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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 for the fiscal year ended December 31, 2022**

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
Date of event requiring this shell company report

Commission file number: 001-37891

AC IMMUNE SA
(Exact name of Registrant as specified in its charter)

Switzerland
(Jurisdiction of incorporation)

EPFL INNOVATION PARK
Building B
1015 Lausanne
Switzerland
(Address of principal executive offices)

Andrea Pfeifer
Tel: +41 21 345 91 21
EPFL INNOVATION PARK
Building B
1015 Lausanne
Switzerland
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Copies to:

Derek J. Dostal
Davis Polk & Wardwell LLP
450 Lexington Avenue
New York, NY 10017
(212) 450-4000

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Shares, nominal value CHF 0.02 per share	ACIU	The Nasdaq Global Market

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

Indicate the number of outstanding shares of each of the issuer's classes of capital stock or common stock as of the close of the period covered by the annual report.

Common shares: 83,620,364

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

☐ Yes ☒ No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

☐ Yes ☒ No

Note – Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

☒ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

☒ Yes ☐ No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or an emerging growth company. See definition of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☒	Non-accelerated filer ☐
		Emerging growth company ☐

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by checkmark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report

☒ Yes ☐ No

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b).

☐

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐	International Financial Reporting Standards as issued by the International Accounting Standards Board ☒	Other ☐

If "Other" has been checked in response to the previous question indicate by check mark which financial statement item the registrant has elected to follow.

☐ Item 17 ☐ Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

☐ Yes ☒ No

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PRESENTATION OF FINANCIAL AND OTHER INFORMATION

Unless otherwise indicated or the context otherwise requires, all references in this annual report on Form 20-F (the "Annual Report") to "AC Immune," "ACIU," "Company," "we," "our," "ours," "us" or similar terms refer to AC Immune SA together with its subsidiary. The Company owns various registered and unregistered trademarks, for some of which protection has been obtained or is being sought, including Morphomer™, SupraAntigen® and its corporate name, logo and Nasdaq Global Market symbol. All other trademarks, trade names and service marks of other companies appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report may be referred to without the respective ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. The Company does not intend to use or display other companies' trademarks and/or trade names to imply a relationship with, or endorsement or sponsorship of the Company by, any other companies.

Financial statements

Our consolidated financial statements are presented in Swiss Francs and in accordance with International Financial Reporting Standards (IFRS), as issued by the International Accounting Standards Board (IASB). None of the consolidated financial statements was prepared in accordance with generally accepted accounting principles in the United States (U.S.). The terms "dollar" and "USD" refer to U.S. dollars, and the terms "Swiss Franc" and "CHF" refer to the legal currency of Switzerland, unless otherwise indicated. We have made rounding adjustments to some of the figures included in this Annual Report. Accordingly, any numerical discrepancies in any table between totals and sums of the amounts listed are due to rounding.

FORWARD-LOOKING STATEMENTS

This Annual Report contains statements that constitute forward-looking statements. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, product candidates, product pipeline, ongoing and planned clinical studies, including those of our collaboration partners, regulatory approvals, research and development (R&D) costs, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. Many of the forward-looking statements contained in this Annual Report can be identified by the use of forward-looking words such as "anticipate," "believe," "could," "expect," "should," "plan," "intend," "estimate," "will" and "potential," among others.

Forward-looking statements appear in a number of places in this Annual Report and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management's beliefs and assumptions, and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified under "Item 3. Key information—D. Risk factors" in this Annual Report. These risks and uncertainties include multiple factors:

- the success of our and our collaboration partners' clinical studies, and our and their ability to obtain and maintain regulatory approval and to commercialize our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589) and to a lesser extent our preclinical candidates;
- the preclinical and clinical safety, efficacy and utility of our product candidates;
- the ability of our competitors to discover, develop or commercialize competing products before or more successfully than we do;
- our plans to research, develop and commercialize our product candidates;
- the identification of serious adverse, undesirable or unacceptable side effects related to our product candidates;

- our ability to maintain our current strategic relationships with our collaboration partners;
- our ability to protect and maintain our, and not infringe on third parties', intellectual property rights throughout the world;
- our ability to raise capital when needed in order to continue our product development programs or commercialization efforts;
- our ability to attract and retain qualified employees and key personnel;
- the acceptance by the Food and Drug Administration (FDA) and applicable foreign regulatory authorities of data from studies that we and our collaboration partners conduct within and outside the U.S. now and in the future;
- our foreign private issuer (FPI) status, the loss of which would require us to comply with the Exchange Act's domestic reporting regime, and cause us to incur significant legal, accounting and other expenses;
- our incorporation in Switzerland, the laws of which govern our corporate affairs and may differ from those applicable to companies incorporated in the U.S.; and
- the other risk factors discussed under "Item 3. Key information—D. Risk factors."

These forward-looking statements are applicable only as of the date of this Annual Report, and are subject to a number of risks, uncertainties and assumptions described under the sections in this Annual Report entitled "Item 3. Key information—D. Risk factors" and "Item 5. Operating and financial review and prospects," and elsewhere in this Annual Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

A. Directors and senior management

Not applicable.

B. Advisers

Not applicable.

C. Auditors

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

A. Offer statistics

Not applicable.

B. Method and expected timetable

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and indebtedness

Not applicable.

C. Reasons for the offer and use of proceeds

Not applicable.

D. Risk factors

You should carefully consider the risks and uncertainties described below and the other information in this Annual Report before making an investment in our common shares. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common shares could decline and you could lose all or part of your investment. This Annual Report also contains forward-looking statements that involve risks and uncertainties. See "Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors.

The below provides a summary of our principal risk factors:

Risks related to our business:

- We depend heavily on the success of our clinical and, to a lesser extent, preclinical products:

a. Our ability to generate product revenues, which we do not expect to occur for several years, will depend on clinical and regulatory success which have low probabilities of success in the central nervous system (CNS) space in which we operate.

- Results of early preclinical and clinical studies may not be predictive of future results:

  a. Products that show positive or timely preclinical or early clinical results may not show sufficient safety or efficacy in later-stage clinical studies and therefore may fail to obtain regulatory approvals.

- Our products may not gain market acceptance or may be preempted by competitors:

  a. Even if our products obtain regulatory approval, they may not be accepted by healthcare providers, patients or the medical community.

  b. Our success is dependent on the ability to discover, develop and obtain marketing approval for our products. We face and will continue to face intense competition from a variety of businesses, including large fully integrated biopharmaceutical and pharmaceutical companies and others that may have greater financial, technical and human resources.

  c. A competitor may enter with a generic of an approved innovator product.

- We may not be successful in using and expanding our Morphomer and SupraAntigen proprietary technology platforms.

- We operate in highly competitive and rapidly changing industries, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

- Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel including members of our Executive Committee.

Risks related to our relationships with third parties:

- If we fail to maintain, or realize the benefits from, our current strategic relationships with our current and potential future license and collaboration partners our financial condition may be materially adversely affected.

- We may seek to form additional strategic alliances in the future with respect to our product candidates, and if we do not realize the benefits of such alliances, our business, financial condition, commercialization prospects and results of operations may be materially adversely affected.

- Our collaboration agreements may make us an attractive acquisition target under certain circumstances.

Risks related to intellectual property:

- We or our licensing or collaboration partners may not have sufficient patent terms to protect our products and business effectively which may adversely affect our product sales and technology development.

- If we fail to comply with the obligations to obtain and maintain patent protection such as compliance with intellectual property agreements, including those under which we license intellectual property and other rights to or from third parties, or otherwise experience disruptions to our business relationships with our licensees, our licensors and collaboration partners, we could lose intellectual property rights that are important to our business.

- We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Risks related to our financial condition and capital requirements:

- We are a clinical stage biopharmaceutical company with a history of losses. We anticipate incurring losses for the foreseeable future. As such, if we fail to obtain additional funding via product revenues, license and collaboration agreements, equity offerings or other forms of financing, we may need to delay, reduce or eliminate certain of our product development programs.

- If we fail to obtain additional funding, we may delay, reduce or eliminate our product development programs or commercialization efforts.

Risks related to the regulatory environment:

- We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

- Even if we obtain regulatory approvals in one jurisdiction, we may not be able to obtain approval in other jurisdictions. Additionally, we will be subject to ongoing obligations and review which may result in significant additional expense.

- We have conducted and may in the future conduct clinical studies for our product candidates outside the U.S., and the FDA and applicable foreign regulatory authorities may not accept data from such studies.

- Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

Risks related to our common shares:

- We have limited free float in our common shares which may have a negative impact on the liquidity and market price of our common shares.

- Certain of our existing shareholders exercise significant control over us, and your or other shareholders' interests may conflict with the interests of such shareholders.

- We are a Swiss corporation. The rights of our shareholders may be different from the rights of shareholders in companies governed by the laws of U.S. jurisdictions.

- We are an FPI and, as a result, we are not subject to U.S. proxy rules and are subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

- As an FPI, and as permitted by the listing requirements of Nasdaq, we rely on certain home country governance practices rather than the corporate governance requirements of Nasdaq. Should we lose our FPI status, we would be required to comply with the Exchange Act's domestic reporting regime, which would cause us to incur significant legal, accounting and other expenses.

- We were likely a passive foreign investment company (PFIC) for our 2022 taxable year and we may be a PFIC for 2023 or future taxable years. If we are a PFIC for any taxable year during which a U.S. investor owns our common shares, the investor generally will be subject to adverse U.S. federal income tax consequences.

Risks related to our business

We depend heavily on the success of our clinical and, to a lesser extent, preclinical products. Our clinical product candidates include our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589). If our clinical studies are unsuccessful, if we or our collaboration partners do not obtain regulatory approval or if we or our collaboration partners are unable to commercialize our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589), or if we experience significant delays in doing so, our business, financial condition and results of operations will be materially adversely affected.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589), all of which are in clinical development as well as other preclinical candidates such as our small molecule programs including therapeutics (Morphomer Tau), our TDP-43 antibody, Morphomer a-syn and inflammasome. Our ability to generate product revenues, which we do not expect will occur for at least the next several years, if ever, will depend heavily on successful clinical development, obtaining regulatory approval and eventual commercialization of these product candidates. In this regard, we rely heavily on our collaboration partners for clinical development of certain of our product candidates, and they may choose to discontinue the clinical development process in certain cases. In addition, we currently generate no revenues from sales of any drugs or diagnostics, and we may never be able to develop or commercialize a marketable drug or diagnostic. The success of our current and future product candidates will depend on several factors, including, but not limited to, the following:

- completing preclinical and clinical studies that demonstrate the efficacy, safety and clinical utility of our preclinical and clinical product candidates;
- receiving marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities;
- launching commercial sales, marketing and distribution operations;
- acceptance of our product candidates by patients, the medical community and third-party payors;
- a continued acceptable safety profile following approval;
- competing effectively with other therapies or diagnostic approaches; and
- obtaining, maintaining, enforcing and defending our intellectual property rights and claims and not infringing on third parties' intellectual property rights.

If we or our collaboration partners do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our current or future product candidates, which would materially adversely affect our business, financial condition and results of operations.

Results of early clinical studies may not be predictive of future study results.

Positive or timely results from preclinical or early-stage clinical studies do not ensure positive or timely results in mid- to late-stage clinical studies or product approval by the U.S. FDA, the European Medicines Agency (EMA), or comparable foreign regulatory authorities. Products that show positive preclinical or early clinical results may not show sufficient safety or efficacy in later-stage clinical studies and therefore may fail to obtain regulatory approvals. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that

believed their product candidates performed satisfactorily in preclinical and clinical studies have nonetheless failed to obtain marketing approval for the product candidates. The FDA, the EMA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether regulatory approval will be obtained for any of our product candidates. Even if we believe that the data collected from clinical studies of our product candidates are promising, such data may not be sufficient to support approval by the FDA, the EMA or any other regulatory authority.

In some instances, there can be significant variability in safety and/or efficacy results between different studies of the same product candidate due to numerous factors, including changes in study procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other study protocols, and the rate of dropout among clinical study participants. In the case of our later-stage clinical product candidates, results may differ in general on the basis of the larger number of clinical study sites and the additional countries and languages involved in these clinical studies.

Clinical studies may include subject-reported outcomes, some of which may be captured with electronic diaries. We have no assurance and cannot rely on past experience that the high frequency of questioning is not influencing the measured outcome. In addition, low compliance with daily reporting requirements may impact the studies' validity or statistical power. We cannot assure you that any Phase 2, Phase 3 or other clinical studies that either we or our collaboration partners are conducting and may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

If we or our collaboration partners are required to conduct additional clinical studies or other testing of any of our current or future product candidates that we or our collaboration partners develop, beyond the studies and testing that we or our collaboration partners contemplate, if we or our collaboration partners are unable to successfully complete clinical studies of our product candidates or other testing, if the results of these studies or tests are unfavorable or are only modestly favorable, or if there are safety concerns associated with our current or future product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to conditional approval or otherwise to additional post-marketing studies or other requirements; or
- remove the product from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or receiving marketing approvals and we may be required to obtain additional funds to complete clinical studies. We cannot assure you that our clinical studies will begin as planned or be completed on schedule, if at all, or that we will not need to amend our studies after they have begun. Significant clinical study delays could also shorten any periods during which we or our collaboration partners may have the exclusive right to commercialize our product candidates, or allow our competitors to bring products to market before we do, which may harm our business and results of operations. In addition, some of the factors that cause, or lead to, clinical study delays may ultimately lead to the denial of regulatory approval of our product candidates.

We may undertake one or more significant corporate transactions that may not achieve their intended results, may adversely affect our financial condition and our results of operations or result in unforeseeable risks to our business.

We continuously evaluate the acquisition or disposition of operating businesses and assets and may in the future undertake one or more significant transactions, such as our purchase in 2021 of Affiris AG's (Affiris) program portfolio of therapeutics targeting a-syn, notably our ACI-7104.056, a clinically-validated active vaccine candidate for the treatment of Parkinson's disease (PD). Any such transaction could be material to our business and could take any number of forms, including mergers, joint ventures and the purchase of equity interests, amongst others. The consideration for such acquisitive transactions may include, among other things, cash, common shares or equity interests in us or our subsidiary, or a contribution of equipment to obtain equity interests, and in conjunction with a transaction we might incur additional indebtedness. We also routinely evaluate the benefits of disposing of certain of our assets.

These transactions may present significant risks such as insufficient revenue to offset liabilities assumed, potential loss of significant revenue and income streams, increased or unexpected expenses, inadequate return of capital, regulatory or compliance issues, the triggering of certain covenants in our debt agreements (including accelerated repayment) and unidentified issues not discovered in due diligence. In addition, such transactions could distract management from current operations. As a result of the risks inherent in such transactions, we cannot guarantee that any such transaction will ultimately result in the realization of its anticipated benefits or that it will not have a material adverse effect on our business, financial condition and results of operations. If we were to complete such an acquisition, disposition, investment or other strategic transaction, we may require additional debt or equity financing that could result in a significant increase in our amount of debt and our debt service obligations or the number of outstanding common shares, thereby diluting holders of our common shares outstanding prior to such acquisition.

Additional competitors could enter the market with generic versions of our products, which may result in a material decline in sales of affected products.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application (ANDA), seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit a new drug application (NDA) under Section 505(b)(2) that references the FDA's prior approval of the innovator product. A 505(b)(2) NDA product may be submitted for a new or improved version of the original innovator product. Hatch-Waxman also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA or 505(b)(2) NDA. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan-drug exclusivity. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in the ANDA what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must also be given to the innovator, and if within 45 days of receiving notice the innovator, in order to protect its patents, sues the company that manufactures the generic, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589) are approved, competitors could file ANDAs for generic versions of our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589) or 505(b)(2) NDAs that reference our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589), respectively. If there are patents listed in the Orange Book for our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589), respectively, those ANDAs and 505(b)(2) NDAs would be required to include a certification for each listed patent, indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot

predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product, and our results of operations and cash flows could be materially and adversely affected.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage and reimbursement levels and pricing policies.

The successful commercialization of our product candidates will depend, in part, on the extent to which coverage and reimbursement for our products will be available from government and health administration authorities, private health insurers and other third-party payors. To manage healthcare costs, many governments and third-party payors increasingly scrutinize the pricing of new technologies and require greater levels of evidence of favorable clinical outcomes and cost-effectiveness before extending coverage. For example, the Inflation Reduction Act (IRA) of 2022, among other things, incentivizes the renegotiation with the U.S. government of the prices of certain pharmaceutical drugs and imposes penalties for Medicare drugs that increase in price faster than the rate of inflation. See "—Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set" below. In light of such challenges to prices and the requirement for increasing levels of evidence of the benefits and clinical outcomes of new technologies, we cannot be sure that coverage will be available for any of our current or future product candidates that we or our collaboration partners will commercialize or, if available, that the reimbursement rates will be adequate in each respective region. If we are unable to obtain adequate levels of coverage and reimbursement for our product candidates, their marketability will be negatively and materially impacted.

Third-party payors may deny coverage and reimbursement status altogether for a given drug product, or may cover the product but also establish prices at levels that are too low to enable us to realize an appropriate return on our investment in product development. Because the rules and regulations regarding coverage and reimbursement change frequently, in some cases at short notice, even when there is favorable coverage and reimbursement, future changes may occur that adversely impact the favorable status. Further, the net reimbursement for drug products may be subject to additional reductions in the future depending on policy changes enacted by the U.S. Congress.

The unavailability or inadequacy and variability of third-party coverage and reimbursement could have a material adverse effect on the market acceptance of our product candidates and the future revenues we may expect to receive from those products. In addition, we are unable to predict what additional legislation or regulation relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future, or what effect such legislation or regulation would have on our business.

Our products may not gain market acceptance, in which case we or our collaboration partners may not be able to generate product revenues, which will materially adversely affect our business, financial condition and results of operations.

Even if the FDA, the EMA or any other regulatory authority approves the marketing of any product candidates that we develop, physicians, healthcare providers, patients or the medical community may not accept or use them. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our current or future product candidates does not achieve an adequate level of acceptance, we or our collaboration partners may not generate significant product or royalty revenues or any

profits from operations. The degree of market acceptance of our product candidates that are approved for commercial sale will depend on a variety of factors, including:

- how clinicians and potential patients perceive our novel products;
- the timing of market introduction;
- the number and clinical profile of competing products;
- our ability to provide acceptable evidence of safety and efficacy or clinical utility;
- the prevalence and severity of any side effects;
- relative convenience and ease of administration;
- cost-effectiveness;
- patient diagnostics and screening infrastructure in each market;
- marketing and distribution support;
- availability of coverage, reimbursement and adequate payment from health maintenance organizations and other third-party payors, both public and private; and
- other potential advantages over alternative treatment methods.

If our product candidates fail to gain market acceptance, this will have a material adverse impact on our ability to generate revenues to provide a satisfactory, or any, return on our investments. Even if some products achieve market acceptance, the market may prove to not be large enough to allow us to generate significant revenues.

In addition, the potential market opportunity of our product candidates is difficult to estimate precisely. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge and publications, third-party research reports and other surveys. These assumptions involve the exercise of significant judgment on the part of our management and are inherently uncertain, and the reasonableness of these assumptions could not have been assessed by an independent source in every detail. If any of the assumptions proves to be inaccurate, then the actual market for our product candidates could be smaller than our estimates of the potential market opportunity. If the actual market for our product candidates is smaller than we expect, or if any approved products fail to achieve an adequate level of acceptance by physicians, healthcare payors and patients, our product or royalty revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

We depend on enrollment of patients in our clinical studies for our product candidates. If we are unable to enroll patients in our clinical studies, our research and development efforts could be materially adversely affected.

Successful and timely completion of clinical studies will require that we enroll a sufficient number of patient candidates. Studies may be subject to delays as a result of patient enrollment taking longer than anticipated or by patient withdrawal. Patient enrollment depends on many factors, including the size and nature of the patient population, the eligibility criteria for the study, the proximity of patients to clinical sites, the design of the clinical protocol, the existence of competing clinical studies, the availability of new drugs approved for the indication the clinical study is investigating, and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies.

Generally, the specific target population of patients and therapeutic time windows may make it difficult for us to enroll enough patients to complete clinical studies for our product candidates in a timely and cost-effective manner.

Delays in the completion of any clinical study of our product candidates will increase our costs, slow down our product candidate development and approval process, and delay or potentially jeopardize our or our collaboration partners' ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

If serious adverse, undesirable or unacceptable side effects are identified during the development of our product candidates or following approval, if any, we may need to abandon our development of such product candidates, the commercial profile of any approved label may be limited, or we may be subject to other significant negative consequences following marketing approval, if any.

If our product candidates are associated with serious adverse, undesirable or unacceptable side effects, we may need to abandon their development or limit development to certain uses or subpopulations in which such side effects are less prevalent, less severe or more acceptable from a risk–benefit perspective. Many compounds that initially showed promise in preclinical or early-stage testing were later found to cause side effects that restricted their use and prevented further development of the compound for larger indications.

Occurrence of serious procedure- or treatment-related side effects could impede clinical study enrollment and receipt of marketing approval from the FDA, the EMA and comparable foreign regulatory authorities. Adverse events (AEs) could also adversely affect physician or patient acceptance of our product candidates.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including the following:

- regulatory authorities may withdraw approvals of such product and require us or our collaboration partners to take any approved products off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered, to conduct additional studies or to change the labeling of the product;
- we or our collaboration partners may be subject to limitations in how we promote the product;
- sales of the product may decrease significantly;
- we could be sued and held liable for harm caused to patients; and
- our reputation and physician or patient acceptance of our products may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

We operate in highly competitive and rapidly changing industries, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The biopharmaceutical and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. Our success is highly dependent on our ability to discover, develop and obtain marketing approval

for new and innovative products on a cost-effective basis and to market them successfully. In doing so, we face and will continue to face intense competition from a variety of businesses, including large, fully integrated pharmaceutical companies, specialty pharmaceutical companies and biopharmaceutical companies, academic institutions, government agencies and other private and public research institutions in Europe, the U.S. and other jurisdictions. Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments, and the commercialization of those treatments. Mergers and acquisitions in the pharmaceutical and biopharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors.

The highly competitive nature of and rapid technological changes in the pharmaceutical and biopharmaceutical industries could render our product candidates or our technology obsolete or noncompetitive. The commercial opportunity for our products could be reduced or eliminated if our competitors:

- develop and commercialize products that are safer, more effective, less expensive, or more convenient or easier to administer;
- obtain quicker FDA or other regulatory approval for their products;
- establish superior intellectual property and proprietary positions;
- have access to more manufacturing capacity;
- implement more effective approaches to sales, marketing and distribution; or
- form more advantageous strategic alliances.

Should any of these occur, our business, financial condition and results of operations could be materially adversely affected.

We believe that our key competitor product candidates are (i) AADvac1 (Axon Neuroscience) for ACI-35.030; (ii) UB-311 (Vaxxinity) and ABvac-40 (Araclon Biotech) for ACI-24.060; (iii) UB-312 (Vaxxinity) for ACI-7104.056; (iv) bepranemab (UCB/Roche), E-2814 (Eisai) and JNJ63733657 (Janssen) for semorinemab; (v) ADUHELM (Biogen), Leqembi (BioArctic/Eisai), donanemab (Eli Lilly and Company) and solanezumab (Eli Lilly and Company) for crenezumab; (vi) HMTM (TauRx Pharmaceuticals) for Morphomer Tau; (vii) Tauvid (Eli Lilly and Company), florzolotau (Aprinoia Therapeutics), MK-6240 (Cerveau/Merck) and GTP1 (Genentech) for PI-2620; and (viii) UCB-2897 (UCB) for ACI-12589, as described under “Item 4. Information on the Company—B. Business overview—Competition.”

We may not be successful in our efforts to use and expand our Morphomer and SupraAntigen proprietary technology platforms to build additional product candidates for our pipeline.

A key element of our strategy is to use and expand our Morphomer and SupraAntigen proprietary technology platforms to create unique therapies and diagnostics misfolded proteins in diseases, such as AD, PD and others (including NeuroOrphan diseases e.g. ALS and PSP), and progress these product candidates through clinical development. Although our research and development efforts to date have resulted in a pipeline of product candidates, we may not be able in the future to develop product candidates that are safe and effective. Even if we are successful in continuing to build our pipelines, the potential product candidates that we identify may not be suitable for clinical development, potentially as a result of having harmful side effects or other characteristics indicating they may be unlikely to receive marketing approval and achieve market acceptance.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. We and a number of our suppliers and collaborative and clinical study relationships are located outside the U.S.. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing regulatory requirements for drug approvals in non-U.S. countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions such as sanctions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Moreover, at the end of 2021 and into 2022, tensions between the United States and Russia escalated when Russia amassed large numbers of military ground forces and support personnel on the Ukraine-Russia border and, in February 2022, Russia invaded Ukraine. In response, NATO has deployed additional military forces to Eastern Europe, including to Lithuania, and the Biden administration announced certain sanctions against Russia. The invasion of Ukraine and the retaliatory measures that have been taken, or could be taken in the future, by the United States, NATO, and other countries have created global security concerns that could result in a regional conflict and otherwise have a lasting impact on regional and global economies, any or all of which could disrupt our supply chain, adversely affect our ability to conduct ongoing and future clinical trials of our product candidates, and adversely affect our ability to commercialize our products (subject to regulatory approval) in this region. Currently, none of our clinical development or business activities are conducted directly or otherwise in Russia or Ukraine.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, rising interest rates and high inflation may cause our cost of doing business to materially increase and may adversely impact our ability to operate or may adversely impact other parties upon whom we rely for research and development capabilities to operate. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

The Covid-19 pandemic has adversely impacted, and may continue to impact, our business, including preclinical and clinical trials and regulatory approvals.

Since the beginning of the Covid-19 pandemic, governments, public institutions, and other organizations in countries and localities where Covid-19 cases have been identified have taken certain preventative or protective measures to combat the transmission of the virus, including the implementation of travel restrictions or bans, closures of non-essential businesses, limitations of public gatherings, other social distancing and shelter-in-place measures, and delays or cancellations of elective surgeries. The Covid-19 pandemic poses the risk that the Company, our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time due to shutdowns that may be requested or mandated by state and federal governmental authorities.

As a result of Covid-19, we have experienced disruptions impacting our business and clinical trials and we may continue to experience disruptions that could materially impact our business and planned clinical trials, including:

- delays or difficulties in conducting preclinical research and clinical trials;
- interruption in global manufacturing and shipping that may affect the manufacturing and/or transport of clinical trial materials and other materials, including testing equipment and personal protective equipment, used at our or our contract research organizations' (CROs') and contract manufacturing organizations' (CMOs') facilities;
- changes in local regulations as part of a response to the Covid-19 coronavirus outbreak which may require us to change the way in which clinical trials are conducted and may result in unexpected costs; and
- impact our ability to secure additional financing.

In addition, the outbreak of Covid-19 could disrupt our operations due to absenteeism by infected or ill members of Executive Management or other employees, or absenteeism by members of Executive Management and other employees who elect not to come to work due to the illness affecting others in our office or laboratory facilities, or due to quarantines. Covid-19 illness could also impact members of our Board and its ability to hold meetings. Further information concerning details of the impact of Covid-19 on our programs can be found under "Item 5: Operating and financial review and prospects."

Our ability to effectively monitor and respond to the rapid and ongoing developments and expectations relating to environmental, social and governance (ESG) matters, including related social expectations and concerns, may impose unexpected costs on us or result in reputational or other harm to us that could have a material adverse effect on our business, financial condition and results of operations.

If we are not able to adequately recognize and respond to the rapid and ongoing developments and governmental and social expectations relating to ESG matters such as climate change and access to health care and affordable drugs, this failure could result in missed corporate opportunities, additional regulatory, social or other scrutiny of us and our

business, the imposition of unexpected costs or in damage to our reputation or our various relationships with governments, customers, employees, third parties and the communities in which we operate, in each case that could have a material adverse effect on our business, financial condition and results of operations.

We have no history of commercializing biologics or pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We began our operations in 2003. Our operations to date have been limited to financing and staffing our company, developing our technology and developing our product candidates as well as early-stage clinical trials. We have not yet demonstrated an ability to successfully complete a large-scale, pivotal clinical study, obtain marketing approval, manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing biologics or pharmaceutical products.

Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.

Our success depends upon the continued contributions of our key management, scientific and technical personnel, many of whom have substantial experience with or been instrumental for us and our projects. Members of our key management include Dr. Andrea Pfeifer, our Chief Executive Officer; Dr. Marie Kosco-Vilbois, our Chief Scientific Officer; Dr. Johannes Rolf Streffer, our Chief Medical Officer; Piergiorgio Donati, our Chief Technical Operations Officer; Jean-Fabien Monin, our Chief Administrative Officer; Christopher Roberts, our Vice President (VP) Finance and Interim CFO; Dr. Julien Rongère, our Senior Vice President (SVP) for Regulatory Affairs and Quality Assurance; Dr. Olivier Sol, our VP Head of Clinical Development; Dr. Bojana Portmann, our VP for Intellectual Property and Business Development (VP IP and BD); Alexandre Caratsch, our General Counsel; and Mark Danton, our VP Information Systems, Security and Digital Technologies.

The loss of our key managers and senior scientists could delay our research and development activities. Laws and regulations on executive compensation, including legislation in our home country, Switzerland, may restrict our ability to attract, motivate and retain the required level of qualified personnel. In Switzerland, legislation affecting public companies is in force that, among other things, imposes an annual binding shareholders' "say on pay" vote with respect to the total compensation of executive management, including executive officers and the board of directors, and prohibits severance or similar payment, bonuses for company purchases and sales, and additional contracts as consultants to or employees of other companies in the group. In addition, the competition for qualified personnel in the pharmaceutical and biopharmaceutical field is intense, and our future success depends upon our ability to attract, retain and motivate highly skilled scientific, technical and managerial employees. We face competition for personnel from other companies, universities, public and private research institutions and other organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to implement our business strategy, which could have a material adverse effect on our business.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage or as a result of claims against our directors and officers; and our liability insurance may not cover all damages from such claims.

We are exposed to potential clinical trial liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical or biopharmaceutical products. Currently we have no products that have been approved for commercial sale, however, our current and future use of product candidates in clinical studies, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, by healthcare providers, or by pharmaceutical or biopharmaceutical companies or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially adversely affect the market for our product candidates or any prospects for commercialization of our product candidates.

Although the clinical study process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical studies or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates.

We purchase liability insurance in connection with the clinical studies that we undertake and for the purpose of indemnifying our directors and officers for claims against them in amounts that we consider to be consistent with industry norms. It is possible that our liabilities could exceed our insurance coverage. For example, if we obtain marketing approval for any of our product candidates, we will intend to expand our insurance coverage to include the sale of commercial products. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Should any of the events described above occur, this could have a material adverse effect on our business, financial condition and results of operations.

We may seek to obtain orphan-drug designation for certain of our product candidates. Orphan-drug designation may not ensure that we will enjoy market exclusivity in a particular market, and if we fail to obtain or maintain orphan-drug exclusivity for such product candidates, we may be subject to earlier competition and our potential revenue will be reduced.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S.. In the European Union (EU), the EMA's Committee for Orphan Medicinal Products grants orphan-drug designation to promote the development of products that meet the following criteria: a) they are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the EU or for products that are intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product; and b) there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the U.S., orphan-drug designation entitles a party to financial incentives such as opportunities for grant funding toward clinical study costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan-drug exclusivity, which means that the FDA cannot approve any other application to market the same drug for the same indication for a period of 7 years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or if the manufacturer is unable to assure sufficient product quantity. In the EU, orphan-drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity for the orphan indication following drug or biological product approval, provided that the criteria for orphan designation are still applicable at the time of the granting of the marketing authorization. This period may be reduced to 6 years if at the end of the fifth year, the orphan-drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

We may not be able to obtain orphan-drug designation for any of our product candidates, and even if we do, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical or biopharmaceutical products. Further, even if we obtain orphan-drug designation for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Orphan-drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Due to our limited resources and access to capital, we must prioritize development of certain product candidates.

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each. Our decisions concerning the allocation of research, collaboration, management and financial resources toward particular compounds, product candidates or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain product development programs may also prove not to be optimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the market potential of our product candidates or misread trends in the pharmaceutical or biopharmaceutical industry, in particular for neurological disorders, our business, financial condition and results of operations could be materially adversely affected.

Our research and development activities could be affected or delayed as a result of possible restrictions on animal testing.

Certain laws and regulations require us to test our product candidates on animals before initiating clinical studies in humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent that the activities of these groups are successful, our research and development activities may be interrupted, delayed or become more expensive.

A breakdown or breach of our information technology systems and cybersecurity efforts, or those of our key business partners, CROs or service providers, could subject us to liability or reputational damage or interrupt the operation of our business.

We are increasingly dependent upon technology systems and data. Our computer systems continue to increase in multitude and complexity due to the growth in our business, making them potentially vulnerable to breakdown, malicious intrusion and random attack. Despite the implementation of security measures, our internal computer systems and those of our key business partners, CROs and service providers may be vulnerable to damage from computer viruses, unauthorized access or other similar cyber-attacks or incidents. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations.

Data privacy or security breaches, cyber-attacks and other cybersecurity incidents, including those by individuals authorized to access our technology systems or others, may pose a risk that sensitive data, including intellectual property, trade secrets or personal information belonging to us, our patients, study subjects or other business partners, may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity, and are becoming increasingly difficult to detect. They are often carried out by motivated, well-resourced, skilled and persistent actors, including nation states, organized crime groups, “hacktivists” and employees or contractors acting with malicious intent. Cyber-attacks could include the deployment of harmful malware and key loggers, ransomware, a denial-of-service attack, a malicious website, phishing attacks, computer viruses, social engineering and other means to affect the confidentiality, integrity and availability of our technology systems and data. Our key business partners, CROs and service providers face similar risks and any security breach of their systems could adversely affect our security posture. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and on other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. Our ability to evaluate and monitor our CROs’, contractors’ and consultants’ data security practices are limited, and due to applicable laws and regulations or contractual obligations, we may be held responsible for any security breaches or cybersecurity attack attributed to them as they relate to the information we share with them. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary information or personal data of our employees, partners or study subjects, we could incur liability

including notification obligations (including to the impacted individuals and applicable regulators or supervisory authorities), and the further development and commercialization of our product candidates could be delayed.

Although we continue to build and improve our systems and infrastructure, and to implement technical, organizational and legal security measures, and believe we have taken appropriate security measures to reduce these risks to our data and information technology systems, there can be no assurance that our efforts will prevent, detect or appropriately respond to breakdowns or breaches in our systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, including personal information, which could result in financial, legal, business or reputational harm to us. We continue to invest in industry standard IS/IT solutions and managed services that often include the relevant, layered protection and monitoring practices surrounding our data and IT systems and related infrastructure. These investments reduce further these risks in that they enable organizations such as ours to leverage the resources necessary to monitor IT systems and infrastructure for any current or potential threats. We also regularly perform risk and impact assessments, the results of which generally lead to the implementation of certain measures designed to increase our level of data protection. These investments are costly, and as cyber threats continue to evolve, we may be required to expend significant, additional resources to continue to modify and/or enhance our protective, detective and responsive measures required to remediate any identified information security vulnerabilities. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches. We may be required to expend significant capital and other resources to protect against and respond to any attempted or existing cybersecurity incidents. In addition, our remediation efforts may not be successful.

In addition, certain global geo-political events can increase our cybersecurity risk. For example, due to the recent Russia-Ukraine conflict, there have been publicized threats to increase cyber-attack activity against the critical infrastructure of any nation or organization that retaliates against Russia for its invasion of Ukraine. Any such increase in such attacks on us or our key business partners, CROs or service providers could adversely affect our systems or other operations.

Changes in laws, rules or regulations relating to data privacy and security, or any actual or perceived failure by us to comply with such laws, rules, regulations and standards, or contractual or other obligations relating to data privacy and security, could result in claims, changes to our business practices, penalties, increased cost of operations and could have a material adverse effect on our reputation, results of operations, financial condition and cash flows.

We are, and may increasingly become, subject to various laws, rules, regulations, treaties, decisions and standards, as well as contractual obligations, relating to data privacy and security in the jurisdictions in which we operate. The regulatory environment related to data privacy and security is increasingly rigorous, with new and constantly changing requirements applicable to our business, and enforcement practices are likely to remain uncertain for the foreseeable future. These laws, rules, regulations, treaties, decisions and standards may be interpreted and applied differently over time and from jurisdiction to jurisdiction and in a manner that is inconsistent with our data practices and that could have a material adverse effect on our results of operations, financial condition and cash flows. New laws, amendments to or reinterpretations of existing laws, rules, regulations, treaties, decisions, standards and other obligations may require us to incur additional costs and restrict our business operations, and may require us to change how we use, collect, store, transfer or otherwise process certain types of personal information and to implement new processes to comply with those laws.

In the U.S., there are numerous federal and state laws and regulations related to the privacy and security of personal information. Regulations promulgated pursuant to the U.S. Health Insurance Portability and Accountability Act of 1996 (HIPAA) establish privacy and security standards that limit the use and disclosure of protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and to ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. Numerous states have enacted or are in the process of enacting state level data privacy laws and regulations governing the collection, use, and other processing of state residents' personal information, such as the California Consumer Privacy Act (CCPA) as

amended by the California Privacy Rights Act of 2020 (CPRA), which provides new and enhanced data privacy rights to California residents, such as affording California residents the right to access and delete their information and to opt out of certain sharing and sales of personal information. In addition, laws in all 50 states require businesses to provide notice to individuals whose personal information has been disclosed as a result of a data breach.

Internationally, laws, regulations and standards in many jurisdictions apply broadly to the collection, use, retention, security, disclosure, transfer and other processing of personal information. For example, the EU General Data Protection Regulation (GDPR), which became effective in May 2018, greatly increased the European Commission's jurisdictional reach of its laws and adds a broad array of requirements for handling personal data. EU Member States are tasked under the GDPR to enact, and to have enacted, certain implementing legislation that adds to and/or further interprets the GDPR requirements and potentially extends our obligations and potential liability for failing to meet such obligations. The GDPR, together with national legislation, regulations and guidelines of the EU Member States and Switzerland (via its Federal Data Protection Act) governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, use, retain, protect, disclose, transfer and otherwise process personal data. In particular, the GDPR includes obligations and restrictions concerning the consent and rights of individuals to whom the personal data relates (and the obligations of sponsors of clinical trials acting as data controllers), the transfer of personal data out of the European Economic Area (EEA), the notification of security breaches and the security and confidentiality of personal data. The GDPR authorizes fines for certain violations of up to 4% of global annual revenue or EUR 20 million, whichever is greater. The GDPR also applies to our key business partners, CROs and service providers, whether or not they are located in Europe, with which we share personal data subject to the GDPR. Additionally, following Brexit, we also are subject to the UK General Data Protection Regulation (UK GDPR) (i.e., a version of the GDPR as implemented into UK law), exposing us to two parallel regimes with potentially divergent interpretations and enforcement actions for certain violations. While the European Commission issued an adequacy decision intended to last for at least four years in respect of the UK's data protection framework, enabling data transfers from EU Member States to the UK to continue without requiring organizations to put in place contractual or other measures in order to lawfully transfer personal data between the territories, the relationship between the UK and the EU in relation to certain aspects of data privacy and security law remains unclear. Although we do not have material operations in the UK, we cannot rule out potential disruptions in relation to the clinical regulatory framework applicable to our clinical studies in the UK, and to data privacy and security rules with respect to personal data sharing with vendors and clinical investigators in the UK, and we cannot predict future implications.

All of these evolving compliance and operational requirements impose significant costs, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, distract management or divert resources from other initiatives and projects. For instance, the European Union Court of Justice and the Swiss Data Protection Authority have declared the U.S. Privacy Shield to be inadequate for transfers of personal data out of the EU and Switzerland, which increased our compliance burden. If we are unable to properly protect the privacy and security of personal information, including protected health information, we could be found to have breached our contracts. In addition, any failure or perceived failure by us to comply with any applicable federal, state or similar foreign laws and regulations relating to data privacy and security could result in damage to our reputation and our relationship with our customers, as well as proceedings or litigation by governmental agencies, customers, partners, collaborators and/or study subjects, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, sanctions, awards, penalties or judgments, all of which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, CROs, CMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. Moreover, at the end of 2021 and into 2022, tensions between the United States and Russia escalated when Russia amassed large numbers of military ground forces and support

personnel on the Ukraine-Russia border and, in February 2022, Russia invaded Ukraine. In response, North Atlantic Treaty Organization, or NATO has deployed additional military forces to Eastern Europe, including to Lithuania, and the Biden administration announced certain sanctions against Russia. The invasion of Ukraine and the retaliatory measures that have been taken, or could be taken in the future, by the United States, NATO, and other countries have created global security concerns that could result in a regional conflict and otherwise have a lasting impact on regional and global economies, any or all of which could disrupt our supply chain, adversely affect our ability to conduct ongoing and future clinical trials of our product candidates, and adversely affect our ability to commercialize our products (subject to regulatory approval) in this region. Currently, none of our clinical development or business activities are conducted directly or otherwise in Russia or Ukraine. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or by other business interruption.

The vast majority of our operations including our corporate headquarters are located in Ecublens, near Lausanne, Canton of Vaud, Switzerland. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

We have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize our products on our own or together with suitable partners.

We have never commercialized a product candidate, and we currently have no sales force, marketing or distribution capabilities. To achieve commercial success for our product candidates, we will have to develop our own sales, marketing and supply organization or outsource these activities to third parties.

Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates, and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization. In addition, successful commercialization also requires an enhanced regulatory organization which we currently do not have. If we are unable to build our own distribution and marketing capabilities, are unable to find suitable partners for the commercialization of our product candidates or do not successfully obtain the necessary regulatory capabilities, we may not generate revenues from them or be able to reach or sustain profitability.

Risks related to our relationships with third parties

If we fail to maintain our current strategic relationships with Genentech, a member of the Roche Group, Eli Lilly and Company (Lilly), Janssen Pharmaceuticals Inc. (Janssen) part of the Janssen Pharmaceutical Companies of Johnson & Johnson, Life Molecular Imaging SA (LMI) (formerly Piramal Imaging SA) and other of our current or future strategic partners, our business, commercialization prospects and financial condition may be materially adversely affected.

We have two partnerships with Genentech. In 2006, we granted Genentech an exclusive, worldwide license for crenezumab. In 2012, we entered into a second partnership to commercialize anti-Tau antibodies for use as immunotherapies. In December 2018, we signed a license agreement with Lilly to research and develop Morphomer Tau small molecules for the treatment of AD and other neurodegenerative diseases (NDD). This collaboration commenced in Q1 2019. We are in a partnership with Janssen to develop and commercialize therapeutic anti-Tau vaccines for the treatment of AD and potentially other Tauopathies. We also have a diagnostic partnership with LMI for one of our compounds from our Morphomer chemical library, which bind pathological Tau for use as a PET tracer. Our collaboration partners each have the right to terminate their agreements with us for any reason upon providing us with a

certain notice period. If Genentech, Lilly, Janssen, LMI or other of our current or future strategic partners terminates its agreement with us at any time, it could delay or prevent development of our product candidates and materially harm our business, financial condition, commercialization prospects and results of operations.

Good relationships with Genentech, Lilly, Janssen, LMI and other of our current or future strategic partners are important for our business prospects. If our relationships with Genentech, Lilly, Janssen, LMI or other of our current or future strategic partners were to deteriorate substantially or if Genentech, Lilly, Janssen, LMI or other of our current or future strategic partners were to challenge our use of their intellectual property or our calculations of the payments we are owed under our agreements, our business, financial condition, commercialization prospects and results of operations could be materially adversely affected.

Lastly, our collaboration agreements with Genentech, Lilly, Janssen and LMI provide each partner with control over, and responsibility for, the clinical development process, including obtaining regulatory and marketing approvals, manufacturing costs and sales and marketing costs. Future collaboration agreements may also relinquish development control to our partners. Genentech or our other current or future collaboration partners may and do separately pursue competing products, therapeutic approaches or technologies to develop treatments for the diseases targeted by us or our collaborative efforts. Even if our partners continue their contributions to the collaborative agreements to which we are a party, they may nevertheless determine not to actively pursue the development or commercialization of any resulting products. Our partners may also fail to perform their obligations under the collaboration agreements or may be slow in performing their obligations. Any of these circumstances could result in a material adverse impact on our business, financial condition, commercialization prospects or results of operations.

We may seek to form additional strategic alliances in the future with respect to our product candidates, and if we do not realize the benefits of such alliances, our business, financial condition, commercialization prospects and results of operations may be materially adversely affected.

Our product development programs and the potential commercialization of our product candidates will require substantial additional liquidity to fund expenses and may require expertise, such as sales and marketing expertise, which we do not currently possess. Therefore, in addition to our relationships with Genentech, Lilly, Janssen and LMI, we may decide to enter into strategic alliances or to create joint ventures or collaborations with pharmaceutical or biopharmaceutical companies for the further development and potential commercialization of those and other of our product candidates.

We face significant competition in seeking appropriate collaborators. Collaborations are complex and time-consuming to negotiate, document and manage. Any delays in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market. We may also be restricted under existing and future collaboration agreements from entering into strategic partnerships or collaboration agreements on certain terms with other potential collaborators. We may not be able to negotiate collaborations on acceptable terms, or at all, for any of our existing or future product candidates and programs because the potential partner may consider that our research and development pipeline is insufficiently developed to justify a collaborative effort, or that our product candidates and programs do not have the requisite potential to demonstrate safety and efficacy in the target population. If we are unsuccessful in establishing and maintaining a collaboration with respect to a particular product candidate, we may have to curtail the development of that product candidate, reduce the scope of or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of our sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense, for which we have not budgeted. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market and generate product revenue. Even if we are successful in establishing a new strategic partnership or entering into a collaboration agreement, we cannot be certain that, following such a strategic transaction or license, we will be able to progress the development and commercialization of the applicable product candidates as envisaged, or that we will achieve the revenues that would

justify such transaction, and we could be subject to the following risks, each of which may materially harm our business, commercialization prospects and financial condition:

- we may not be able to control the amount and timing of resources that the collaboration partner devotes to the product development program;
- the collaboration partner may experience financial difficulties;
- we may be required to grant or otherwise relinquish important rights such as marketing, distribution and intellectual property rights;
- a collaboration partner could move forward with a competing product developed either independently or in collaboration with third parties, including our competitors; or
- business combinations or significant changes in a collaboration partner's business strategy may adversely affect our willingness to continue any arrangement.

We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates, and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third-party clinical CROs, to monitor and manage data for our ongoing preclinical and clinical programs, including the clinical studies of our product candidates. We rely on these parties for execution of our nonclinical and clinical studies and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the clinical CROs does not relieve us of our regulatory responsibilities. We and our clinical CROs and other vendors are required to comply with current Good Manufacturing Practice (cGMP), current Good Clinical Practice (cGCP), and current Good Laboratory Practice (cGLP), which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the EU and comparable foreign regulatory authorities for our product candidates in nonclinical and clinical development (where applicable). Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites and other contractors. If we or any of our clinical CROs or vendors fail to comply with applicable regulations, the data generated in our nonclinical and clinical studies may be deemed unreliable and the EMA, FDA, other regulatory authorities may require us to perform additional nonclinical and clinical studies before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that all of our clinical studies comply with cGCP regulations. In addition, our clinical studies must be conducted with products produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical studies, which would delay the regulatory approval process.

If any of our relationships with these third-party clinical CROs terminates, we may not be able to enter into arrangements with alternative clinical CROs or do so on commercially reasonable terms. In addition, our clinical CROs are not our employees, and except for remedies available to us under our agreements with such clinical CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing nonclinical and clinical programs. If clinical CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Clinical CROs may also generate higher costs than anticipated. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

Switching or adding additional clinical CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new clinical CRO commences work. As a result, delays occur, which

could materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our clinical CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We currently rely on third-party suppliers and other third parties for production of our product candidates and our dependence on these third parties may impair the advancement of our research and development programs and the development of our product candidates.

We currently rely on, and expect to continue to rely on, third parties for the manufacturing and supply of chemical and biological compounds and formulations for the clinical studies of our current and future product candidates. For the foreseeable future, we expect to continue to rely on such third parties for the manufacture of any of our product candidates on a clinical or commercial scale, if any of our product candidates receives regulatory approval. Reliance on third-party providers may expose us to different risks than if we were to manufacture product candidates ourselves. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other regulatory authorities, pursuant to inspections that will be conducted after we submit our NDA or comparable marketing application to the FDA or other regulatory authority. We do not have control over a supplier's or manufacturer's compliance with these laws, regulations and applicable cGMP standards and other laws and regulations, such as those related to environmental health and safety matters. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control (QC), quality assurance (QA) and qualified personnel. If we are compelled or we wish to find alternative manufacturing facilities, this could significantly impact our ability to develop, obtain regulatory approval for or market our product candidates. Any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our product candidates or that obtained approvals could be revoked, which would adversely affect our business and reputation.

Third-party providers may breach agreements they have with us because of factors beyond our control. Contract manufacturers often encounter difficulties involving production yields, QC and QA, as well as shortages of qualified personnel. They may also terminate or refuse to renew their agreements because of their own financial difficulties or business priorities, potentially at a time that is costly or otherwise inconvenient for us. If we are unable to find adequate replacement or another acceptable solution in time, our clinical studies could be delayed or our commercial activities could be harmed.

In addition, the fact that we are dependent on our suppliers and other third parties for the manufacture, storage and distribution of our product candidates means that we are subject to the risk that our product candidates and, if approved, commercial products may have manufacturing defects that we have limited ability to prevent or control. The sale of products containing such defects could result in recalls or regulatory enforcement action that could adversely affect our business, financial condition and results of operations.

Growth in the costs and expenses of components or raw materials, in particular as a result of rising inflation, may also adversely influence our business, financial condition and results of operations. Supply sources could be interrupted from time to time and, if interrupted, we cannot be certain that supplies could be resumed (whether in part or in whole) within a reasonable timeframe and at an acceptable cost or at all. Our current and anticipated future dependence upon others for the manufacturing of our current and future product candidates may adversely affect our future profit margins and our, or our collaboration partners', ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Our collaboration arrangements with our strategic partners may make us an attractive target for potential acquisition under certain circumstances.

Under certain circumstances, due to the structure of our collaboration arrangements with our strategic partners, our strategic partners may prefer to acquire us rather than pay the milestone payments or royalties under the collaboration

arrangements, which may bring additional uncertainties to our business development and prospects. For example, under our collaboration arrangements with Genentech, Lilly and Janssen, we may become entitled to substantial milestone payments and royalties. As a result, rather than paying the milestone payments or royalties, Genentech, Lilly or Janssen, or one of their affiliates including Roche or Johnson & Johnson, may choose to acquire us.

Risks related to intellectual property

We may not have sufficient patent terms to protect our products and business effectively.

Patents have a limited lifespan. In the U.S., the natural expiration of a patent is generally 20 years after it is filed. Although various extensions or adjustments may be available, such as adjustments based on certain delays caused by the U.S. Patent and Trademark Office (USPTO) the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned, co-owned and licensed patent portfolios may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage. Even if patents covering our product candidates are obtained and unchallenged, once the patent life has expired for a product, we may be open to competition from generic medications.

Although patent term extensions under the Hatch-Waxman Act, in the U.S. and under supplementary protection certificates (SPCs) in Europe may be available to extend the patent exclusivity term for our products, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. The Hatch-Waxman Act permits a patent extension term of up to 5 years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. However, we may not be granted any extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. It is not possible to base an SPC in Europe on a patent in a European Member State if that patent expires before the Market Authorization (MA) of the clinical product, protected by the patent, is obtained. As the “product” (active ingredient(s)) must be “protected by a basic patent in force,” only a granted patent that is in force, and remains in force until it reaches the end of its full term, can serve as a “basic patent” upon which an SPC can be based. Therefore, expired patents and pending patent applications cannot serve as the basis for an SPC. Given the relatively long clinical development timelines of biologicals and new chemical entities for therapeutic purposes, we may not be granted any patent extensions as we might fail to apply for the extensions prior to expiration of relevant patents. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or if the term of any such extension is less than we request, such result could have a material adverse effect on our business.

We or our licensing or collaboration partners may become subject to intellectual property-related litigation or other proceedings to protect or enforce our patents or the patents of our licensors or licensees and collaborators, any of which could be expensive, time-consuming, and unsuccessful, and may ultimately result in our loss of ownership of intellectual property.

Competitors may infringe our patents or the patents of our licensors or collaborators. To counter such infringement, we may be required to file infringement claims against those competitors, which can be expensive and time-consuming. If we or one of our licensing or collaboration partners were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable or that the defendant’s products do not infringe our or our licensing collaborators’ patents or that we or our licensing collaborators infringe the defendant’s patents. In patent litigation in the U.S., defendant counterclaims alleging invalidity, unenforceability and non-infringement are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, obviousness-type double patenting, lack of written description, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld

relevant information from the USPTO, or made a misleading statement, during prosecution. In addition, third parties may raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference and derivation proceedings as well as equivalent proceedings in foreign jurisdictions, such as opposition proceedings in Europe. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Such proceedings or patent litigations could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates or otherwise provide any competitive advantage. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing or collaboration partners were unaware during prosecution. A court may also refuse to stop a third party from using the technology in question on the grounds that our patents do not cover that technology. An adverse result in any proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly, which could have a material adverse effect on our business and financial condition.

Interference, derivation or other proceedings provoked by third parties, brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors, licensees or collaborators. An unfavorable outcome could require us or our licensing or collaboration partners to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be materially harmed if the prevailing party does not offer us or our licensing or collaboration partners a license on commercially reasonable terms or at all. If we or our licensing or collaboration partners are unsuccessful in any interference, derivation or other proceedings, we may lose our ownership of intellectual property or our patents may be narrowed or invalidated. There can be no assurance as to the outcome of the interference, derivation or other proceedings, and any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations or prospects.

Our defense of litigation, interference, derivation or other proceedings or other intellectual property-related proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and could substantially reduce the funds necessary to continue our clinical studies and research programs or force us to license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market. We may not be able to prevent, alone or with our licensing or collaboration partners, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S..

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, decisions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common shares.

If we or our licensing or collaboration partners are unable to obtain and maintain effective patent rights for our technologies, product candidates or any future product candidates, or if the scope of the patent rights obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our, or our collaboration partners' ability to successfully commercialize our products and technology may be adversely affected.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large part on our and our licensing or collaboration partners' ability to obtain and maintain patent and other intellectual property protection in the U.S., the EU and other countries with respect to our proprietary technologies and product candidates. In particular, Genentech, Lilly, Janssen or our other licensing or collaboration partners may be dependent on a license with a third party for the development and future commercialization of our product candidates. If such license is not granted or is terminated, Genentech, Lilly, Janssen or other licensing or collaboration partners may be required to cease development and commercialization of our product candidates, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

We have sought to protect our proprietary position by filing patent applications in the U.S. and abroad related to any of our novel technologies and products that are important to our business. This process is expensive, time-consuming, and complex, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our or our licensing or collaboration partners' research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license to or from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biopharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. As a result, the inventorship, issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. The pending or future patent applications that we own, co-own or in-license may fail to issue, fail to result in issued patents with claims that cover our product candidates in the U.S. or in other foreign countries, or fail to effectively prevent others from commercializing competitive technologies and product candidates. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

We may not be aware of all third-party intellectual property rights potentially relating to our technologies or product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions remain confidential for a period of time after filing, and some remain so until issued. Therefore, we cannot be certain that we were the first to file any patent application related to our product candidates or technologies, or whether we were the first to make the inventions claimed in our owned or co-owned patents or pending patent applications, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file.

There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable or invalidated, which could allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our or our collaboration partners' inability to manufacture or commercialize products without infringing third-party patent rights. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. Any of these outcomes could impair our ability to prevent competition from third parties, which may have a material adverse effect on our business.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest or title in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants, CROs, CMOs, academic institutions or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our ownership of our patents or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or the right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, thereby impairing our ability to protect our technologies and products.

Changes in either the patent laws or interpretation of the patent laws in the U.S., EU or elsewhere could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming the other requirements for patentability are met, in the U.S. prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, whereas outside the U.S., the first to file a patent application was entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act (the Leahy-Smith Act), enacted on September 16, 2011, the U.S. has moved to a first-to-file system. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether a third party was the first to invent the invention. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications are prosecuted and may also affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by the USPTO administered during post grant proceedings, including re-examination proceedings, *inter partes* review, post-grant review and derivation proceedings. Therefore, the Leahy-Smith Act and its implementation increases the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, future actions by the U.S. Congress, the federal courts and the USPTO could cause the laws and regulations governing patents to change in unpredictable ways. Any of the foregoing could harm our business, financial condition and results of operations.

In Europe, the Unified Patent Court (UPC) and Unified Patent are expected to enter into force in June 2023, assuming that Germany deposits its ratification in February 2023, as anticipated. The UPC will provide a new centralized forum for pan-European litigation in contracting EU Member States (17 out of 27 EU Member States). Litigation of European patents in European Patent Convention countries outside of the EU (e.g. Switzerland, UK, Turkey) and in non-contracting EU countries (e.g. Spain, Poland) will continue to be on a country-by-country basis in front of national courts, as currently. During a transition period (initially seven-years), patent owners can elect to keep their European patents outside of the jurisdiction of the UPC ("opt-out"). Whilst European patents may be opted-out of the UPC during such transition period, after expiry of such transition period EU legislation provides that the UPC jurisdiction will apply, in respect of the UPC contracting states for all European patents. Accordingly, the emergence of the UPC and its implementation increase the uncertainties surrounding the enforcement or defense of issued patents and related costs, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future in the U.S..

If we are unable to maintain effective proprietary rights for our technologies, product candidates or any future product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce, and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the U.S. are less willing or unwilling to protect trade secrets. The EU has introduced a Directive on trade secrets increasing the standards for protection. Because we rely on our advisors, employees and third-party contractors and consultants to research and develop and to manufacture our product candidates, we must, at times, share our intellectual property with them. We seek to protect our intellectual property and

other proprietary technology in part by entering into confidentiality agreements and master service agreements, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, contractors, consultants, licensing and collaboration partners, and other third parties with confidentiality provisions. These agreements typically limit the rights of these third parties to use or disclose our confidential information, including our intellectual property and trade secrets. These agreements also typically restrict the ability of third parties to publish data potentially relating to our intellectual property, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future may expect to be granted rights to publish data arising out of such collaboration, provided that we may have the right to be notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. We also conduct joint research and development programs that may require us to share intellectual property under the terms of our research and development or similar agreements. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or other confidential information or proprietary technology and processes, or that such agreements will not be breached or that our trade secrets or other confidential information will not otherwise be disclosed. Despite the contractual provisions employed when working with these advisors, employees and third-party contractors and consultants, the need to share intellectual property and other confidential information increases the risk that such confidential information becomes known by our competitors, is inadvertently incorporated into the product development of others or is disclosed or used in violation of these agreements. Additionally, our grant agreements typically provide for dissemination of results to academic institutions and to the general public. As a result, our information may be disseminated with the loss of protection status.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining the physical security of our premises and the physical and electronic security of our information technology systems. Despite our efforts to protect our intellectual property, our competitors may discover our trade secrets through breach of our agreements by third parties, for which we may not have adequate remedies for any breach, or publication of information by any of our CROs, academic partners, funding organizations or our licensing or collaboration partners. Additionally, if the steps we take or that we impose on our CROs maintain our trade secrets are deemed inadequate by law, we may have insufficient recourse against third parties for misappropriating such trade secrets. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent such competitor or other third party from using that technology or information to compete with us. A competitor's or other third party's discovery of our intellectual property would impair our competitive position and have a material adverse effect on our business.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S.. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition and results of operations.

Despite confidentiality clauses within our employment and other agreements with employees, we cannot ensure that departing employees will not breach any post-termination commitments in such agreements by allowing others to access our trade secrets.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document-submission, fee-payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on a patent and patent application are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and patent application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee-payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply with these requirements and we are also dependent on our

licensors or collaboration partners to take the necessary action to comply with these requirements with respect to certain of our intellectual property. Although an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, nonpayment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The patent protection and patent prosecution for some of our product candidates is dependent on third parties.

Although we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product candidates, there may be times when the filing and prosecution activities for patents relating to our product candidates are controlled by our licensors or collaboration partners. If any of our current or future licensing or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our or our collaboration partners' ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Additionally, we may be adversely affected or prejudiced by actions or inactions of our external and internal patent counsels working solely on our projects or our joint patent counsels representing us and our collaboration partners.

If we fail to comply with the obligations in our intellectual property agreements, including those under which we license intellectual property and other rights to or from third parties, or otherwise experience disruptions to our business relationships with our licensees, our licensors and collaboration partners, we could lose intellectual property rights that are important to our business.

We are a party to a number of intellectual property license and co-ownership agreements and research and development collaborations that are important to our business and expect to enter into additional such agreements in the future. Under certain circumstances, the royalties payable to us under these agreements are subject to certain reductions, which may have a materially adverse effect on our business, financial condition, results of operations and prospects. In addition, our existing agreements impose, and we expect that future agreements will impose, various diligence, commercialization, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise regarding intellectual property subject to a licensing or co-ownership agreement, including:

- the scope of rights granted under the agreement, any restrictions in licensed fields and other interpretation-related issues;
- the extent to which our technology and processes infringe or otherwise violate the intellectual property of any third parties;
- the sublicensing of patents and other IP rights;

- the diligence, development and commercialization obligations under the agreement and what activities satisfy those obligations;
- the ownership of inventions and know-how resulting from the joint or mutual creation or use of intellectual property by our licensors or collaboration partners and us;
- non-compete commitments; and
- consequences for changes in control.

If disputes over intellectual property and other rights that we own, have licensed or co-own prevent or impair our ability to maintain our current licensing or exclusivity arrangements on acceptable terms, we or our collaboration partners may be unable to successfully develop and commercialize the affected product candidates.

In addition, certain provisions in the agreements under which we currently license intellectual property or technology to and from third parties may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, increase what we believe to be our financial or other obligations under the relevant agreement, or decrease the third party's financial or other obligations under the relevant agreement, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We or our licensors or licensees and collaborators may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

Our or our licensors or licensees and collaborators programs may require the use of proprietary rights held by third parties in the future, and the growth of our business will likely depend in part on our ability to acquire, in-license, maintain or use these proprietary rights. In addition, our product candidates may require specific processes and/or formulations to work effectively and efficiently and the rights to these processes and/or formulations may be held by others. We or our licensors or licensees may be unable to acquire or in-license from third parties any compositions, methods of use, processes, or other third-party intellectual property rights that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We or our licensors or licensees also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

For example, we sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our applicable product candidate or program.

If we are unable to successfully obtain a license to third-party intellectual property rights necessary for the development of a product candidate or program, we may have to abandon development of that product candidate or program and our business and financial condition could suffer.

Third-party claims of intellectual property infringement may expose us to substantial liability or may prevent or delay our or our collaboration partners' development and commercialization efforts.

Numerous U.S.- and foreign-issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. For example, we are aware of third-party patents or patent

applications that may be construed to cover one or more of our product candidates. If these patents are asserted against us or our licensing or collaboration partners and either we or our licensing or collaboration partners are found to infringe any of these patents, and are unsuccessful in demonstrating that such patents are invalid or unenforceable, then we and our licensing or collaboration partners could be required to pay substantial monetary damages or cease further development or commercialization of one or more of our product candidates or be compelled to enter into onerous licenses with such third parties. There may also be other third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods of treatment related to the use or manufacture of our product candidates and technology. Although we generally conduct a freedom-to-operate search and review with respect to our product candidates, we cannot guarantee that our search and review is complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the U.S. and abroad that is relevant or necessary to the manufacturing or commercialization of our product candidates or use of our technology. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may file and obtain additional patents in the future and claim that use of our technologies infringes upon these patents.

Third parties may assert infringement claims against us based on existing patents or on patents that may be granted in the future, regardless of merit. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our or our collaboration partners' ability to commercialize our product candidates or technologies covered by the asserted third-party patents.

Parties making claims against us may also obtain injunctive or other equitable relief, which could effectively block our or our collaboration partners' ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Any of the foregoing could have a material and adverse effect on our business, financial conditions, results of operations and prospects.

In addition, claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

There could also be public announcements of the results of hearings, motions, decisions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common shares.

Some of our competitors may have substantially greater resources and more mature and developed intellectual property portfolios than we do, and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent-holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the pharmaceutical and biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. The uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ and utilize the services of individuals who were previously employed or provided services to universities or other pharmaceutical or biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees,

consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employees', consultants' or independent contractors' former employers or of other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

In addition, although it is our policy to require our employees, consultants and independent contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. may be less extensive than those in the U.S.. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as the laws in the U.S.. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. In the ordinary course of prosecution and maintenance activities, we determine whether to seek patent protection outside the U.S. and in which countries. This also applies to patents we have acquired or in-licensed from third parties. In some cases, we, or our predecessors in interest or licensors of patents within our portfolio, have sought patent protection in a limited number of countries for patents covering our product candidates. Competitors may use our technologies and products in jurisdictions where we have not obtained or are unable to adequately enforce patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the U.S.. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing, which would have a material adverse effect on our business and financial positions.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement, misappropriation or other violations of our intellectual property and proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest, our names and brands may be misappropriated by third parties, and our business may be adversely affected.

We have filed trademark applications seeking protection for our corporate name, logo, Nasdaq Global Market symbol and selected names of our technology platforms in selected geographies. While we have been granted registrations in certain geographies for certain trademarks, there is no guarantee that our trademark applications will be approved by the respective authorities at all or that we will not be required to narrow the scope of protection in certain or all geographies. Our applications have in the past faced and may in the future face opposition from third parties, potentially resulting in the lack of protection or narrower protection. Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. We may not be able to protect

our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names, domain names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks and domain names may be ineffective and could result in substantial costs and diversion of resources, and could adversely affect our business, financial condition, results of operations and growth prospects.

Risks related to our financial condition and capital requirements

We are a clinical-stage company and have a history of operating losses. We anticipate that we will continue to incur losses for the foreseeable future.

We are a clinical-stage biopharmaceutical company. Since 2003, although we have received upfront and milestone payments from our collaboration partners and certain other contract revenue, we have also incurred significant operating losses. We incurred net losses (defined as net loss attributable to owners of the Company) of CHF 70.8 million for the year ended December 31, 2022. In addition, we had accumulated losses of CHF 264.0 million as of December 31, 2022.

Our losses have resulted principally from research and development expenses and from general business and administrative expenses. We expect to continue to incur significant operating losses in the future as we continue our research and development efforts for our current and future product candidates and seek to obtain regulatory approval and commercialization of such product candidates.

To date, the Company has financed its liquidity requirements primarily from its public offerings, share issuances, contract revenues from license and collaboration agreements and grants. We have no products approved for commercialization and have never generated any revenues from product sales. Biopharmaceutical and pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. It may be several years, if ever, before we or our collaboration partners complete pivotal clinical studies and have a product candidate approved for commercialization and we begin to generate revenue or royalties from product sales.

Although we have generated revenues from upfront and milestone payments related to our license and collaboration agreements, we have never generated any revenue from product sales and may never be profitable.

Although we have generated contract revenue from upfront and milestone payments related to our license and collaboration agreements, we have no products approved for commercialization and have never generated any revenue from product sales. Our ability to generate revenue and achieve profitability depends on our and our licensors' and collaboration partners' ability to successfully complete the development of, and obtain the marketing approvals necessary, to commercialize one or more of our product candidates. We do not anticipate generating revenue from product sales unless and until we or our collaboration partners obtain regulatory approval for, and commercialize, our product candidates. Our ability to generate future revenue from product sales depends heavily on our and our collaboration partners' success in many areas, including but not limited to:

- successfully completing research and clinical development of our product candidates, by us or our collaboration partners, as the case may be;

- obtaining marketing approvals for our clinical product candidates, including our vaccines (ACI-35.030, ACI-24.060 and ACI-7104.056), monoclonal antibodies (semorinemab and crenezumab) and diagnostics (Tau-PET tracer PI-2620 and a-syn PET tracer ACI-12589), for which we or our collaboration partners complete clinical studies;

- developing a sustainable and scalable manufacturing process for any approved product candidates, and maintaining supply and manufacturing relationships with third parties that can conduct the process and provide adequate (in amount, quality and time) products to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our product candidates as viable treatment or diagnostic options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other similar arrangements into which we may enter;
- maintaining, protecting, acquiring and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties with biopharmaceutical and pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses and when, or if, we will be able to achieve profitability. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other regulatory agencies, domestic or foreign, to change our manufacturing processes, or to perform clinical, nonclinical or other types of studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, the treatment population is narrowed by competition, physician choice or treatment guidelines or other commercial related factors we may not generate significant revenue from sales of such products, even if approved. Accordingly, we may not be profitable in the future from the sale of any approved products.

We or our collaboration partners may be unable to develop and commercialize any of our current or future product candidates and, even if we do, may not achieve profitability in the future. Even if we do achieve profitability in the future, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to be profitable in the future would decrease the value of our company and could impair our ability to raise capital, expand our business or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

If we fail to obtain additional funding, we may delay, reduce or eliminate our product development programs or commercialization efforts.

We are currently advancing our clinical product candidates through clinical development, either together with a collaboration partner (ACI-35.030, semorinemab, crenezumab and PI-2620) or independently (ACI-24.060, ACI-7104.056 and ACI-12589). We expect our research and development expenses to continue to increase in connection with our ongoing activities, particularly as we and/or our collaboration partners continue our ongoing studies and initiate new studies of ACI-35.030, ACI-24.060, ACI-7104.056, Morphomer Tau, PI-2620 and ACI-12589 and initiate preclinical and clinical development of our other product candidates.

As of December 31, 2022, we had cash and cash equivalents of CHF 31.6 million and short-term financial assets of CHF 91.0 million resulting in a total liquidity position of CHF 122.6 million. We currently believe that our existing

capital resources, not including potential milestone payments, will be sufficient to meet our projected operating requirements into Q3 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our capital resources sooner than we currently expect. In addition, changing circumstances, including inflation, may cause us to adjust our projected spending to amounts more than currently expected. We may also need to raise additional funds sooner than we anticipate due to various factors such as the scope and rate of progress of our development activities, regulatory approval outcomes and emergence of competing technologies, among others.

We expect that we will require additional capital to develop and commercialize certain of our product candidates. If we receive regulatory approval for our current and future product candidates, and if we have not already licensed such product candidate to a collaboration partner and choose to commercialize such product candidate independently, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing, distribution and establishing a regulatory structure, depending on where we choose to commercialize. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy, in particular as a result of inflation. Additionally, we may be dependent on the status of the capital markets at the time such capital is sought. In addition, our ability to raise sufficient capital under our "at the market" program may be diminished depending on the market price of our shares. If we are not able to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Raising additional capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our intellectual property or future revenue streams.

Until such time, if ever, as we can generate substantial product royalty revenue, we expect to finance our liquidity needs through a combination of equity offerings, debt financings, grants, and license and development agreements in connection with collaborations. In September 2020, the Company established an "at the market offering" (ATM) for the sale of up to USD 80.0 (CHF 74.6) million worth of our common shares from time to time by entering into an Open Market Sale Agreement (Sales Agreement) with Jefferies LLC (Jefferies). In Q2 2021, we filed a new registration statement on Form F-3 and entered into a new Sales Agreement to replace and extend the ATM program. We do not have any material committed external source of funds. In the event we need to seek additional funds, we may raise additional capital through the sale of equity, convertible debt or other securities. In such an event, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of our common shares. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or proposing dividends to our shareholders.

If we raise additional funds through collaborations, strategic alliances, or marketing, distribution or licensing arrangements with third parties, we may have to grant or otherwise relinquish valuable rights to our intellectual property or future revenue streams.

Our ability to use tax loss carry-forwards in Switzerland may be limited.

As of December 31, 2022, we reported tax loss carry-forwards from financial years 2016 until 2022 for purposes of Swiss corporate income tax in the aggregate amount of CHF 264.1 million, which could be available to offset future taxable income. If not used, these tax losses will expire 7 years after the year in which they were incurred. Due to our limited income, there is a high risk that the tax loss carry-forwards will expire partly or entirely and we will not be able to use them to offset future taxable income thereafter for Swiss corporate income tax purposes.

Exchange rate fluctuations may materially affect our results of operations and financial condition.

Under our existing agreements, we receive and make a significant amount of payments in Swiss Franc, USD and EUR. As a result, changes and fluctuations in currency exchange rates between the Swiss Franc and other currencies, especially the USD and EUR, could have a materially adverse effect on our operating results. As our reporting currency is the Swiss Franc, financial line items are converted into Swiss Francs at the applicable exchange rates. We also expect that in the future, a significant portion of our revenues and expenses will be denominated in Swiss Franc, USD and EUR.

Therefore, unfavorable developments in the value of the Swiss Franc as compared to the USD and EUR or any other currency could have a material adverse effect on our business, financial condition and results of operations.

Our significant in-process research and development (IPR&D) asset may become impaired.

Our consolidated balance sheet contains a material IPR&D asset. For an IPR&D asset, the risk of failure is significant, and there can be no certainty that the asset will become a successful candidate. Our ability to realize value on this significant investment is often contingent upon, among other things, regulatory approvals and market acceptance. As such, this IPR&D may become impaired and/or be written off at some time in the future if the associated R&D effort is abandoned or is curtailed.

Risks related to the regulatory environment

We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

Our future success is dependent on our and our collaboration partners' ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We currently have two product candidates that have completed Phase 2 clinical studies and six that are in a Phase 2 clinical study. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA, EMA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates.

We cannot be certain that any of our product candidates will be successful in clinical studies or receive regulatory approval. Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA, EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical studies;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- we may be unable to demonstrate to the FDA, EMA or comparable foreign regulatory authorities that a product candidate's benefit-risk ratio for its proposed indication is acceptable;
- the FDA, EMA or other regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may change significantly in a manner rendering our clinical data insufficient for approval.

We generally plan to seek regulatory approval to commercialize our product candidates in the U.S., the EU and in additional foreign countries where we have commercial and typically intellectual property rights. To obtain regulatory approval in other countries, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies, commercial sales, pricing, marketing

and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. Failure to obtain marketing authorization for our product candidates will result in our being unable to market and sell such products, which would materially adversely affect our business, financial condition and results of operations. If we fail to obtain approval in any jurisdiction, the geographic market for our product candidates could be limited. Similarly, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. If clinical studies of our product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our product candidates on a timely basis or at all.

To obtain the necessary regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical and clinical studies that our products are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical study process. The results of preclinical and early clinical studies of our product candidates may not be predictive of the results of later-stage clinical studies. For example, the positive results generated to date in clinical studies for our product candidates do not ensure that later clinical studies will demonstrate similar results. Product candidates in later stages of clinical studies may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical studies. A number of companies in the pharmaceutical or biopharmaceutical industry, including us, have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies. Our future clinical study results may not be successful.

Clinical studies must be conducted in accordance with the legal requirements, regulations and guidelines of the FDA, EMA and comparable foreign regulatory authorities, and are subject to oversight by these governmental agencies and Institutional Review Boards (IRBs) at the medical institutions where the clinical studies are conducted. In addition, clinical studies must be conducted with supplies of our product candidates produced under cGMP and other requirements. We depend on medical institutions and CROs to conduct our clinical studies in compliance with cGCP standards. To the extent the CROs fail to enroll participants for our clinical studies, fail to conduct the study to cGCP standards or are delayed for a significant time in the execution of studies, including achieving full enrollment, we may be affected by increased costs, program delays or both, which may harm our business.

To date, neither we nor our collaboration partners have completed all clinical studies required for the approval of any of our product candidates.

The completion of clinical studies for our product candidates may be delayed, suspended or terminated as a result of many factors, including but not limited to:

- the delay or refusal of regulators or IRBs to authorize us to commence or amend a clinical study at a prospective study site or changes in regulatory requirements, policies and guidelines;
- delays or failure to reach agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and study sites;
- delays in patient enrollment and variability in the number and types of patients available for clinical studies;
- the inability to enroll a sufficient number of patients in studies to ensure adequate statistical power to detect statistically significant treatment effects;
- negative or inconclusive results, which may require us to conduct additional preclinical or clinical studies or to abandon projects that we expected to be promising;

- safety or tolerability concerns, which could cause us to suspend or terminate a study if we find that the participants are being exposed to unacceptable health risks;
- regulators or IRBs requiring that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or safety concerns, among others;
- lower than anticipated retention rates of patients and volunteers in clinical studies;
- our CROs or clinical study sites failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, deviating from the protocol or dropping out of a study;
- delays relating to adding new clinical study sites;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- delays in establishing the appropriate dosage levels;
- the quality or stability of the product candidate falling below acceptable standards;
- the inability to produce or obtain sufficient quantities of the product candidate to complete clinical studies; and
- exceeding budgeted costs due to difficulty in accurately predicting costs associated with clinical studies.

Any delays in completing our clinical studies will increase our costs, slow our product candidate development and approval process, and jeopardize our ability to commence product sales and generate sales revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

Even if we obtain and maintain approval for our product candidates from one jurisdiction, we may never obtain approval for our product candidates in other jurisdictions, which would limit our market opportunities and adversely affect our business.

Sales by us of our approved drugs will be subject to U.S. and non-U.S. regulatory requirements governing clinical studies and regulatory approval, and we plan to seek regulatory approval to commercialize our product candidates in the U.S., the European Economic Area (EEA), and other countries. Clinical studies conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. For example, approval in the U.S. by the FDA does not ensure approval by the regulatory authorities in other countries or jurisdictions, and similarly, approval by a non-U.S. regulatory authority, such as the EMA, does not ensure approval by regulatory authorities in other countries, including by the FDA. Approval processes and regulatory requirements vary among countries and can involve additional drug testing and validation and additional administrative review periods. Even if a drug is approved, the FDA or EMA, as the case may be, may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling, or require expensive and time-consuming clinical studies or reporting as conditions of approval. In many countries outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that would be charged for a drug is also subject to approval. Regulatory authorities in other countries also have their own requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining non-U.S. regulatory approvals and compliance with such non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our current and any future drugs, in certain countries. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our product candidates will be unrealized.

Even if our product candidates obtain regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

If a marketing authorization is obtained for any of our product candidates, the product will remain subject to continual regulatory review and therefore authorization could be subsequently withdrawn or restricted. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical studies and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA or a comparable foreign regulatory authority approves any of our product candidates, we will be subject to ongoing regulatory obligations and oversight by regulatory authorities, including with respect to the manufacturing processes, labeling, packing, distribution, adverse event reporting, storage, advertising and marketing restrictions, and record-keeping and, potentially, other post-marketing obligations, all of which may result in significant expense and limit our or our collaboration partners' ability to commercialize such products. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and cGCP requirements for any clinical studies that we conduct post-approval. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical studies;
- refusal by the FDA or an applicable foreign regulatory authority to approve pending applications or supplements to approved applications filed by us or our collaborations partners, or suspension or revocation of product license approvals;
- regulatory constraints in promotion and distribution of drug products in various markets;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

If any of these events occurs, our ability to sell such product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could materially adversely affect our business, financial condition and results of operations. The FDA's or those of an applicable foreign regulatory authority's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We have conducted and may in the future conduct clinical studies for our product candidates outside the U.S., and the FDA and applicable foreign regulatory authorities may not accept data from such studies.

We have conducted and may in the future choose to conduct one or more of our clinical studies outside the U.S., including in Germany, Austria, Denmark, Sweden, Finland, the UK, Poland, Spain and the Netherlands. The acceptance of study data from clinical studies conducted outside the U.S. or another jurisdiction by the FDA or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical studies are intended

to serve as the basis for marketing approval in the U.S., the FDA will not approve the application on the basis of foreign data alone unless the following are true: the data are applicable to the U.S. population and U.S. medical practice; the studies were performed by clinical investigators of recognized competence; and the data are considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical study requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar requirements. In addition, such foreign studies would be subject to the applicable local laws of the foreign jurisdictions in which the studies are conducted. There can be no assurance that the FDA or any applicable foreign regulatory authority will accept data from studies conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional studies, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our drugs or product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the U.S., the EU and some foreign jurisdictions, there have been a number of adopted and proposed legislative and regulatory changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any of our product candidates for which we obtain regulatory approval.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") changed the way Medicare covers and pays for pharmaceutical products. Cost reduction initiatives and other provisions of this legislation could limit the coverage and reimbursement rate that we receive for any of our approved product candidates. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the Health Care Reform Law), was enacted. The Health Care Reform Law was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Health Care Reform Law increased manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate amount for both branded and generic drugs and revised the definition of "average manufacturer price" ("AMP"), which may also increase the amount of Medicaid drug rebates manufacturers are required to pay to states. The legislation also expanded Medicaid drug rebates and created an alternative rebate formula for certain new formulations of certain existing products that is intended to increase the rebates due on those drugs. The Centers for Medicare & Medicaid Services, which administers the Medicaid Drug Rebate Program, also has proposed to expand Medicaid rebates to the utilization that occurs in the territories of the U.S., such as Puerto Rico and the Virgin Islands. Further, beginning in 2011, the Health Care Reform Law imposed a significant annual fee on companies that manufacture or import branded prescription drug products. Legislative and regulatory proposals have been introduced at both the state and federal level to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products.

We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing approval testing and other requirements.

In addition, there has been heightened governmental scrutiny in the U.S. of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to

product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At both the federal and state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. One significant example of recent legislative action is the Inflation Reduction Act of 2022 (the "IRA"), which has been considered a scaled-back version of the Build Back Better Act. The IRA was signed into law on August 16, 2022. While the IRA is still subject to rulemaking (with more information to come via guidance documents from the responsible federal agencies), the IRA, as written, will, among other changes, give HHS the ability and authority to directly negotiate with manufacturers the price that Medicare will pay for certain high-priced drugs. The IRA will also require manufacturers of certain Part B and Part D drugs to issue to HHS rebates based on certain calculations and triggers (i.e., when drug prices increase and outpace the rate of inflation). At this time, we cannot predict the implications the IRA provisions will have on our business.

Additionally, in the EU, the new clinical trial regulation came into force on January 31, 2022. This new legislation enforces the centralization of clinical trial applications (CTAs) and approvals, which eliminates redundancy, but in some cases, this may extend timelines for clinical study approvals, due to potentially longer wait times. Austerity measures in certain European nations may also affect the prices we are able to seek if our products are approved. Both in the U.S. and in the EU, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biopharmaceutical products. We do not know whether additional legislative changes will be enacted, whether the regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be.

We could be subject to liabilities under environmental, health and safety laws or regulations, or fines, penalties or other sanctions, if we fail to comply with such laws or regulations or otherwise incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws, regulations, and permitting requirements, including those governing laboratory procedures, decontamination activities, and the handling, transportation, use, remediation, storage, treatment and disposal of hazardous materials, human substances and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials that produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials or wastes either at our sites or at third-party disposal sites. In the event of such contamination or injury, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, human substances or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws, regulations or permitting requirements. Such laws, regulations and requirements are becoming increasingly more stringent and may impair our research, development or production efforts. Failure to comply with these laws, regulations and permitting requirements also may result in substantial fines, penalties or other sanctions.

Our relationships with clinical centers are, and potentials customers and payors will be, subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable healthcare laws and regulations include the following:

- the U.S. healthcare Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under U.S. government healthcare programs such as Medicare and Medicaid;

- the U.S. False Claims Act imposes criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the U.S. HIPAA imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the transparency requirements under the Health Care Reform Law require manufacturers of drugs, devices, biologics and medical supplies to report to the U.S. Department of Health and Human Services information related to payments and other transfers of value made by such manufacturers to physicians and teaching hospitals, and ownership and investment interests held by physicians or their immediate family members; and

- analogous laws and regulations, such as state anti-kickback and false claims laws, will apply to sales or marketing arrangements, consultancy and service agreements, and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers, and some state laws require pharmaceutical and biopharmaceutical companies to comply with the pharmaceutical and biopharmaceutical industries' voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute, it is possible that some of our future business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare-reform legislation has strengthened these laws. For example, the Health Care Reform Law, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Jurisdictions outside of the U.S. have enacted laws and regulations defining the framework of business practices of pharmaceutical organizations in their interactions with government offices, medical institutions and healthcare professionals (HCP) in order to safeguard the independence of medical judgement and of prescription and purchasing decisions. These regulations typically prohibit illegitimate payments and other transfers of values to institutional players and HCPs and regulate the bases for their remuneration, such as for consultancy and other service arrangements, as well as the reimbursement of costs; in certain jurisdictions, regulations prescribe the disclosure of the existing relationships and/or the remunerations paid. In addition to government regulations, pharmaceutical industry associations, such as the European Federation of Pharmaceutical Industries and Associations (EFPIA), of which we have been a member since 2021, have enacted industry codes of conduct providing their own rules of compliance for their members' interactions with government offices, medical institutions and HCPs.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other

governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government-funded healthcare programs, such as Medicare and Medicaid, other foreign healthcare reimbursement and procurement programs, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business with is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Risks from the improper conduct of employees, agents, contractors, or collaborators could adversely affect our reputation and our business, prospects, operating results, and financial condition.

We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors, collaborators, or other parties, which would violate the laws or regulations of the jurisdictions in which we operate, including, without limitation, healthcare, employment, foreign corrupt practices, environmental, competition, and patient privacy and other privacy laws and regulations. Such improper actions could subject us to civil or criminal investigations, and monetary and injunctive penalties, and could adversely impact our operating results, our ability to conduct business and our reputation.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA or EMA regulations, to provide accurate information to the FDA or the EMA, or intentional failures to report financial information or data accurately or to disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation. In April 2022, we amended our code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Our business activities may be subject to the Foreign Corrupt Practices Act (FCPA), and similar anti-bribery and anti-corruption laws.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the UK Bribery Act. The FCPA generally prohibits offering, promising, giving or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation, and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals or biopharmaceuticals and the investigators who perform our studies are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these decision makers are subject to regulation under the FCPA. The Securities and Exchange Commission (SEC) and the Department of Justice have increased their FCPA enforcement activities with respect to pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, collaborators, or other parties or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results and financial condition.

Risks related to our common shares

The price of our common shares is volatile and may fluctuate due to factors beyond our control.

The share prices of publicly traded pharmaceutical, biopharmaceutical and drug discovery and development companies have been highly volatile and are likely to remain highly volatile in the future. The market price of our common shares may fluctuate significantly due to a variety of factors, including:

- positive or negative results of testing and clinical studies by us, strategic partners, or competitors;
- delays in entering into strategic relationships with respect to development and/or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to us;
- the sentiment of retail investors, including the perception of our clinical trial results by such retail investors, which investors may be subject to the influence of information provided by social media, third party investor websites and independent authors distributing information on the internet;
- technological innovations or commercial product introductions by us or our collaboration partners or competitors;
- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our product candidates;
- financing or other corporate transactions;
- publication of research reports or comments by securities or industry analysts or key opinion leaders;
- general market conditions in the pharmaceutical or biopharmaceutical industry or in the economy as a whole; or
- other events and factors beyond our control.

Broad market and industry factors may materially affect the market price of companies' stock, including ours, regardless of actual operating performance. Furthermore, issuers such as ourselves, whose securities have historically had limited trading volumes and/or have been susceptible to relatively high volatility levels, can be particularly vulnerable to short-seller attacks and trading in our common shares by non-fundamental investors such as hedge funds and others who may enter and exit positions in our common shares frequently and suddenly, causing increased volatility of our share price. Short selling is the practice of selling securities that the seller does not own but rather has borrowed or intends to borrow from a third party with the intention of buying identical securities at a later date to return to the lender, and profit from a decline in the value of the securities in the process. The publication of any commentary by short sellers with the intent of creating negative market momentum may bring about a temporary, or possibly long-term, decline in the market price of our common shares.

There is only a limited free float of our common shares; this may have a negative impact on the liquidity of and the market price for our common shares.

As of the date hereof, certain principal shareholders controlling 5% or more of our common shares as well as our executive officers and directors together beneficially own approximately 60.1% of our common shares. The limited free float may have a negative impact on the liquidity of our common shares and result in a low trading volume of our common shares, which could adversely affect the price of our common shares.

Certain of our existing shareholders exercise significant control over us, and your interests may conflict with the interests of such shareholders.

Certain principal shareholders as well as our executive officers and directors together beneficially own approximately 60.1% of our common shares. Depending on the level of attendance at our general meetings of shareholders, these shareholders may be in a position to determine the outcome of decisions taken at any such general meeting. To the extent that the interests of these shareholders may differ from the interests of the Company's other shareholders, the latter may be disadvantaged by any action that these shareholders may seek to pursue. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our common shares.

Future sales, or the possibility of future sales, of a substantial number of our common shares could adversely affect the price of our common shares.

Future sales of a substantial number of our common shares, or the perception that such sales will occur, could cause a decline in the market price of our common shares. If certain of our shareholders sell substantial amounts of common shares in the public market, or the market perceives that such sales may occur, the market price of our common shares and our ability to raise capital through an issue of equity securities in the future could be adversely affected. We also entered into a registration rights agreement in connection with the Series E Private Placement with certain investors in the Series E Private Placement, pursuant to which we agreed under certain circumstances to file a registration statement to register the resale of the common shares held by certain of our existing shareholders, as well as to cooperate in certain public offerings of such common shares. In October 2020 and August 2018, we filed registration statements on Form F-3 to register the resale of two of our shareholder's common shares pursuant to the requirements of their registration rights agreements. In addition, in 2019, we adopted a new omnibus equity incentive plan under which we have the discretion to grant a broad range of equity-based awards to eligible participants. These shares were registered pursuant to the registration statement on Form S-8 that we filed with the SEC and, therefore, can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. If a large number of our common shares are sold in the public market after they become eligible for sale, the sales could reduce the trading price of our common shares and impede our ability to raise future capital.

We have broad discretion in the use of our cash and cash equivalents and short-term financial assets (liquidity) and may not use them effectively.

Our management has broad discretion in the application of our cash and cash equivalents and short-term financial assets. Our or our collaboration partners' decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the pharmaceutical or biopharmaceutical industry, in particular for neurodegenerative diseases, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

We do not expect to pay dividends in the foreseeable future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that any earnings will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. Based on Swiss law and our articles of association, the declaration of dividends requires a resolution passed by a simple majority of the votes cast at a shareholders' meeting regardless of abstentions and empty or invalid votes. The proposal to pay future dividends to shareholders will in addition effectively be at the discretion of our board of directors after considering various factors

including our business prospects, liquidity requirements, financial performance and new product development. In addition, payment of future dividends is subject to certain limitations pursuant to Swiss law or by our articles of association compliance with which must be confirmed by our auditors. Accordingly, investors cannot rely on dividend income from our common shares and any returns on an investment in our common shares will likely depend entirely upon any future appreciation in the price of our common shares.

We are a Swiss corporation. The rights of our shareholders may be different from the rights of shareholders in companies governed by the laws of U.S. jurisdictions.

We are a Swiss corporation. Our corporate affairs are governed by our articles of association and by the laws governing companies, including listed companies, incorporated in Switzerland. The rights of our shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and directors of companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board of directors is required by Swiss law to consider the interests of our Company first, then of our shareholders, our employees and other stakeholders, in all cases, with due observation of their fiduciary duties of care and loyalty. It is possible that some of these parties will have interests that are different from, or in addition to, your interests as a shareholder. Swiss corporate law limits the ability of our shareholders to challenge resolutions made or other actions taken by our board of directors in court. Our shareholders generally are not permitted to file a suit to reverse a decision or an action taken by our board of directors but are instead only permitted to seek damages for breaches of their fiduciary duties by the directors. As a matter of Swiss law, shareholder claims against a member of our board of directors for breach of fiduciary duty would have to be brought in Lausanne, Switzerland, or the country in which the relevant member of our board of directors is domiciled. In addition, under Swiss law, any claims by our shareholders against us must be in principle brought exclusively in Lausanne, Switzerland (except for certain U.S. securities and other claims that may be brought in U.S. federal court).

Our common shares are issued under the laws of Switzerland, which may not protect investors in a similar fashion afforded by incorporation in a U.S. state.

We are organized under the laws of Switzerland. There can be no assurance that Swiss law will not change in the future in a way detrimental to shareholders or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the U.S., which could adversely affect the rights of investors.

Our status as a Swiss corporation may limit our flexibility with respect to certain aspects of capital management and may cause us to be unable to make distributions without subjecting our shareholders to Swiss withholding tax.

The Swiss law effective at the time according to which our current Articles were established allowed our shareholders to authorize share capital that can be issued by the board of directors without additional shareholder approval. This authorization is limited to 50% of the existing registered share capital and must be renewed by the shareholders once expired. As of January 1, 2023, the new Swiss corporate law introducing the capital band mechanism has come into force. It will no longer be possible to renew the Company's current Authorized Share Capital beyond June 24, 2024. Instead, the Company can only introduce the capital band pursuant to Article 653s et seq. of the revised Swiss Code of Obligations which requires an amendment of the Articles of Association by way of a resolution of a duly convened general meeting of shareholders of the Company. Under the capital band mechanism, the general meeting of shareholders can authorize the board of directors at any time within a maximum of five years to increase or decrease the share capital by a maximum amount of 50% of the current share capital.

Additionally, as a principle, Swiss law grants pre-emptive subscription rights to existing shareholders to subscribe to any new issuance of shares. Any common share capital increase resolution preserving pre-emptive subscription rights expires after 3 months and requires a simple majority of the votes cast at the shareholder’s meeting regardless of abstentions and empty or invalid votes. Swiss law also does not provide as much flexibility in the various terms that can attach to different classes of shares as do the laws of some other jurisdictions. Swiss law also reserves for approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, dividends must be approved by shareholders. These Swiss law requirements relating to our capital

management may limit our flexibility, and situations may arise in which greater flexibility would have provided substantial benefits to our shareholders.

Under Swiss law, a Swiss corporation may pay dividends only if the corporation has sufficient distributable profits from previous fiscal years, or if the corporation has distributable reserves, each as evidenced by its audited statutory balance sheet. Freely distributable reserves are generally booked either as "free reserves" or as "capital contributions" (*apports de capital*, contributions received from shareholders) in the "reserve from capital contributions." Distributions may be made out of issued share capital—the aggregate nominal value of a company's issued shares—only by way of a capital reduction. To the extent the Company introduces the capital band, only net proceeds from capital increase using the capital band (less certain expenses and net of repayments from the Company) will be recognized as reserves from capital contributions at the end of validity period of the respective capital band). As of December 31, 2022, the Company has CHF 432.6 million of reserves from capital contributions confirmed by the Swiss Federal Tax Administration and CHF 1,794,907 of issued share capital (consisting of 89,745,365 common shares each with a nominal value of CHF 0.02 and no preferred shares) on its audited statutory balance sheet. Of the total issued shares and issued share capital, the Company holds 6,214,021 fully paid-in treasury shares representing CHF 124,280 of issued share capital.

Generally, Swiss withholding tax of 35% is due on dividends and similar distributions to our shareholders, regardless of the place of residency of the shareholder, unless the distribution is made to shareholders out of (i) a reduction of nominal value or (ii) assuming certain conditions are met, reserves from capital contributions accumulated on or after January 1, 1997. We expect the aggregate of the reserves from capital contributions confirmed by the Swiss Federal Tax Administration and share capital, less the total losses brought forward (to the extent set off against reserves from capital contributions or share capital), less the treasury shares (to the extent booked against reserves from capital contributions), less the lowest legally possible issued share capital and legal reserve of together CHF 150,000 to represent the maximum amount potentially available for future dividends or capital reductions on a Swiss withholding tax-free basis. We would also be able to pay dividends out of distributable profits or freely distributable reserves but such dividends would be subject to Swiss withholding taxes. There can be no assurance that we will have sufficient distributable profits, free reserves, reserves from capital contributions or registered share capital to pay a dividend or effect a capital reduction, that our shareholders will approve dividends or capital reductions proposed by us, or that we will be able to meet the other legal requirements for dividend payments or distributions as a result of capital reductions.

A U.S. investor who qualifies for benefits under the Convention Between the United States of America and the Swiss Confederation for the Avoidance of Double Taxation with Respect to Taxes on Income, which we refer to as the "U.S.-Swiss Treaty," may apply for a refund of the tax withheld in excess of the 15% treaty rate (or in excess of the 5% reduced treaty rate for qualifying corporate shareholders with at least 10% participation in our voting stock, or for a full refund in the case of qualified pension funds). There can be no assurance that we will have sufficient reserves from capital contributions to pay dividends free from Swiss withholding tax, or that Swiss withholding tax rules will not be changed in the future. In addition, we cannot provide assurance that the current Swiss law with respect to distributions out of reserves from capital contributions will not be changed or that a change in Swiss law will not adversely affect us or our shareholders, in particular as a result of distributions out of reserves from capital contributions becoming subject to additional corporate law or other restrictions. If we are unable to make a distribution through a reduction in nominal value or out of confirmed reserves from capital contributions, we will not be able to make distributions without subjecting our shareholders to Swiss withholding taxes.

U.S. shareholders may not be able to obtain judgments or enforce civil liabilities against us or our executive officers or members of our board of directors.

We are organized under the laws of Switzerland and our registered office and domicile is located in Ecublens, near Lausanne, Canton of Vaud, Switzerland. Moreover, a number of our directors and executive officers are not residents of the U.S., and all or a substantial portion of the assets of such persons are located outside the U.S.. As a result, it may not be possible for investors to effect service of process within the U.S. upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the U.S.. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or of actions for enforcement of judgments of U.S. courts, for civil liabilities to the extent solely predicated upon the federal and state securities laws of the U.S.. Original actions against persons in Switzerland based solely upon the U.S. federal or state securities laws are governed, among other things, by

the principles set forth in the Swiss Federal Act on Private International Law. This statute provides that the application of provisions of non-Swiss law by the courts in Switzerland shall be precluded if the result is incompatible with Swiss public policy. Additionally, certain mandatory provisions of Swiss law may be applicable regardless of any other law that would otherwise apply.

Switzerland and the U.S. do not have a treaty providing for reciprocal recognition and enforcement of judgments in civil and commercial matters. The recognition and enforcement of a judgment of the courts of the U.S. in Switzerland is governed by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides in principle that a judgment rendered by a non-Swiss court may be enforced in Switzerland only if:

- the non-Swiss court had jurisdiction pursuant to the Swiss Federal Act on Private International Law;
- the judgment of such non-Swiss court has become final and non-appealable;
- the judgment does not contravene Swiss public policy;
- the court procedures and the service of documents leading to the judgment were in accordance with the due process of law; and
- no proceeding involving the same parties and the same subject matter was first brought in Switzerland, or adjudicated in Switzerland, or was earlier adjudicated in a third state for which the decision is recognizable in Switzerland.

Our status as a Swiss corporation means that our shareholders enjoy certain rights that may limit our flexibility to raise capital, issue dividends and otherwise manage ongoing capital needs.

Swiss law reserves for approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, the payment of dividends and cancellation of treasury shares must be approved by shareholders. Swiss law also requires that our shareholders themselves resolve, or authorize our board of directors, to increase our share capital. Although under the current Swiss law our shareholders may resolve a capital band which authorizes the board of directors to increase or decrease the share capital without additional shareholder approval, Swiss law limits this authorization to 50% of the issued share capital at the time of the authorization. The authorization, furthermore, has a limited duration of up to five years and must be renewed by the shareholders from time to time thereafter.

Since January 1, 2023, the new Swiss corporate law introducing the capital band mechanism has come into force. It will no longer be possible to renew the Company's current Authorized Share Capital beyond June 24, 2024. Instead, the Company can only introduce the capital band pursuant to Article 653s et seq. of the revised Swiss Code of Obligations which requires an amendment of the Articles by way of a resolution of a duly convened general meeting of shareholders of the Company.

Additionally, subject to specified exceptions, including exceptions explicitly described in our articles of association, Swiss law grants pre-emptive subscription rights to existing shareholders to subscribe for new issuances of shares. Swiss law also does not provide as much flexibility in the various rights and regulations that can attach to different categories of shares as do the laws of some other jurisdictions. These Swiss law requirements relating to our capital management may limit our flexibility, and situations may arise where greater flexibility would have provided benefits to our shareholders.

Swiss law restricts our ability to pay dividends.

See “Item 10. Additional information—E. Taxation—Swiss tax considerations” for a summary of certain Swiss tax consequences regarding dividends distributed to holders of our common shares.

Shareholders in countries with a currency other than Swiss Francs face additional investment risks from currency exchange rate fluctuations in connection with their holding of our common shares.

Any future payments of dividends, if any, will likely be denominated in Swiss Francs. The foreign currency equivalent of any dividend, if any, paid on our common shares or received in connection with any sale of our common shares could be adversely affected by the depreciation of the Swiss Franc against such other currency.

We are a foreign private issuer and, as a result, we are not subject to U.S. proxy rules and are subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

We are reporting under the Exchange Act as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act and although we are subject to Swiss laws and regulations with regard to such matters and intend to furnish quarterly financial information to the SEC, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and their liability for insiders who profit from trades made in a short period of time; and (iii) the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or of current reports on Form 8-K, upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until 4 months after the end of each financial year, whereas U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

As a foreign private issuer and as permitted by the listing requirements of Nasdaq, we rely on certain home country governance practices rather than the corporate governance requirements of Nasdaq.

We are a foreign private issuer. As a result, in accordance with Nasdaq Listing Rule 5615(a)(3), we comply with home country (in this case, Swiss) governance requirements and certain exemptions thereunder rather than complying with certain of the corporate governance requirements of Nasdaq. Swiss law does not require that a majority of our board of directors consist of independent directors. Our board of directors therefore may include fewer independent directors than would be required if we were subject to Nasdaq Listing Rule 5605(b)(1). In addition, we are not subject to Nasdaq Listing Rule 5605(b)(2), which requires that independent directors regularly have scheduled meetings at which only independent directors are present.

While Swiss law also requires that our board of directors elects an audit and finance committee from among its members, as a foreign private issuer, the independence of the members of such committee is determined by home country regulations and the conditions of Section 10B of the Securities Exchange Act, excluding any Nasdaq Listing Rules. Section 10B of the Securities Exchange Act also prescribes qualification requirements for the audit and finance committee. Swiss law also requires that we elect a compensation committee, we follow home country requirements with respect to such committee and our compensation, nomination and corporate governance committee is tasked with certain director nomination and governance responsibilities. As a result, our practice varies from the requirements of Nasdaq Listing Rule 5605(d), which sets forth certain requirements as to the responsibilities, composition and independence of compensation committees, and from the independent director oversight of director nominations requirements of Nasdaq Listing Rule 5605(e).

Furthermore, in accordance with Swiss law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. Our practice thus varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock. Our articles of association provide for an independent proxy holder elected by our shareholders, who may represent our shareholders at

a general meeting of shareholders, and we must provide shareholders with an agenda and other relevant documents for the general meeting of shareholders. Our practice varies from the requirement of Nasdaq Listing Rule 5620(b), which sets forth certain requirements regarding the solicitation of proxies. In addition, we have opted out of shareholder approval requirements for the issuance of securities in connection with certain events such as the acquisition of stock or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us, and certain private placements. To this extent, our practice varies from the requirements of Nasdaq Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

For an overview of our corporate governance principles, see "Item 16G. Corporate governance." As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

We may lose our foreign private issuer status, which would then require us to comply with the Exchange Act's domestic reporting regime and cause us to incur significant legal, accounting and other expenses.

We are a foreign private issuer and therefore we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. We may no longer be a foreign private issuer as of June 30, 2023 (or the end of our second fiscal quarter in any subsequent fiscal year), which would require us to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers as of January 1, 2024 (or the first day of the fiscal year immediately succeeding the end of such second quarter). In order to maintain our current status as a foreign private issuer, either (a) a majority of our common shares must be either directly or indirectly owned of record by non-residents of the U.S. or (b) (i) a majority of our executive officers or directors may not be U.S. citizens or residents, (ii) more than 50 percent of our assets cannot be located in the U.S. and (iii) our business must be administered principally outside the U.S.. If we lost this status, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and stock exchange rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time-consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common shares.

Our management is responsible for establishing and maintaining adequate internal controls over financial reporting. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud, among other objectives. Any failure to implement any required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or any testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting, which are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement.

Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our common shares could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional

financial and management resources. Furthermore, investor perceptions of our company may suffer if deficiencies are found, and this could cause a decline in the market price of our common shares. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results and harm our reputation. If we are unable to implement these requirements effectively or efficiently, it could harm our operations, financial reporting, or financial results and could result in an adverse opinion on our internal control over financial reporting from our independent registered public accounting firm.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, the price of our common shares and our trading volume could decline.

The trading market for our common shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. If no or too few securities or industry analysts cover our company, the trading price for our common shares would likely be negatively affected. In addition, if one or more of the analysts who cover us downgrade our common shares or publish inaccurate or unfavorable research about our business, the price of our common shares would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common shares could decrease, which might cause the price of our common shares and trading volume to decline.

We were likely a passive foreign investment company (PFIC) for our 2022 taxable year and we may be a PFIC for 2023 or future taxable years. If we are a PFIC for any taxable year during which a U.S. investor owns our common shares, the investor generally will be subject to adverse U.S. federal income tax consequences.

As discussed in our Annual Report on Form 20-F for 2019 and 2020, we were likely a PFIC for these years. We were also likely a PFIC for 2022.

Under the Internal Revenue Code of 1986, as amended (the "Code"), we will be a PFIC for any taxable year in which, after the application of certain look-through rules with respect to subsidiaries, either (i) 75% or more of our gross income consists of passive income (the "income test") or (ii) 50% or more of the average value of our assets (generally determined on a quarterly basis) consists of assets that produce, or are held for the production of, passive income (the "asset test"). Passive income generally includes dividends, interest, certain non-active rents and royalties, and gains from financial investments. Cash is generally a passive asset. Goodwill (the value of which may be determined by reference to the excess of the sum of a corporation's market capitalization and liabilities over the value of its assets) is generally an active asset to the extent attributable to business activities that produce active income. For purposes of the above calculations, we will be treated as if we hold our proportionate share of the assets of, and directly receive our proportionate share of the income of, any other corporation in which we directly or indirectly own at least 25% of the shares of such corporation by value.

We have not obtained valuations of our assets (including goodwill or going concern value) for 2022 and thus are not in a position to make a definitive determination regarding whether we were a PFIC for 2022. However, we believe that we were likely a PFIC for 2022 due to the decline and volatility of our market capitalization in 2022. If the value of our goodwill or going concern value is determined by reference to our market capitalization then we were a PFIC for 2022. For the same reason there is a significant risk that we will also be a PFIC for 2023, and possibly other taxable years. Because our PFIC status is a factual annual determination that can be determined only after the end of the relevant taxable year, we cannot express a view regarding our PFIC status for 2023 or any future taxable year.

In addition, the application of the income test to a company like us (whose overall losses from research and development activities significantly exceed its gross income) is not entirely clear. We will be a PFIC for any taxable year under the income test if 75% or more of our gross income (as determined for U.S. federal income tax purposes) for such year consists of interest and other passive income. Prior to the commercialization and sales of any of our product candidates, our gross income may consist primarily of upfront or milestone payments and grants (which we believe are likely to be treated as active income) and interest (which is passive income). The receipt of upfront payments is non-recurring in nature, and the receipt of grants or milestone payments is subject to various conditions. Therefore, there can be no assurance as to the amount of grants, milestone payments or upfront payments (if any) that we will receive for any taxable year. Moreover, we may earn income from sublicensing, which may be passive unless certain conditions are satisfied. There is no assurance that the Internal Revenue Service ("IRS") will not challenge the classification of any of

our income items for PFIC purposes for any taxable year. Accordingly, there is no assurance that we will not be a PFIC for any taxable year under the income test.

If we are a PFIC for any taxable year and a U.S. investor owns our common shares during any portion of that year, we will continue to be treated as a PFIC with respect to the U.S. investor, even if we are not a PFIC for any subsequent taxable year, unless the U.S. investor makes a "deemed sale" election with respect to our common shares.

U.S. investors that own our common shares during any taxable year in which we are (or were) a PFIC generally will be subject to adverse U.S. federal income tax consequences, including (i) the treatment of all or a portion of any gain on disposition of our common shares as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) the requirement to file certain reports to the IRS. We do not intend to provide the information that would enable investors to make a "qualified electing fund" election which, if available, could materially affect the U.S. federal income tax consequences if we are a PFIC for any taxable year.

For further discussion, see "Item 10. Additional information—Section E. Taxation."

ITEM 4. INFORMATION ON THE COMPANY

A. History and development of the company

We are a Swiss stock corporation (*société anonyme*) organized under the laws of Switzerland. We were formed as a Swiss limited liability company (*société à responsabilité limitée*) on February 13, 2003 with our registered office and domicile in Basel, Switzerland. We converted to a Swiss stock corporation (*société anonyme*) under the laws of Switzerland on August 25, 2003. Our Swiss enterprise identification number is CHE-109.878.825. Our domicile and registered office is in Ecublens, at the École Polytechnique Fédérale Lausanne (EPFL) Innovation Park Building B, 1015 Lausanne, Vaud, Switzerland. Our common shares were admitted to trading on Nasdaq Global Market on September 23, 2016, and trade under the symbol ACIU.

Our general telephone number is (41) 21 345 91 21 and our internet address is www.acimmune.com. References to our website address do not constitute incorporation by reference of the information contained on the website, and the information contained on the website is not part of this document or any other document that we file with or furnish to the SEC. The SEC maintains an internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, which can be found at http://www.sec.gov. Our agent for service of process in the United States is Cogency Global Inc. located at 122 East 42nd Street, 18th Floor, New York, New York 10168.

Our principal expenditures since January 1, 2020 have been our research and development expenses, as more fully described elsewhere in this Annual Report.

B. Business overview

AC Immune is a leading, clinical stage biopharmaceutical company advancing one of the broadest portfolios focused on pioneering Precision Medicine for neurodegenerative diseases. Our highly differentiated approach integrates novel therapeutics and diagnostics to overcome the fundamental challenge in this therapeutic area – the high number of co-pathologies driving disease development and progression and the urgent need for more tailored therapeutic regimens.

Leveraging our dual proprietary technology platforms, SupraAntigen and Morphomer, we have built a comprehensive pipeline of first-in-class or best-in-class candidates spanning multiple treatment modalities and targeting both established and emerging neurodegenerative pathologies. We are currently advancing 16 therapeutic and diagnostic programs, with seven currently in clinical trials, targeting five different types of misfolded pathological proteins related to Alzheimer's disease (AD), Parkinson's disease (PD) and other neurodegenerative disorders. Our pipeline assets are further validated by the multiple partnerships we have established with leading global pharmaceutical companies. We believe our clinically validated technology platforms and multi-target, multimodal approach position AC Immune to revolutionize the treatment paradigm for neurodegenerative disease by shifting it towards Precision Medicine and disease prevention.

Figure 1: AC Immune investment highlights

(1) As of December 31, 2022; excluding treasury shares; (2) As of December 31, 2022

Our Team

We have assembled an outstanding management team with relevant scientific, clinical and regulatory expertise. Our scientific founders, Jean-Marie Lehn, Claude Nicolau, and Fred van Leuven, are regarded as pioneers in their respective scientific domains, including in the study of AD. Our co-founder and Chief Executive Officer, Andrea Pfeifer, a Pharmacologist with a Ph.D. in cancer research and a former National Institute of Health researcher, has a 30-year track record in product innovation and implementation, and was formerly Head of Nestlé Global Research and the co-founder of Nestlé Venture Fund. Marie Kosco-Vilbois, our Chief Scientific Officer, brings more than 20 years of experience in various aspects of discovery research and drug development, including work on multiple drug development programs. Johannes Rolf Streffer, our Chief Medical Officer, is a Neurologist and Psychiatrist with extensive expertise in AD including biomolecular modalities such as PET, volumetric and functional MRI, genetics, cognition and cerebrospinal fluid (CSF) marker.

Unmet need in neurodegenerative diseases

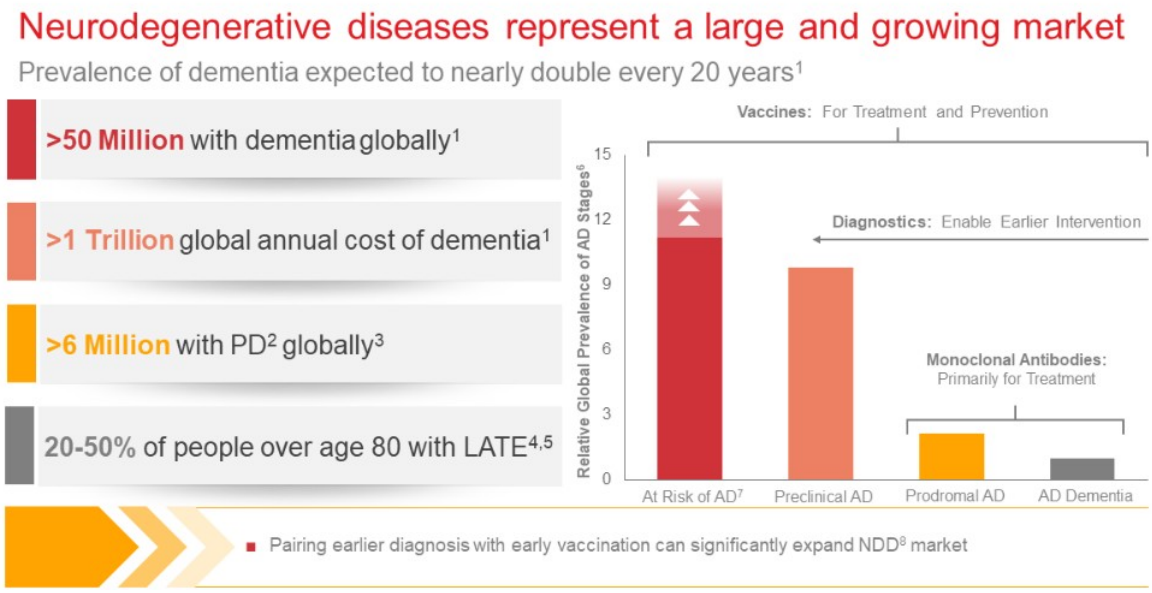
Neurodegenerative diseases, including dementias and motor disorders associated with protein misfolding, are prevalent, but there is currently an absence of reliable, early-stage diagnosis and disease-modifying treatments for these diseases. The growth in the number of people with neurodegenerative diseases has been significant, as evidenced by the prevalence of people affected by AD and PD, two of the most common neurodegenerative diseases.

- The World Health Organization recognizes dementia as a global public health priority**.** Worldwide, there is a new case of dementia every 3 seconds, with an estimated global patient population of greater than 50 million in 2020. This is predicted to increase to 139 million by 2050 (Alzheimer's Disease International).

- The estimated total healthcare costs for the treatment of Alzheimer's disease in the United States in 2022 is USD 321 billion per the Alzheimer's Association. The worldwide cost for dementia is expected to increase to

approximately USD 2.8 trillion annually by 2030 as the population ages (Alzheimer's Disease International). If the estimated global costs of dementia were a country, it would be the 14th largest economy in the world.

Figure 2: Neurodegenerative diseases represent a large and growing market



(1) Alzheimer's Disease International; (2) Parkinson's disease; (3) Michael J Fox Foundation; (4) Limbic-predominant age-related TDP-43 encephalopathy; (5) Nelson et al. Brain 2019; (6) Gustavsson et al. Alzheimer's Dement. 2022; 1- 13. https://doi.org/10.1002/alz.12694; (7) Alzheimer's disease; (8) Neurodegenerative disease

Diagnosis typically takes the form of observation of cognitive, functional and behavioral impairment and other symptoms of the diseases, which are generally only apparent after irreversible neuronal damage has already occurred. In the United States, through Q1 2023, there were seven approved therapies for AD, five addressing symptoms and two being disease-modifying treatments. These provided incomplete clinical efficacy, presented non-negligible safety risks and failed to halt disease progression. Despite these shortcomings, marketed therapies, such as Eisai and Pfizer's Aricept, have achieved peak annual global sales of approximately USD 2.4 billion prior to loss of exclusivity. Similarly, in the treatment of PD, the current standard of care is intended only to alleviate clinical symptoms.

In July 2022, the FDA accepted Eisai Co., Ltd.'s Biologics License Application (BLA) for lecanemab, an investigational anti-amyloid beta protofibril antibody for early AD that is partnered with Biogen Inc. In September 2022, Eisai and Biogen announced that lecanemab's confirmatory Phase 3 AD study met its primary endpoint. As a result, lecanemab was granted accelerated approval as a treatment for AD in the U.S. by the U.S. FDA on January 6, 2023. Eisai submitted a Supplemental BLA to the FDA for approval under the traditional pathway on the same day.

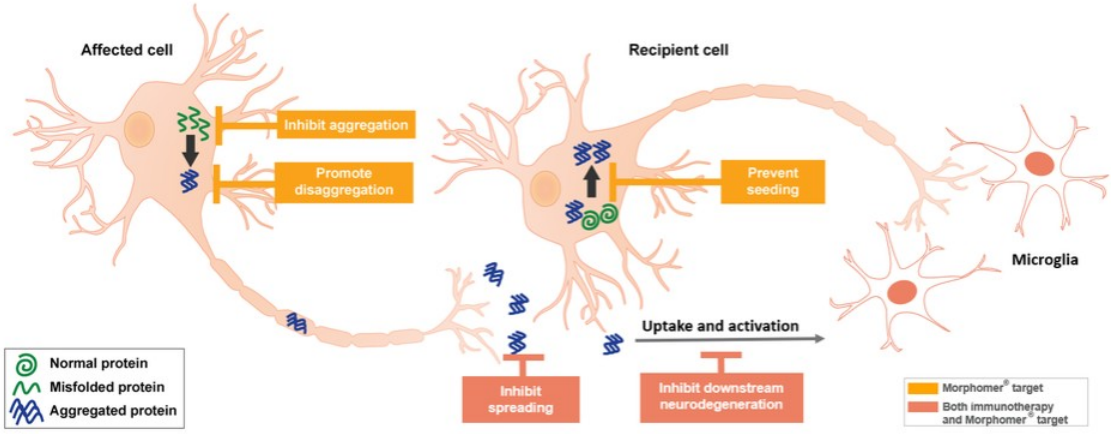
In Europe, Eisai submitted marketing authorization application to the EMA on January 9, 2023. In China, Eisai initiated submission of data for BLA to the National Medical Products Administration (NMPA) on December 23, 2022. On January 16, 2023, Eisai filed its marketing authorization application in Japan.

Neurodegenerative disease overview

Folding and unfolding of proteins are important ways of regulating the biological activity and cellular location of those proteins. Misfolding of proteins occurs due to a breakdown of cellular quality control systems and is a common feature of many neurodegenerative diseases. Misfolded proteins are unable to carry out their normal functions and aggregate to form insoluble deposits in the brain, which eventually lead to neuronal damage and cell death. The

progression of neurodegenerative diseases, such as AD and PD, is linked to the spread of misfolded, pathological protein aggregates throughout the brain. Figure 3 shows how misfolded proteins play a key role in the pathology of neurodegenerative diseases.

Figure 3: Misfolded proteins key impact on the pathology of neurodegenerative diseases



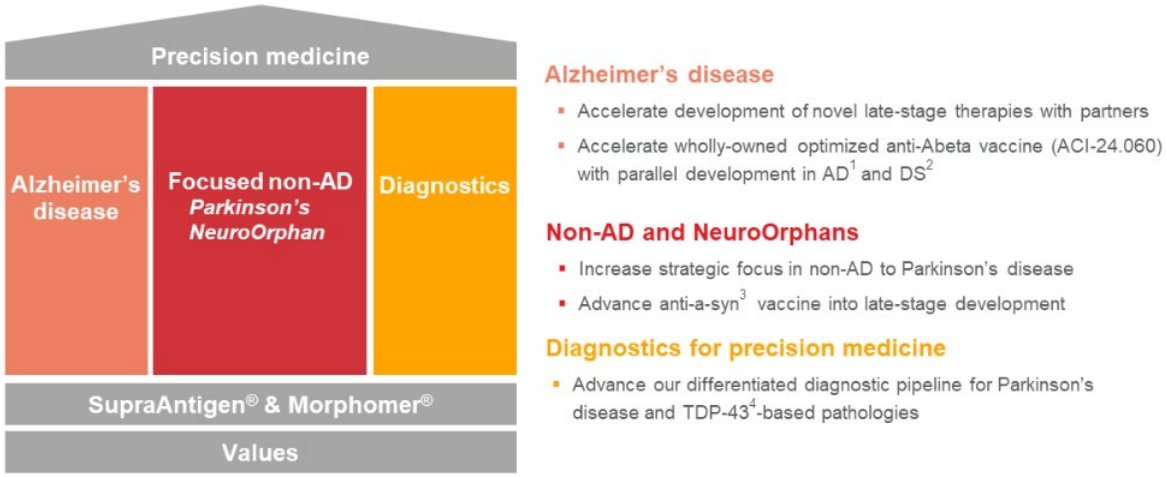
Typically, protein misfolding occurs in response to cellular stress, which can be triggered by many different, largely unknown, causes. A cascade of molecular events begins with the misfolding of single proteins within a cell, which then aggregate and ultimately form larger aggregates including plaques and tangles. These misfolded proteins are then exported or shed from dying neurons where they can spread to healthy cells nearby. Once inside, misfolded proteins can interact with normal proteins and cause them to misfold in a process known as “seeding,” leading to spreading of the disease pathology throughout the brain, increased neuronal death and a progressive decline in cognitive function.

The Figure above also shows how our therapies are designed to intervene and prevent key pathological steps in the progression of neurodegenerative diseases. They are designed to (i) prevent initial misfolding; (ii) promote disaggregation of misfolded proteins; (iii) inhibit spreading of pathological protein to healthy cells; (iv) prevent seeding of new misfolded protein aggregates inside healthy cells; and (v) inhibit downstream neurodegeneration. This robust approach to targeting neurodegenerative diseases is enabled by our two validated technology platforms, SupraAntigen and Morphomer, which generate highly specific biologics and small molecule inhibitors that can distinguish normal from misfolded proteins and inhibit key disease pathways both inside and outside of cells.

Our strategic vision

Our goal is to continue leveraging our proprietary discovery platforms, SupraAntigen and Morphomer, to shift the treatment paradigm for neurodegenerative disease towards Precision Medicine and disease prevention. We are executing a clear business strategy built on three pillars: (i) accelerate development of novel therapeutics in AD with our partners; (ii) expand our strategic focus in Parkinson’ disease (PD) and non-AD neurodegenerative diseases, including NeuroOrphan indications and limbic-predominant age-related TDP-43 encephalopathy (LATE); and (iii) a continued focus on diagnostics enabling Precision Medicine to be an ultimate differentiator for the Company.

Figure 4: AC Immune's three-pillar strategy



(1) Alzheimer's disease; (2) Down syndrome; (3) alpha-synuclein; (4) TAR DNA-binding protein 43

Our three-pillar execution strategy reflects our unique Precision Medicine approach, which ultimately creates differentiation due to our ability to address the high levels of co-pathologies present in AD and other neurodegenerative diseases. Much like cancer, neurodegenerative diseases are heterogeneous and may require multiple therapeutic interventions tailored to patients' specific disease drivers, to be used in combination in order to slow or stop the disease course. Ultimately, it is our belief that Precision Medicine will increase the chance of treatment success by enabling clinical trial participants to be better defined by their various proteinopathies, allowing for treatment with the right therapies at the right time.

AC Immune has established itself as a leader in developing Precision Medicines for neurodegenerative diseases by utilizing our diagnostic capabilities to enable improved diagnosis of co-pathologies, patient selection and assessment of clinical trial outcomes. Our dual technology platforms allow for a multi-modal approach encompassing a portfolio of vaccines, antibodies and small molecules tailored to the underlying pathology driving patients' disease. In addition to generating targeted monotherapies, this approach creates the potential for combination regimens, which may treat a broader spectrum of disease and offer greater efficacy.

Precision Medicine for neurodegenerative diseases

The development of therapeutics for neurodegenerative diseases is moving towards treating early-stage disease to delay or prevent progression by preserving neurological function before it is irretrievably lost. Therefore, early detection of neurodegenerative diseases will be critical to enhancing the effectiveness of both symptomatic and disease-modifying therapies.

This begins with a real challenge. The commonly used approach of taking a biopsy of the affected tissue to detect the corresponding pathology is not possible with diseases of the brain. Given these complexities, it becomes more important that we develop improved methods to fully characterize the underlying pathologies in different patients to ultimately provide better opportunities for therapeutic intervention at all stages of disease. Samples of blood or cerebrospinal fluid can be used to monitor biomarker levels indirectly but neither of these fluids provide exact anatomical information on where protein misfolding and aggregation occur.

At AC Immune, we have a strong track record in discovering highly sensitive and specific imaging agents to detect and quantify pathological proteins and their aggregated forms directly in patients' brains using PET scans. These agents

can provide critical information to confirm or exclude certain diagnoses and thus to determine which might be the most appropriate therapeutic strategy for a patient.

We are developing an integrated diagnostic and therapeutic strategy to deliver, for the first time, Precision Medicine for patients with neurodegenerative conditions. This will lead to a combination therapy approach to treat each patient's unique disease by addressing the right proteinopathy, in the right patient, at the right time.

Vaccines for Alzheimer's and Parkinson's disease

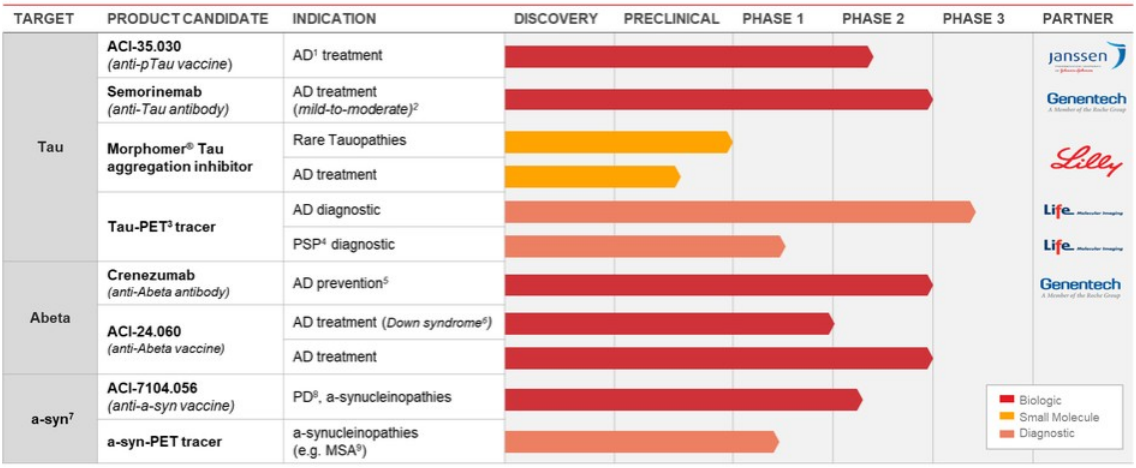
Consistent with this approach, we are progressing our vaccines targeting the hallmark proteins driving neurodegenerative diseases such as amyloid beta, Tau, and alpha-synuclein. Our clinical stage vaccine programs, ACI-35.030 (anti-pTau vaccine), ACI-24.060 (anti-Abeta vaccine) and ACI-7104.056 (anti-a-syn vaccine) have been shown to stimulate a patient's own immune system to produce antibodies directed specifically against the pathological species of these target proteins.

We believe that these antibodies will modify the course of disease by supporting clearance of toxic protein aggregates (as recent clinical data from certain monoclonal antibodies have shown), or by preventing their spreading and accumulation, thereby preserving neuronal health and function. Importantly, the use of vaccines over the longer-term and in people identified as "at risk" before symptomatic disease development will provide the rational, targeted approach consistent with our Precision Medicine strategy.

Key elements of our approach include:

1. Execution on advancing our product candidates, in partnership or alone, from clinical development to regulatory approval and potential commercialization

Figure 5: Our broad and robust clinical stage pipeline



(1) Alzheimer's disease; (2) Open label extension study is ongoing; (3) Positron emission tomography; (4) Progressive supranuclear palsy; (5) Prevention trial API-ADAD in Colombia; (6) Down syndrome-related Alzheimer's disease; (7) alpha-synuclein; (8) Parkinson's disease; (9) Multiple system atrophy

Our clinical stage product candidates include:

- ***ACI-35.030.*** AC Immune and Janssen Pharmaceuticals, Inc. (Janssen), part of the Janssen Pharmaceutical Companies of Johnson & Johnson, are evaluating the anti-phosphorylated-Tau (anti-pTau) vaccine candidate ACI-35.030 in a Phase 1b/2a study in subjects with early AD (NCT04445831). Interim results show that ACI-35.030 vaccination generated a strong antigen-specific antibody response against pTau in 100% of participants, achieving anti-pTau antibody levels of about two orders of magnitude higher than pre-vaccination levels, whereas anti-ePHF (enriched paired helical filaments) antibody titers increased by one order of magnitude from baseline as early as two weeks after the second injection at week 8 of the mid-dose of ACI-35.030. Based on these results, the second highest dose cohort was expanded in Q2 2021 to facilitate plans for further late-stage development. The safety and the tolerability have been good in the study, and so far the Data Safety Monitoring Board has always stated that the trial may continue without modification. Two serious adverse events (SAEs) (injection site rash and dizziness occurring on one occasion) were considered probably/possibly related to the study active immunotherapy while none of the other 6 SAEs that occurred in the study to date were considered to be possibly or probably related to the study active immunotherapy. ACI-35.030 specifically targets pathological pTau species and is eventually intended as a disease-modifying treatment for AD and other Tauopathies.

  In Q4 2022, it was announced that, based on the Phase 1b/2a interim data, ACI-35.030 had been selected for further development. New clinical data from the Phase 1b/2a trial showed that ACI-35.030 treatment rapidly leads to the strong and durable induction of antibodies specific for pathological forms of Tau such as pTau and its aggregated form, ePHF. The ACI-35.030-induced antibody response was sustained and could be periodically boosted over a period of 72 weeks. The decision to select ACI-35.030 follows the comparison demonstrating its strengths relative to an alternative anti-pTau protein conjugate vaccine, JACI-35.054.

- ***ACI-24.060 for AD and for AD in DS.*** The original formulation of our wholly owned anti-amyloid-beta vaccine candidate was shown to be safe and well tolerated along with preliminary evidence of immunogenicity and pharmacodynamic effects in patients with AD and in people with DS. Based on these results, the optimized formulation, ACI-24.060, which incorporates Abeta unrelated T-helper cell epitopes to increase the magnitude and the boost-ability of the antibody response, was advanced into the ABATE Phase 1b/2 trial.

  ABATE is a multicenter, adaptive, double-blind, randomized, placebo-controlled study designed to assess the safety, tolerability, immunogenicity, and pharmacodynamic effects of ACl-24.060 in subjects with prodromal AD and subsequently in adults with DS is ongoing. The CTA has been approved by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and by the Spanish Agency for Medicines and Health Products (AEMPS) with the first patient dosed in Q2 2022. AC Immune plans for an Investigational New Drug (IND) application in the USA in H1 2023 for the global development of the vaccine candidate.

- ***ACI-7104.056.*** The optimized formulation of the clinically-validated PD vaccine candidate PD01, will advance into an adaptive, biomarker-based Phase 2 study following the recent clearance of the CTA. This trial will evaluate an initial dose-response of ACI-7104.056 focusing on safety and immunogenicity against a-syn and pathological a-syn species. Additionally, the identification or verification of disease-specific biomarkers and progression of motor and non-motor symptoms of Parkinson's disease will be monitored, together with digital, imaging and fluid biomarkers, in the second part of the study. The trial initiation is anticipated in H1 2023.

- ***Semorinemab.*** Our collaboration partner, Genentech, a member of the Roche Group, is developing semorinemab for the treatment of AD. A Phase 2 study (Lauriet) conducted in patients with mild-to-moderate AD was completed in Q3 2021 and data showed a statistically significant reduction on one of two co-primary endpoints, ADAS-Cog11. The second co-primary endpoint, ADCS-ADL, and secondary endpoints were not met. Safety data showed that semorinemab is well tolerated with no unanticipated safety signals. At CTAD 2022, Genentech presented CSF and plasma biomarkers. These data confirmed peripheral target engagement

and reduction in CSF total Tau, pTau181 and pTau217, observed after semorinemab treatment but not with placebo. Genentech reported that the open label portion of the study will continue as planned and that further analyses are ongoing. Semorinemab is designed to slow the spreading of Tau pathology, which coincides with both clinical symptoms and disease progression in AD.

- ***Crenezumab.*** In August 2022, the Company provided an update on the Alzheimer's Prevention Initiative study evaluating crenezumab in autosomal dominant Alzheimer's disease, a specific genetic mutation which causes early-onset Alzheimer's disease. While numerical differences favoring crenezumab over placebo were observed across the co-primary, multiple secondary and exploratory endpoints, none of these effects were statistically significant. Initial data was presented at the Alzheimer's Association International Conference (AAIC) on August 2, 2022. Further plasma biomarker analyses presented at the CTAD 2022 conference further favored crenezumab over placebo. All participants in the study were offered up to one year of continued treatment (crenezumab for all carriers and placebo for all non-carrier) following the end of the double-blind period while primary results and additional analyses were pending. Final efficacy visits have begun.

- ***Morphomer Tau aggregation inhibitors.*** In collaboration with our partner, Lilly, we are researching and developing small molecule Tau aggregation inhibitors with plans to evaluate candidates in AD and NeuroOrphan tauopathies. We completed a Phase 1 clinical study in healthy volunteers with ACI-3024, in Q2 2020, which showed a dose-dependent exposure and brain penetration, achieving the desired levels of ACI-3024 in the CSF. Continued candidate characterization across the research program has also identified new and highly differentiated candidates with excellent cerebrospinal fluid exposure, selectivity for pathological aggregated Tau.

- ***PI-2620.*** PI-2620 is the Tau-PET imaging agent discovered during the collaboration of AC Immune and LMI. We are working with our partner, LMI, to advance PI-2620 as a highly differentiated, best-in-class Tau diagnostic for AD as well as non-AD Tauopathies such as progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD). Results have demonstrated PI-2620's differentiated characteristics as a diagnostic tool for studying Tau-related diseases. Results on the use of PI-2620 in AD patients from an investigator sponsored Phase 2 trial at the Asan Medical Center (NCT03903211) were presented at the 2022 AAIC. Following these, LMI moved PI-2620 into late-stage clinical development in AD and made a milestone payment. The first Alzheimer's patient in ADvance, the pivotal Phase 3 histopathology study in AD (NCT05641688) was imaged in January 2023.

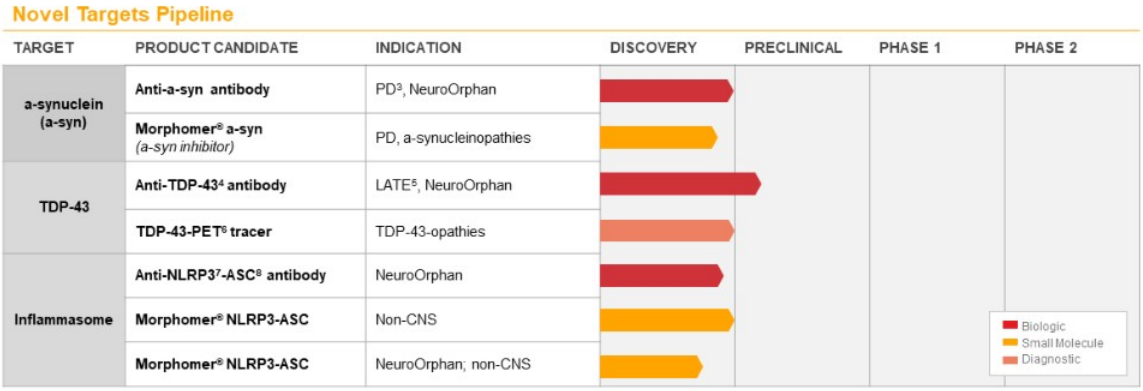
- ***ACI-12589.*** Our next-generation a-syn PET imaging tracer, derived from our Morphomer platform, has shown significant potential to reliably detect and map deposits of pathological alpha-synuclein protein in the brain. Supported by the Michael J. Fox Foundation for Parkinson's Research (MJFF), ACI-12589, our latest diagnostic imaging agent, completed a first-in-human study and an investigator-initiated study in 2022. The readouts of these trials in patients with PD, multiple system atrophy (MSA) and other synucleinopathies were reported at the AD/PD and AAIC 2022 conferences. These images provided the first clinical proof-of-concept for an a-syn PET tracer, as ACI-12589 clearly distinguished patients with MSA from those with other alpha-synucleinopathies and healthy controls. Moreover, our Morphomer platform is delivering additional candidates with improved binding properties and the potential to image a-syn pathology in patients with PD.

2. Expand product development into NeuroOrphan and additional neurodegenerative diseases

Beyond AD, we are pursuing additional neurodegenerative diseases such as Parkinson's disease (PD) and NeuroOrphan indications, specifically Tau-, a-syn- and TDP-43-driven diseases, such as FTLD-Tau (e.g., PSP, CBD, FTLD-MAPT), MSA, and ALS and FTLD-TDP, respectively. As part of this strategic move, AC Immune acquired certain a-syn assets from Affiris in 2021, gaining an advanced, clinical stage and validated a-syn vaccine candidate for development against PD in the process.

Pursuing NeuroOrphan indications may enable us to obtain a streamlined regulatory approval pathway and favorable reimbursement for any approved products. In addition, we are accelerating our novel therapeutic and diagnostic candidates targeting a-syn as a primary pathology in Parkinson's disease and other a-synucleinopathies. See below for a summary of our early-stage diversified novel targets pipeline including non-AD neurodegenerative diseases, with an in-house focus on NeuroOrphan indications.

Figure 6: Robust novel targets pipeline: diversification into non-AD[1] and non-CNS[2] diseases



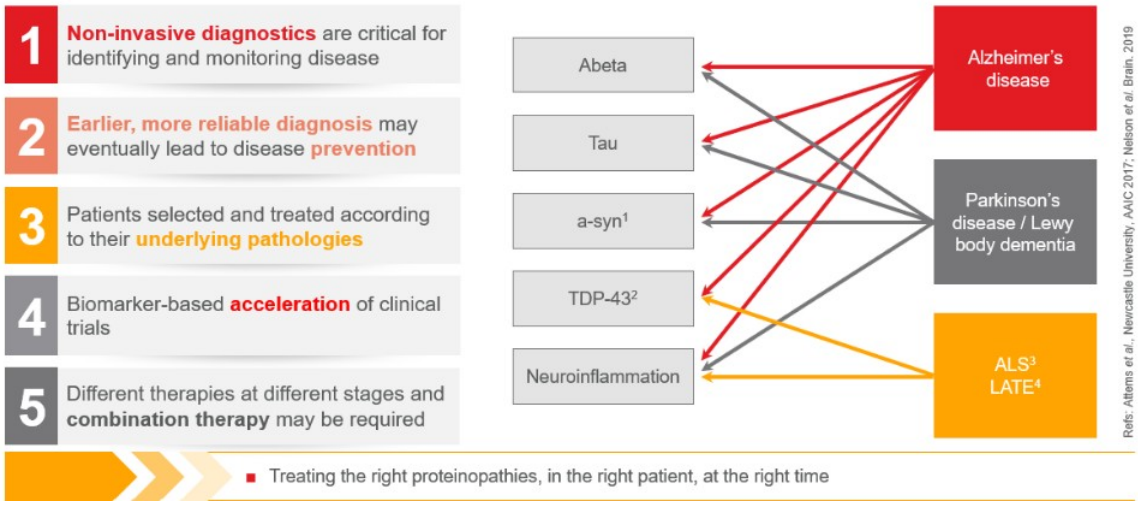
(1) Alzheimer's disease; (2) Central nervous system; (3) Parkinson's disease; (4) TAR DNA-binding protein 43; (5) Limbic-predominant age-related TDP-43 encephalopathy; (6) Positron emission tomography; (7) (NOD)-like receptor protein 3; (8) Apoptosis-associated speck-like protein containing a CARD, also PYCARD

3. Accelerating the advancement of our diagnostic portfolio

Early detection of neurodegenerative diseases may be critical to enhancing the effectiveness of both symptomatic and disease-modifying therapies. As a result, therapeutic development for AD increasingly focuses on treating early-stage disease to delay or prevent progression and to preserve the maximum amount of cognitive function before it is irreversibly lost. Most clinical studies now target mild or even preclinical stages of the disease increasing the need for accurate diagnosis that is independent of potentially subjective cognitive metrics. At least one study estimates that as many as one-third of patients in previous AD studies did not in fact have AD. Accurate and early diagnosis of AD is thus a substantial unmet market need, and diagnostic products will have a key role in generating a new treatment paradigm, including by selecting more uniform and stage-specific clinical study subjects, tracking patient progress and results,

managing patients who are receiving treatment, and ultimately diagnosing disease at its earliest stage for immediate treatment.

Figure 7: The need for Precision Medicine in AD: improved clinical trials, diagnosis and treatment of neurodegenerative diseases



(1) alpha-synuclein; (2) TAR DNA-binding protein 43; (3) Amyotrophic lateral sclerosis; (4) Limbic-predominant age-related TDP-43 encephalopathy

Refs: Attems *et al.*, Newcastle University, AAIC 2017; Nelson et al. Brain. 2019

We are developing a suite of diagnostics designed to be first-in-class or best-in-class, which will enable improved diagnosis of pathologies, patient selection and assessment of clinical trial outcomes. We currently have four diagnostic programs in our pipeline, developed using our proprietary technology platforms and targeting the therapeutic targets: Tau, a-syn and TDP-43.

Leveraging our Morphomer platform, we are developing proprietary PET imaging diagnostics for diseases resulting from the misfolding of a-syn and TDP-43 proteins. No such diagnostics are currently available for these important pathologies and AC Immune has identified promising compounds with high affinity and target specificity, as well as favorable central nervous system (CNS) pharmacokinetic properties. In 2020, the a-syn-PET tracer won the Ken Griffin Alpha-synuclein Imaging Competition from MJFF. In 2022, the Company received a continuation grant from the MJFF for this tracer.

Our novel TDP-43-PET tracer and our antibody-based immuno-assay for biofluid detection of TDP-43 also were awarded highly competitive grants from the EU Joint Programme – Neurodegenerative Disease Research' (JPND) in 2020, The Target ALS Foundation (Target ALS) in 2020 and 2022 and the MJFF in Q1 2023. Our diagnostics for a-syn and TDP-43, if validated clinically, could become the first in the world to effectively diagnose these proteinopathies, which are highly relevant for multiple neurodegenerative diseases.

4. Continuing to optimize our long-term growth by selectively partnering product candidates for global development and commercialization

We have a strong track record of establishing value-driving collaboration agreements with leading pharmaceutical companies, including two collaborations with Genentech, one with Janssen and one with Lilly. This strategy allows us to leverage our partners' scientific, development, manufacturing and commercialization expertise and other resources while

partially monetizing our investments, de-risking and accelerating the development of our product candidates. This strategy also enables us to use non-dilutive partnership revenue to bolster our investment into our early-stage proprietary programs and fuel our continued growth. We have five current collaboration agreements with leading global pharmaceutical companies, summarized in the table below:

Figure 8: External validation and cash generation through external collaborations[1]

	Product	Dev. phase	Total value[2]	Upfront[2]	Milestones received to date[2]	Royalties	Partners
Biologicals	Crenezumab (anti-Abeta antibody)	Phase 2	USD 340	USD 25	USD 40	Mid-single digits to mid-teens	Genentech
Biologicals	Semorinemab (anti-Tau antibody)	Phase 2	CHF 430	CHF 17	CHF 42	Mid-single digits to low-double digits	Genentech
Biologicals	ACI-35.030 (anti-pTau vaccine)	Phase 1b/2a	CHF 500	CHF 26	CHF 5	Low-double digits to mid-teens	janssen
Small molecules	Tau PET[3] imaging agent	Phase 3[4]	EUR 160	EUR 0.5	EUR 7	Mid-single digits to low-teens	Life Molecular Imaging
Small molecules	Tau Morphomer® small molecules	Phase 1[5]	CHF 1,860	CHF 80 +USD 50[6]	CHF 40	Low-double digits to mid-teens	Lilly
	Total (millions)[7]		**CHF ~3,311**	**CHF 155.2[8]**	**CHF 132.4**		

(1) Disclosure limited due to confidentiality agreements with collaboration partners; (2) In millions; (3) Positron emission tomography; (4) In Alzheimer's disease; (5) Phase 1 completed; (6) Equity investment; (7) Converted to CHF on date of receipt; (8) Excludes convertible note agreement of USD 50 million

For any additional product candidates targeting large markets, we may, if appropriate, selectively partner with leading companies that we believe can contribute development, manufacturing and marketing expertise, geographic reach and/or other resources that can enhance the value of our wholly-owned products. We will continue to seek to retain certain indications (e.g., NeuroOrphan) and/or geographies, such that we could begin to grow our own marketing capabilities as we develop AC Immune into a fully integrated pharmaceutical company.

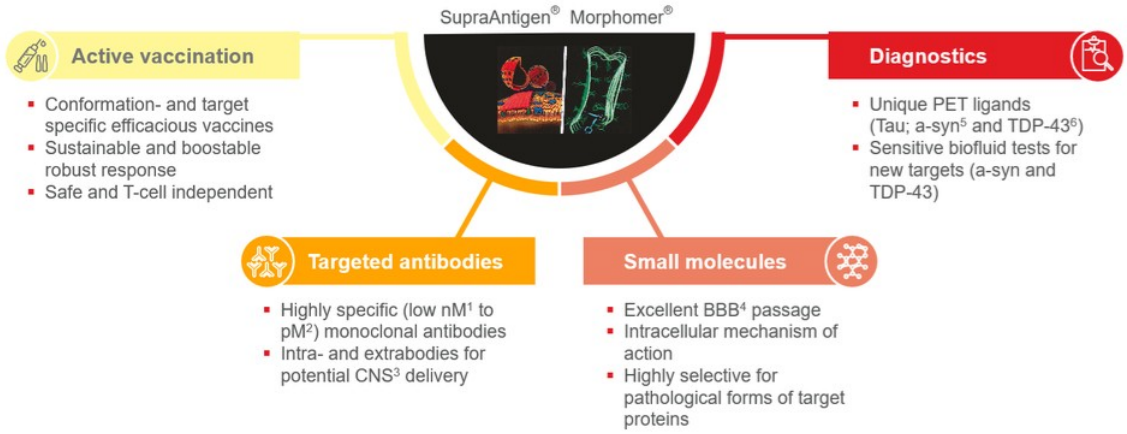
Additionally, in this respect, we established a strategic partnership with WuXi Biologics for its expertise in manufacturing biologicals in China and potential collaborations regarding AC Immune's SupraAntigen platform.

The benefits of our clinically-validated, proprietary technology platforms

The engines that drive our growth are our two unique proprietary and versatile technology platforms: our SupraAntigen platform, which is our biological and immunological platform, and our Morphomer platform, which is our chemical platform. These platforms generate biologics (vaccines and antibodies) and small molecules, respectively, which are designed to selectively interact with the misfolded proteins that are common in a broad range of neurodegenerative diseases. These clinically-validated platforms form the basis of our ongoing pipeline development and the value-driving strategic partnerships we have established to date.

The key aspect of both our SupraAntigen and Morphomer technology platforms is conformational specificity, which we believe is central to the development of effective and safe therapeutics for neurodegenerative diseases. Our SupraAntigen platform targets misfolded proteins through antigens displayed on the surface of liposomes, which mimic the targeted pathological form of the protein. In a complementary approach, our Morphomer platform uses small molecular weight compounds to target the aggregation and seeding process, which prevents the misfolded proteins from aggregating inside the cell and prevents the formation of new misfolded proteins in healthy neighboring cells through a seeding mechanism. Small molecules derived from our Morphomer platform, which we refer to as Morphomers, not only inhibit aggregation of pathological proteins, but also promote disaggregation of already formed aggregates, thereby potentially enhancing their therapeutic potential even in established disease states.

Figure 9: SupraAntigen and Morphomer platforms: an integrated approach to CNS-specific therapies



(1) Nanomolar; (2) Picomolar; (3) Central nervous system; (4) Blood-brain barrier; (5) alpha-synuclein; (6) TAR DNA-binding protein 43

The SupraAntigen platform was first developed by AC Immune's scientific co-founders to overcome a challenge common to neurodegenerative diseases: the lack of immunogenicity of disease-causing self-proteins. The SupraAntigen platform uses liposomes (small spherical vesicles formed by a lipid bilayer) to present specific antigens designed to evoke an immune response. SupraAntigen is used to generate conformation-specific antibodies for immunotherapy in neurodegenerative diseases. The overarching idea behind the platform is that antibodies, which are large in size, are well-suited to target extracellular proteins, interrupt spreading of pathological proteins, and break up and clear aggregates of misfolded proteins through phagocytosis.

AC Immune has acquired advanced mastery of the design and manipulation of liposomes to develop either passive or active immunization techniques to generate antibodies targeting neurodegenerative diseases. When pursuing active immunization approaches, we use liposomes carrying a specific antigen as a vaccine. After vaccination with a liposome, antigen and confirmation-specific antibodies are produced naturally by the host with very high affinity without further optimization. This immune response can be long-lasting and may be ideal to prevent the onset of a disease, as the immune system is now primed to rapidly identify disease-causing misfolded proteins.

Product candidates generated utilizing the SupraAntigen platform include vaccines (i) ACI-35.030, which has been selected for further development based on supporting data from the Phase 1b/2a in early AD, and (ii) ACI-24.060 ABATE Phase 1b/2, study in subjects with prodromal AD and subsequently in adults with DS. Additionally, antibodies include: crenezumab in Phase 2 for AD prevention and the preclinical candidates targeting a-syn and TDP-43 for PD and NeuroOrphan indications.

The Morphomer platform is designed to enable the development of small molecules (Morphomers) able to bind/interact with beta-sheets containing fibrillary aggregates from candidate selection through preclinical proof-of-concept. Morphomers can target pathological protein aggregates in any brain compartment and are equally well suited for therapeutic and diagnostic applications.

The first key component of the Morphomer platform is its library of rationally designed, CNS-optimized non-dye compounds. AC Immune's extensive know-how has enabled the identification of CNS compounds that penetrate the brain and demonstrate high selectivity for the target. This knowledge has been used to focus the Morphomer library to approximately 15,000 compounds that display these favorable characteristics, making this library an ideal starting point when developing molecules to target human proteinopathies of the CNS. Thus, rather than using the non-directed trial and error strategy of the typical drug development process, the Morphomer platform utilizes its bias for successful CNS candidates to improve efficiency and accelerate the early stages of the drug development process. Extensive expertise in

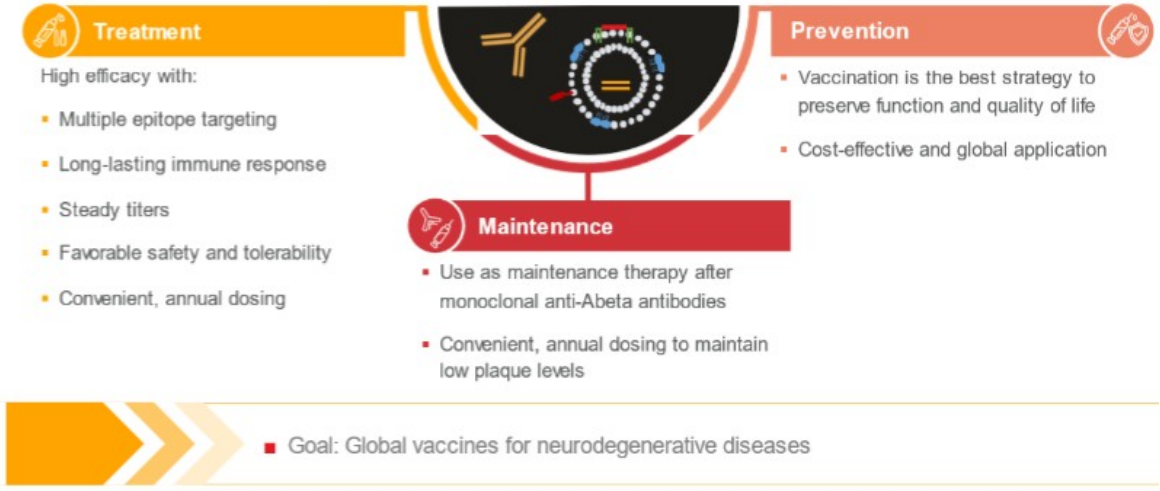
medicinal chemistry and a suite of proprietary assays developed to screen and validate candidate compounds enables AC Immune to rapidly optimize multiple, highly diversified lead compounds for further preclinical and clinical development.

Therapeutic product candidates generated by the Morphomer platform include our Morphomer Tau candidates, including ACI-3024. We also have Morphomer a-syn candidates and the diagnostic programs PI-2620 in Phase 3 and Phase 1 in AD and PSP, respectively, and ACI-12589 in a Phase 1 clinical trial in PD, MSA and other synucleinopathies. Finally, we also have TDP-43-PET imaging agents.

Shifting the current treatment paradigm for neurodegenerative diseases

Modifying the progression of the disease requires targeting the specific underlying biological processes that drive disease progression. Unfortunately, these processes evolve over the course of many years prior to manifestation of symptoms and a high percentage of neurons may be lost prior to clinical manifestation. Earlier intervention or prevention of the disease could have a major impact, but it requires accurate disease detection prior to developing symptoms. Due to recent advancement in biomarker research, people at risk of developing AD can be diagnosed 10-20 years before symptoms occur, opening a completely new market segment for the prevention of NDD when active vaccination will play an important role. This early, and potentially preventative, Precision Medicine approach may ultimately lead to better disease management for patients with neurodegenerative diseases.

Figure 10: Vaccines as a new class of treatment for neurodegenerative diseases



Given the inherent advantages of vaccines compared to monoclonal antibodies, we believe that our programs could have a profound global social and economic impact as a new class of therapy for neurogenerative diseases in various settings.

In regard to treatment, vaccines have potentially improved safety and efficacy profiles. By stimulating the patient's own immune system to produce antibodies, we believe tolerability would be enhanced by avoiding the need to introduce repeated large doses of externally manufactured antibodies. Additionally, due to their ability to target multiple epitopes with a long-lasting and consistent immune response, the polyclonal antibody response generated by a vaccine permits covering multiple pathological species of the targeted protein.

Vaccines are also much simpler to administer. They are amenable to convenient annual or biannual dosing whereas monoclonal antibodies require frequent intravenous infusions (up to twice per month). These dosing regimens position vaccines as an obvious solution for a maintenance therapy for patients who have previously achieved plaque clearance

with antibodies. This approach will reduce the burden for infusion centers and enhance access to a broader patient population.

In addition to these advantages, vaccines allow for more simplified distribution logistics and cost-effectiveness. These factors are crucial to enable their global application as preventative therapies. Given the irreversible nature of neuronal damage, earlier intervention, even before symptoms become visible, promises to be the best strategy to preserve patient function and quality of life.

Figure 11: Market opportunities targeting key primary and co-pathologies

Large Indications			
Indication	Alzheimer's disease	Parkinson's disease	LATE[5]
Prevalence	>5M in U.S.[1]	>6.1M globally[4]	20-50% of individuals over age 80[6]
Target	Tau, NLRP3[2]-ASC[3]	a-synuclein	TDP-43[7]

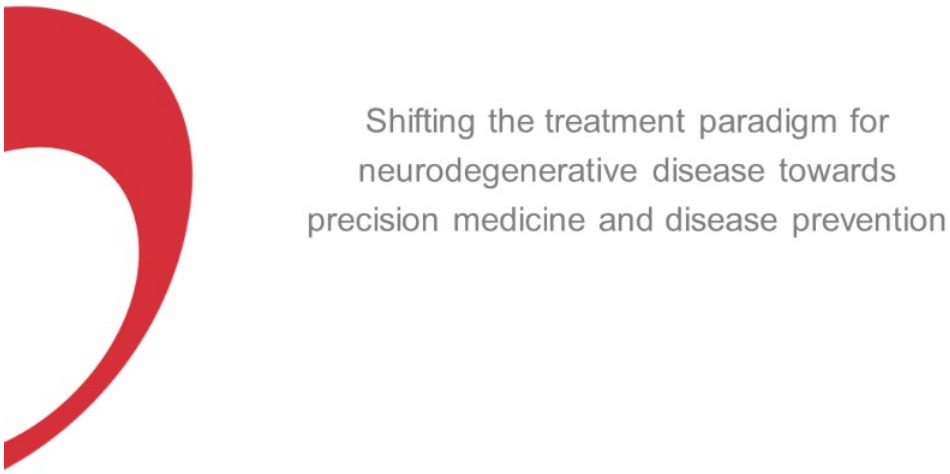
NeuroOrphan Indications				
Indication	Progressive Supranuclear Palsy	Multiple System Atrophy	Amyotrophic Lateral Sclerosis	Frontotemporal Lobar Degeneration
Prevalence	~20K in U.S.[8]	15-50 K in U.S.[9]	15-30K in U.S.[10,11]	20-30K in U.S.[12]
Target	Tau	a-synuclein	TDP-43	TDP-43

(1) Alzheimer's Association; (2) (NOD)-like receptor protein; (3) Apoptosis-associated speck-like protein containing a CARD, also PYCARD; (4) GBD 2016 Parkinson's Disease Collaborators *Lancet Neurology* 2018; (5) Limbic-predominant age-related TDP-43 encephalopathy; (6) Nelson et. al. *Brain* 2019; (7) TAR DNA-binding protein43; (8) National Institute of Neurological Disorders and Stroke (NINDS) Progressive Supranuclear Palsy Fact Sheet; (9) NINDS Multiple System Atrophy Fact Sheer; (10) ALS Association *Rare Disease* 2013; (199) NINDS Amyotrophic Lateral Sclerosis Fact Sheer; (12) Knopman and Roberts *J. Mol. Neurosci.* 2011

Due to the high level of co-pathologies involved in neurodegenerative diseases, future treatment paradigms may involve different combinations of disease modifiers at various stages of a disease. Therefore, combination therapies may include combinations of immunotherapies or combinations of small and large molecules targeting proteinopathies and neuroinflammation. Our therapeutic product candidates seek to modify the course of AD by intervening at an earlier stage of the disease progression, prior to irreversible neuronal damage. Beyond AD, we believe that we can leverage our proprietary platforms to generate and employ molecules that address the pathologies of other neurodegenerative diseases (See Figure above).

In support of shifting the current treatment paradigm from treatment to prevention, we are the leader in discovering new PET imaging agents to improve the timing and accuracy of diagnoses in neurodegenerative diseases. In our pipeline, we have three families of diagnostic candidates that were developed through our Morphomer platform, which target Tau, a-syn and TDP-43. We believe our Tau-PET imaging program has received external validation through our partnership with LMI, a leader in imaging agents, as well as from several investigator-sponsored trials. We are also developing a-syn and TDP-43 PET imaging agents for PD and other neurodegenerative diseases.

With our unique integrated approach focused on Precision Medicine, we believe that our diagnostic product candidate pipeline will complement our disease-modifying treatment product candidate pipeline and potentially reshape the clinical course and treatment of neurodegenerative diseases.



Our clinical programs

Anti-pTau vaccine

In collaboration with Janssen, we are advancing the anti-pTau vaccine program with ACI-35.030 that is directed against a key component of the pathology of AD: phosphorylated Tau proteins, found in Tau tangles. Developed using our SupraAntigen technology, our vaccine is designed to stimulate a patient's immune system to produce antibodies against misfolded and phosphorylated, pathological Tau protein, which aggregates to create the neurofibrillary tangles that characterize AD.

Potential advantages of Tau vaccination over other therapeutic approaches

ACI-35.030 Tau vaccine, which is able to induce a long-lasting and boost-able antibody response, has the potential to be even more advantageous in some aspects than other anti-Tau therapeutic modalities such as small molecules or monoclonal antibodies, which typically show much shorter half-lives *in vivo*, requiring more frequent administration. ACI-35.030 may thus offer a more cost effective and less burdensome approach for the treatment or prevention of Tau pathology, which may be particularly relevant for addressing slow-progressing chronic neurodegenerative Tauopathies such as AD.

Clinical development

ACI-35.030

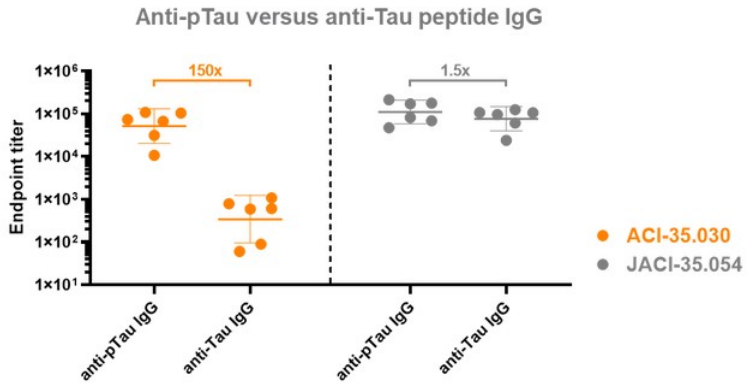
ACI-35.030 is an optimized liposomal anti-pTau vaccine formulation designed to elicit antibodies against extracellular pTau protein in order to prevent and reduce the spread and development of Tau pathology within the brain. In preclinical studies, ACI-35.030 showed that it retains the excellent non-clinical safety profile and the highly specific antibody response against pTau observed with the initial formulation, ACI-35, while demonstrating an enhanced and more uniform antibody response. We are developing ACI-35.030 with Janssen in accordance with our collaboration agreement.

Mechanism of action

- ACI-35.030 comprises a pTau peptide and a T-cell epitope capable of binding to human leukocyte antigen-major histocompatibility complex, class II (HLA-DR) molecules.

- In rhesus monkeys, ACI-35.030 induced IgG antibodies with a strong specificity towards the pTau peptide with a very low to absent binding to the non-pTau peptide (Figure 12). This is meaningful as Tau hyper-phosphorylation is considered an early event in the development of Tau pathology, occurring even several decades before the onset of Tau deposits.

Figure 12: pTau-specific IgG titers in Non-Human Primate (NHP) induced by ACI-35.030 and JACI-35.054



Ref: Kosco-Vilbois, CTAD 2022

- Sera from rhesus monkeys immunized with ACI-35.030 binds specifically to pathological Tau in brain sections with AD as compared to healthy human brain tissue (Kosco-Vilbois, KOL event 'Untangling' Tau Pathology to Treat Alzheimer's and Neurodegenerative Diseases NYC, Nov 2019)

- Epitope mapping analyses revealed that immunization of NHPs with ACI-35.030 induces a wide range of antibodies covering the pTau antigenic sequence (Kosco-Vilbois, CTAD 2022).

JACI-35.054

JACI-35.054 is an alternative pTau vaccine, which is developed with Janssen in accordance with our collaboration agreement. In preclinical studies, JACI-35.054 showed good safety, and induced a strong antibody response against pTau.

Mechanism of action

- JACI-35.054 is an alternative anti-pTau vaccine comprising a pTau peptide antigen conjugated to an immunogenic carrier protein CRM197, combined with adjuvants.

- CRM197 is a well-defined recombinant protein that is a commercially available version of a non-toxic mutant of diphtheria toxin (DT) A chain and has been shown to be a safe carrier protein in commercial prophylactic vaccines and clinical trials for a plethora of different vaccine candidates.

- Immunization of rhesus macaques with JACI-35.054 induces antibodies that bind to pathological Tau structures in human AD brain, and bind similarly to pTau and non-pTau peptides (Figure 12).

In Q4 2022, it was announced that, based on the Phase 1b/2a interim data, ACI-35.030 has been selected over JACI-35.054 for further development.

Clinical development

Phase 1b/2a study

The Phase 1b/2a study (NCT04445831) is a randomized, multicenter, double-blind, placebo-controlled clinical study with a primary objective to assess the safety, tolerability and immunogenicity of different dosages of ACI-35.030 and JACI-35.054 in participants with early AD. Secondary objectives assess additional immunogenicity parameters, while exploratory endpoints include notable biomarkers of progression of AD as well as clinical assessments. This Phase 1b/2a study evaluating ACI-35.030 and JACI-35.054 was initiated in Q3 2019 and is currently ongoing in Europe.

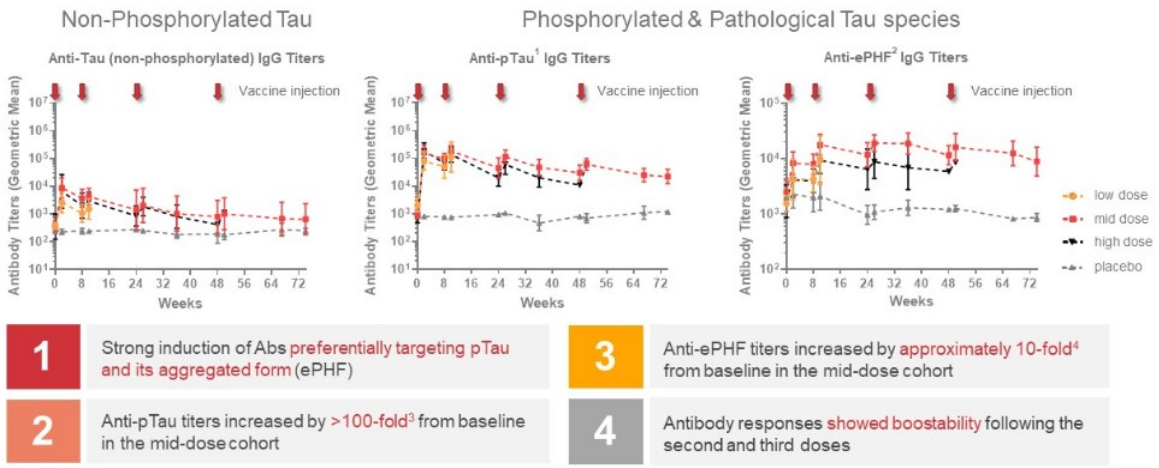
Safety

The recruitment has been completed in the Phase 1b/2a study where 57 subjects have been randomized, of which 41 subjects have been randomized into the Cohort 1 (low-, mid-, or high- dose levels of ACI-35.030 or placebo), and 16 subjects have been randomized into the Cohort 2 (low- or mid-dose levels of JACI-35.054 or placebo). The active/placebo ratio is 3:1 in each Cohort. To-date, eight SAEs have been reported in 6 out of total 57 participants in this study. Two SAEs (injection site rash and dizziness occurring on one occasion) were considered probably/possibly related to the study vaccine. None of the other SAEs were considered to be possibly or probably related to the study vaccine. These SAEs were acute diverticulitis, flare of diverticular disease/diverticulitis, left calf pain due to thrombosed popliteal aneurysm, popliteal aneurysm (both popliteal aneurysms occurred in the same participant), sick sinus syndrome, and lumbar disc prolapse. These SAE were observed in cohort 1 where subjects are receiving either ACI-35.030 or placebo, except the case of lumbar disc prolapse that was observed in cohort 2 where subjects are receiving either JACI-35.054 or placebo.

Antibody response (interim)

Based on interim results from all three dose-level sub-cohorts, in all patients after the first injection ACI-35.030 treatment led to the strong induction of antibodies specific for pathological forms of Tau such as pTau and its aggregated form, ePHF (Figure 13). Anti-pTau IgG titers increased by two orders of magnitude from baseline two weeks after the first injection of the mid-dose of ACI-35.030 and boostable following additional dosing at weeks 8, 24 and 48. Anti-ePHF IgG titers increased by approximately one order of magnitude from baseline as early as two weeks after the second injection at week 8 of the mid-dose of ACI-35.030. The anti-ePHF IgG response was high and boostable following additional dosing at weeks 8, 24 and 48, with a sustained response up to week 74. In contrast, the anti-Tau IgG response decreased from week 2 onwards. Together these data indicate that ACI-35.030 preferentially targets pathological Tau species over non-pathological Tau. Immunization with ACI-35.030 showed class-switching from IgM to IgG. Interim safety data further support ACI-35.030’s favorable safety and tolerability profile.

Figure 13: ACI-35.030: Potent antibody response with preference for pathological Tau
Fast, high, phospho-Tau-specific, and boostable antibody response

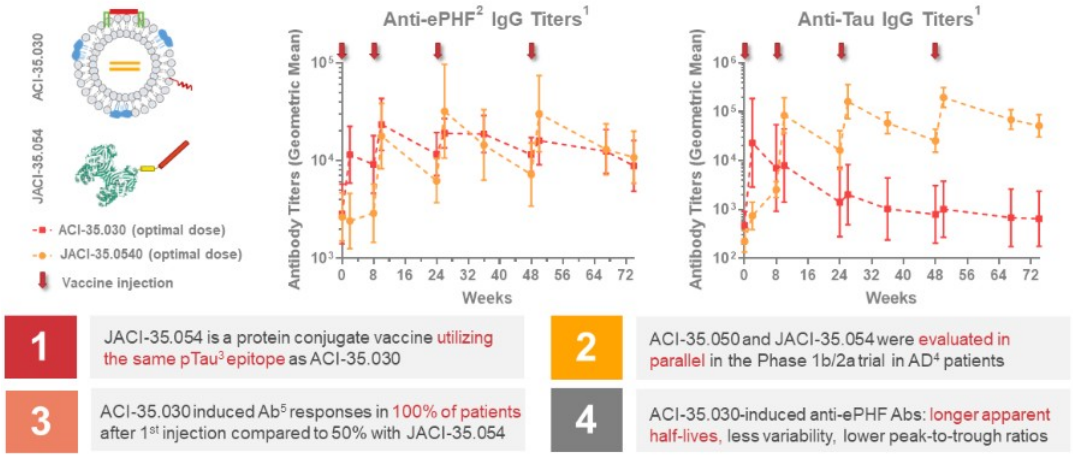


(1) phosphorylated Tau; (2) Enriched paired helical filaments; (3) at weeks 2 and 10; (4) at week 10

Ref: Streffer, CTAD 2022

High responder rates were observed after the first, and all following vaccinations, across all dose levels. A 100% response rate for pTau was observed at the mid-dose at all time points measured. A higher responder rate on ePHF was observed for the mid-dose compared to the high dose at all time points measured.

Figure 14: Comparison of the anti-Tau and anti-ePHF IgG antibody response profiles to ACI-35.030 and JACI-35.054



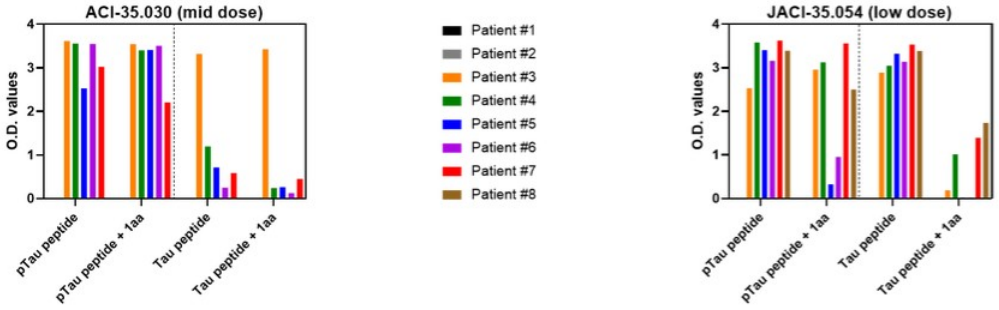
(1) ACI-35.030 original sub-cohort 1.2 data; (2) Enriched paired helical filaments; (3) phosphorylated Tau; (4) Alzheimer's disease; (5) Antibody

Ref: Streffer, CTAD 2022

As seen in the Figure above, the antibody response induced by ACI-35.030 mid-dose preferentially targets pathological Tau species (ePHF) over normal Tau, whereas the antibody response induced by JACI-35.054, a conjugate vaccine, targets both normal Tau and pathological Tau. ACI-35.030 induced anti-ePHF antibodies with longer apparent half-lives, less variability and lower peak-to-trough ratios than those induced by JACI-35.054. ACI-35.030 induced anti-ePHF antibodies in 100% of patients after 1st injection of ACI-35.030 compared to 50% with JACI-35.054.

Binding analyses show that the polyclonal antibodies induced by ACI-35.030 bind preferentially to pTau peptide without binding to the truncated C-terminal end of the peptide (see Figure below). In contrast, JACI-35.054 induces antibodies mostly binding to the very C-terminus of the peptide in a non-phospho specific manner. Together, these data indicate that the presentation of the B-cell peptide upon the surface of the liposomes in ACI-35.030 drives the antibody response towards pathological Tau species.

Figure 15: Mode of binding of antibodies induced by ACI-35.030 and JACI-35.054 towards pTau and Tau peptides



Ref: Streffer, CTAD 2022

The polyclonal sera from 7/8 subjects immunized with either ACI-35.030 (mid-dose) or Placebo, and from 8/8 subjects immunized with JACI-35.054 (low dose) or Placebo, were analyzed for their binding profiles to the pTau or Tau peptide, either without or including 1 additional amino acid (1aa) onto the C-terminal end of the peptide.

ACI-24.060

ACI-24.060 derives from an original AC Immune anti-amyloid-beta vaccine, ACI-24, that was assessed in patients with AD and in subjects with DS. As ACI-24 was shown to be safe and well tolerated with preliminary evidence of immunogenicity and pharmacodynamic effects in these two study populations, the optimized version ACI-24.060 was created. ACI-24.060 contains additional Abeta unrelated T-helper cell epitopes and has demonstrated similar safety and tolerability in NHPs with superior immunogenicity in mouse and NHP studies as compared to the original ACI-24.

The aim of the vaccine is to stimulate the patient's immune system to produce and maintain antibodies that bind and remove pathological Abeta with the goal to prevent plaque accumulation and enhance clearance of toxic Abeta species. The Company is pursuing clinical development of ACI-24.060 in early AD as well as the population of people living with DS exhibiting the presence of brain amyloid pathology.

ACI-24.060 is proprietarily owned.

Mechanism of Action

- ACI-24.060 consists of an immunogenic peptide (Pal1-15) containing the amino acid sequence 1-15 of the human Abeta1-42 protein, an antigenic peptide with Abeta unrelated T-helper cell epitopes and an adjuvant, formulated together as a liposomal suspension. In this formulation, the immunogenic peptide, Pal1-15, is presented to B cells of the immune cells on the surface of the liposomes in a conformational format mimicking the pathological form of the protein. This presentation optimally drives antigen-specific antibody responses that bind to the pathological forms of Abeta (i.e. oligomeric and pyroglutamate (pyroGlu) Abeta). The incorporation of the Abeta unrelated T-helper cell epitopes aims to prime, boost and maintain a strong anti-Abeta IgG response while preserving the well tolerated safety profile observed with the original formulation of ACI-24;

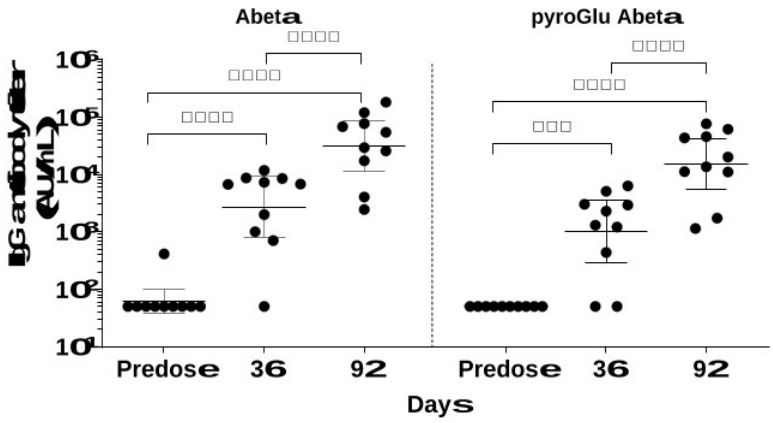
- In preclinical proof of concept studies in models of Abeta pathology, vaccination with the immunogen, Pal1-15 in the original ACI-24 formulation demonstrated anti-Abeta IgG titers with concomitant plaque reduction and restoration of memory;

- In preclinical safety studies, vaccination of NHPs with ACI-24.060 led to the anticipated enhanced anti-Abeta IgG titers (as compared to ACI-24) while maintaining with boosting effect the favorable safety profile, confirming the suitability to add the Abeta-unrelated T-helper cell epitopes to the vaccine;

- Furthermore, assessment of the kinetics and binding profile of the antibodies elicited by vaccination of NHPs with ACI-24.060 demonstrated enhanced antigen specific antibody titers with immunization as well as target binding to Abeta oligomers and pyroGlu Abeta (antibody titers against pyroGlu Abeta shown in the Figure 16);

- Target engagement was confirmed *in situ* using sections from AD patients in which sera from the NHPs vaccinated with ACI-24.060 bound to the Abeta plaques while showing no reactivity to other tissues.

Figure 16: Abeta1-42 and pyroGlu Abeta IgG titers in NHP vaccinated with ACI-24.060



Ref : Fiorini, AAIC 2022

ABATE Phase 1b/2

ABATE Phase 1b/2 study design

The ABATE clinical study (NCT05462106) is a multicenter, adaptive, placebo-controlled, dose-escalation, double-blind, randomized study containing two parts.

Study part 1:

Study part 1 is currently conducted in subjects with prodromal AD to assess the effect of study treatment (ACI-24.060 or placebo) administered over 48 weeks.

The study drug is being administered via intramuscular injections. Initially, a low dose of ACI-24.060 will be tested.

Randomized AD subjects receive five study drug injections (ACI-24.060 or placebo) at weeks 0, 4, 12, 24, and 48. For each study subject, the treatment period will be followed by a 26-week follow-up period.

Up to four cohorts may be included in study part 1. Each cohort will differ from the others in terms of the dose per injection and/or the administration regimen with the possibility to expand any cohort at any time point to better understand antibody response and/or safety and tolerability. The initiation of randomization in the subsequent cohort(s) will be based on interim safety and tolerability data review from the previous cohort(s) and Data and Safety Monitoring Board (DSMB) approval.

Interim analyses will be conducted in each cohort at different predefined study time points.

Study part 1 is conducted in several centers located in the UK and Europe.

Study part 2:

Study part 2 will be conducted in up to 80 non-demented adult subjects with DS and with confirmed presence of amyloid pathology by PET scan to assess the effect of study treatment (ACI-24.060 or placebo) administered over 74 weeks.

Randomized subjects with DS will receive their first five injections (ACI-24.060 or placebo) according to the same schedule administered in part 1, at weeks 0, 4, 12, 24, 48, plus an additional injection at week 74 in order to boost/maintain the response. For each study subject, the treatment period will be followed by a 26-week follow-up period.

Randomization in study part 2 will be initiated with a dose of ACI-24.060 that has been shown to be immunogenic, safe and well tolerated in AD subjects.

The dose level of ACI-24.060 may need to be adjusted in the DS study population based on immunogenicity and safety/tolerability data.

Interim analyses may be conducted at different predefined study time points, during the treatment period and during the follow-up period.

Study part 2 will be conducted in the UK, Europe and the U.S.

The Company’s CTA received approval from the UK MHRA in Q2 2022 and from the AEMPS in Q3 2022 to initiate development of the optimized formulation of ACI-24 in patients with prodromal AD and in adult subjects with DS with presence of brain amyloid pathology.

The first dosing in study part 1 occurred in Q2 2022.

ACI-24 development in AD in DS

The AD pathology that commonly develops in people with DS bears remarkable similarities to familial and sporadic forms of AD and is characterized by a progressive accumulation of brain Abeta amyloid plaques leading to the

appearance of AD-related cognitive decline and a modification of other relevant biomarkers. The Company is pioneering the development of its anti-amyloid-beta vaccine in AD patients and subjects with DS.

Individuals with DS have an extra copy of chromosome 21, which is where the gene for amyloid precursor protein (APP) resides. These individuals develop AD at a rate that is three to five times that of the general population and develop the disease at a much younger age. At autopsy, AD pathology has been reported in 80% of people with DS over the age of 40 and 100% over the age of 60 years. The prevalence of AD in people with DS is more than 50% over the age of 50 and 75–100% over the age of 60 years (Strydom, 2018). It is estimated that there are six million people with DS worldwide, with 250,000 in the U.S.. Preclinical results published by AC Immune in collaboration with Dr. Mobley of the University of California, San Diego in March 2016, showed, in a DS mouse model (Ts65Dn), a significant 20% memory improvement and a 27% reduction of Abeta in the brain following vaccination with ACI-DS-01, the mouse equivalent of ACI-24.

ACI-7104.056 – anti-a-syn vaccine

Neurodegenerative conditions with a-syn accumulation, such as PD, are increasingly linked to dementia and movement disorders in the aging population.

ACI-7104.056 is an optimized peptide-conjugate vaccine formulation designed to induce a-syn-specific antibodies recognizing aggregated a-syn species that have been demonstrated to be toxic to neurons. In contrast, ACI-7104.056-induced antibodies do not bind to the monomeric, physiological form of a-syn and do not cross-react with other members of the synuclein family such as beta- and gamma-synuclein.

A substantial package of preclinical and clinical data has been generated with PD01 (predecessor of ACI-7104.056). This candidate was tested in two different transgenic mouse models of PD and Dementia with Lewy bodies (DLB), the mThy1- and the PDGF-human a-syn transgenic mice. Active vaccination with PD01 resulted in decreased a-syn pathology in brain areas most affected by transgene overexpression, including the substantia nigra and the striatum. This decrease was accompanied by a reduced neurodegeneration in both *in vivo* models and by improvements in motor and memory deficits in the mThy1 and the PDGF-human a-syn transgenic mice, respectively.

PD01 was the first vaccine candidate against pathological a-syn to be tested in a clinical study involving patients with early PD. A series of Phase 1 studies were completed in June 2018. The start of the Phase 2 trial in early PD patients to evaluate ACI-7104.056 is scheduled to commence in H1 2023.

Mechanism of action

- ACI-7104.056 comprises a short engineered antigenic a-syn peptide. This peptide coupled to a carrier protein facilitates the induction of an a-syn-specific antibody response that binds to toxic aggregated a-syn species with high selectivity (Mandler-M *et al*., Acta Neuropathol. 2014).

- Vaccination of wild-type and transgenic mice, resulted in high antibody titres in plasma, which crossed into the cerebrospinal fluid (CSF) and recognized a-syn aggregates. Vaccination resulted in a decreased aggregation and accumulation of a-syn oligomers in brains of transgenic animals (Mandler-M *et al*., Acta Neuropathol. 2014).

- Clearance of a-syn was accompanied by reduced neurodegeneration in both *in vivo* models and by improvements in motor and memory deficits the mThy1 and the PDGF-human a-syn transgenic mice, respectively (Mandler-M *et al*., Acta Neuropathol. 2014).

Clinical development

Phase 1 study design

The safety, tolerability and immunogenicity of the ACI-7104.056 predecessor a-syn vaccine were studied over a three-and-a-half-year period in 24 early PD subjects and have been previously published (Volc *et al*., The Lancet

Neurology 2020). There were four consecutive studies in this group of patients, with patients randomized to receive a lower or higher dose of the alpha synuclein vaccine. After four priming doses, subjects were re-randomized to receive a booster injection at one of the two doses, followed by a second booster injection at the high dose.

Safety

This Phase 1 study series demonstrated a favorable long-term safety profile for PD01.

Antibody response

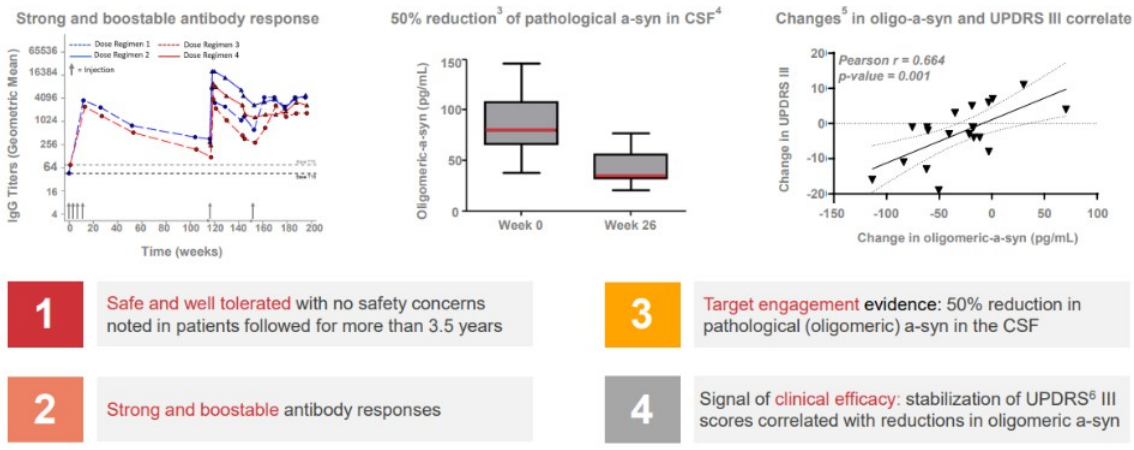
PD01 induced a long lasting and boostable antibody response (Figure 17, left). Such induced antibodies have been shown to bind preferentially the aggregated species of a-syn. The induced antibodies were also demonstrated to bind to a-syn aggregates in human PD and DLB brain tissue.

Pharmacological and clinical effect

Evidence for *in vivo* target engagement and signals for clinical efficacy have been observed in these Phase 1 studies in PD, as immunization was associated with a decrease in oligomeric a-syn in CSF of treated patients and with a stabilization of clinical scores as shown by the MDS-UPDRS part 3 scores (Volc *et al*., The Lancet Neurology, 2020). Post hoc analyses of this study series delivered highly encouraging data with respect to target engagement and identification of a potential biomarker for PD, including:

- *In vivo* target engagement of induced antibodies was demonstrated by lowering of oligomeric a-syn in CSF of vaccinated subjects (Figure 17, middle).
- A highly significant correlation between oligomeric a-syn concentration in CSF and MDS-UPDRS 3 score (motor-symptoms) in PD patients at baseline was shown for the first time.
- The reduction of oligomeric a-syn in CSF correlated significantly with clinical improvement, the changes in MDS-UPDRS 3 score over time (Figure 17, right).

Figure 17: Pharmacokinetic and pharmacodynamic effect of PD01 vaccination in early PD patients



(3) Data from 75 ug dose group; (4) Cerebrospinal fluid; (5) Change in oligomeric a-syn calculated at week 26, change in UPDRS III calculated at week 100; (6) Unified Parkinson's Disease Rating Scale

Ref: Volc *et al*., Lancet Neurology, 2020

These combined data provide a validation of the role of a-syn in disease progression and demonstrate that a-syn directed vaccination has the potential to positively impact clinical outcome. These data also provide an excellent basis for design of the planned Phase 2 study of ACI-7104.056.

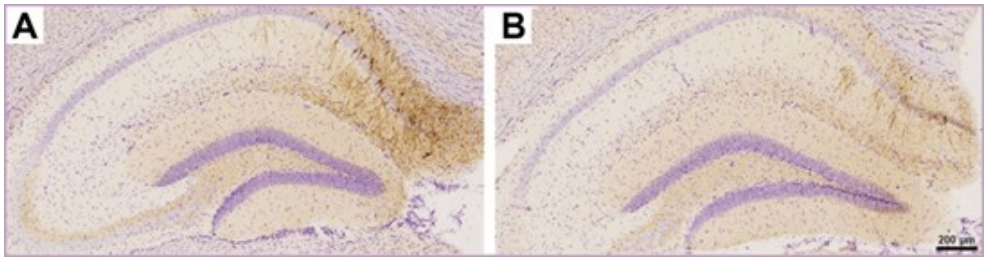
Semorinemab

Semorinemab is a humanized high-affinity IgG4 isotype antibody candidate that binds all forms of Tau. Semorinemab is designed to intercept extracellular Tau, stopping or slowing cell-to-cell spread and propagation of pathological Tau in the brain. Semorinemab is in Phase 2 clinical development for AD as part of an ongoing collaboration, which was established in 2012, with Genentech.

Lead characterization

Our anti-Tau monoclonal antibody program successfully generated multiple humanized antibodies for potential use as passive immunotherapies, which are highly specific for pathological forms of Tau found in AD and other Tauopathies. Results from preclinical studies demonstrated a reduction in pathological Tau and improvement of long-term spatial memory. Efficacy studies run in mouse models of AD and other Tauopathies exhibited dose–response alleviation of Tau pathology with behavioral improvements.

Figure 18: Alleviation of Tau pathology in models of AD



Representative images of hippocampal coronal sections from human Tau-P301L transgenic mice treated with **(A)** control antibody or **(B)** semorinemab, and immunostained for pathological Tau deposits

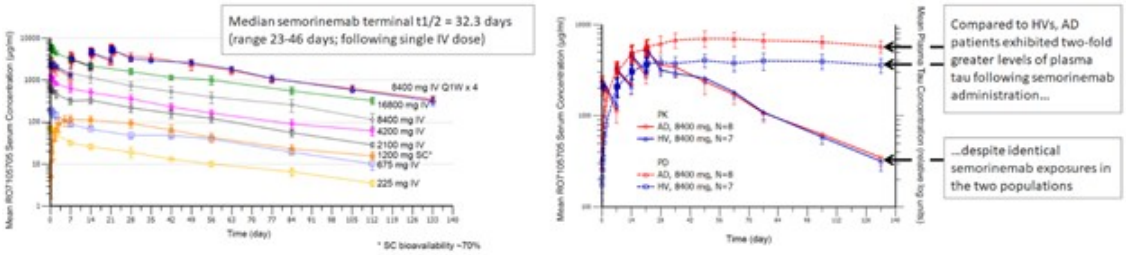
Ref: Ayalon *et al.,* Science Trans. Med., 2021

Clinical development

A Phase 1 clinical trial involving 75 subjects evaluated the safety, tolerability, pharmacokinetics and preliminary data on therapeutic activity of semorinemab in people with AD and in healthy volunteers. This trial was completed in the second quarter of 2017. Semorinemab was administered at single doses of up to 16,800 mg to healthy volunteers, and at multiple doses of 8,400 mg to healthy volunteers and patients with mild-to-moderate AD. No dose-limiting toxicities and no SAEs were observed. No participant withdrawals, modifications or interruptions due to an adverse event were reported. Results were presented at multiple conferences, including the 13th International Conference on Alzheimer's & Parkinson's Diseases and Related Neurological Disorders (AD/PD) in 2017, the AAIC in 2017, and the 10th international CTAD conference in 2017.

Semorinemab exhibited a dose-proportional pharmacokinetic profile and CNS exposure, with a median half-life of 32.3 days. Plasma total Tau concentration increased with increasing drug doses and was doubled in participants with AD compared with healthy volunteers, suggesting a pharmacodynamic signal as shown in the Figure below.

Figure 19: Phase 1 pharmacokinetic and plasma Tau results



Ref: Kerchner *et al.,* CTAD 2017

A Phase 2 clinical trial (Tauriel) commenced in Q4 2017 with the dosing of the first patient. This multicenter trial, which enrolled 457 participants, assessed the safety, tolerability and efficacy of semorinemab in people with prodromal-to-mild AD. Participants received one of three active doses or a placebo for 72 weeks, followed by a 96-week optional open-label extension (OLE). Primary endpoints included safety assessment and the composite functional and cognitive endpoint CDR-SB score.

In September 2020, the Company reported that Genentech informed us of top line results which showed that semorinemab did not meet its primary efficacy endpoint of reducing decline on CDR-SB compared to placebo. Two secondary endpoints, Alzheimer's Disease Assessment Scale-Cognitive Subscale 13 (ADAS-Cog13) and Alzheimer's Disease Cooperative Study Group – Activities of Daily Living Inventory (ADCS-ADL), were also not met. The primary safety endpoint was however met.

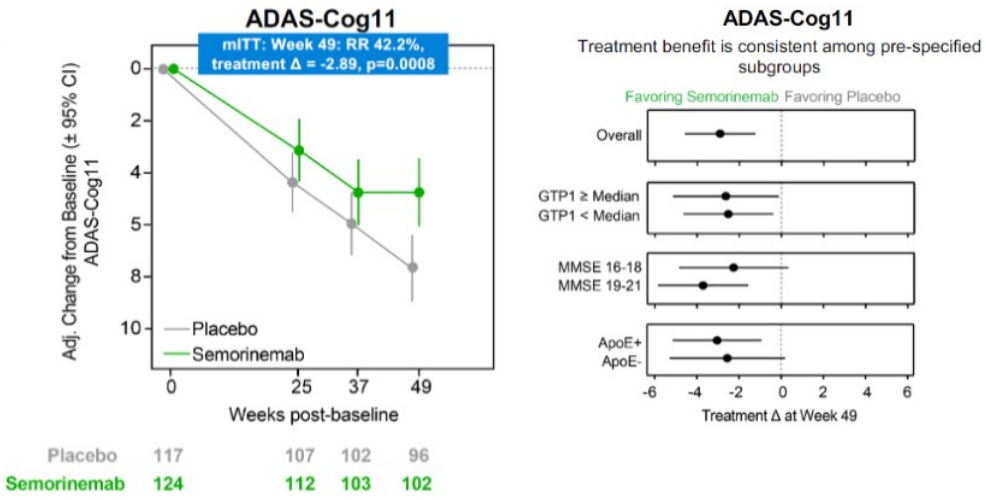
Further analyses revealed a dose-dependent increase in serum pharmacokinetics and evidence of target engagement, measured by an increase in plasma Tau levels, which is consistent with previous Phase 1 study results.

A second Phase 2 trial (Lauriet) was initiated in Q1 2019. This was a multicenter study enrolling 272 participants, and was designed to evaluate the clinical efficacy, safety, pharmacokinetics and pharmacodynamics of semorinemab in patients with moderate AD [Mini Mental State Examination (MMSE) 16–21, CDR-GS 1 or 2]. The study consisted of a screening period, a double-blind treatment period of 49 or 61 weeks, an optional OLE period, and a follow-up period, with the 11-item Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-Cog11) and Alzheimer's Disease Cooperative Study-Activities of Daily Living tools serving as the primary endpoints, and CDR-SB, MMSE and safety as secondary endpoints. Primary completion (last patient, last visit of the double-blind portion of the study) was in Q3 2021.

In August 2021 the Company reported that Genentech had informed the Company that the Lauriet study had met one of its co-primary endpoints, ADAS-Cog 11. The second co-primary endpoint, ADCS-ADL, was not met. Safety data showed that semorinemab was well tolerated with an acceptable safety profile and no unanticipated safety signals. In November 2021, the Company reported that Genentech had presented the full top-line data from the Lauriet study during a late-breaking session at the 14th Clinical Trials on Alzheimer's Disease conference.

272 subjects were randomized into the study and 267 dosed. 49 study centers participated in the U.S., France, Spain and Poland. In a modified intent to treat (mITT) population of all trial participants who had received at least one dose of study drug and had at least one post-baseline ADAS-Cog 11 assessment, there was a 42.2% slowing of cognitive decline compared to placebo, the result being highly statistically significant (p=0.0008).

Figure 20: Positive effect of semorinemab on cognition assessed by ADAS-Cog11

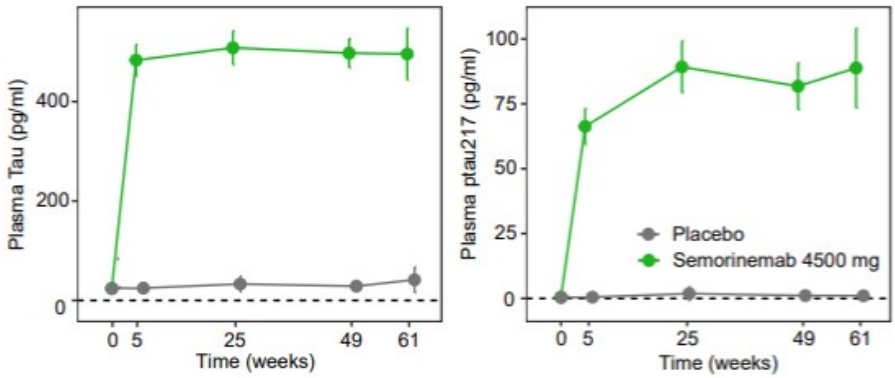


Ref: Monteiro *et al.*, CTAD 2021

The effect on ADAS-Cog 11 was consistently seen at around the same magnitude in subgroup analyses looking at subjects with higher or lower baseline severity assessed by MMSE, brain Tau load assessed by GTP1-PET and different ApoE genotypes. The effect on ADAS-Cog11 was driven by an effect on memory items in the scale. No changes were apparent in the reported functional measures including the co-primary endpoint ADCS-ADL, and the secondary endpoint, CDR-SB, and there was no significant effect in the other secondary endpoint, the MMSE. The reason for the lack of functional effects is unclear. Regular interim analyses in the ongoing extension study are being made to test for later effects on function.

Plasma Tau rose markedly during the study confirming peripheral target engagement, with serum levels of semorinemab in the expected range. The ratio of CSF to plasma semorinemab concentration was 0.29%, in the expected range for similar monoclonal antibodies (Figure 21).

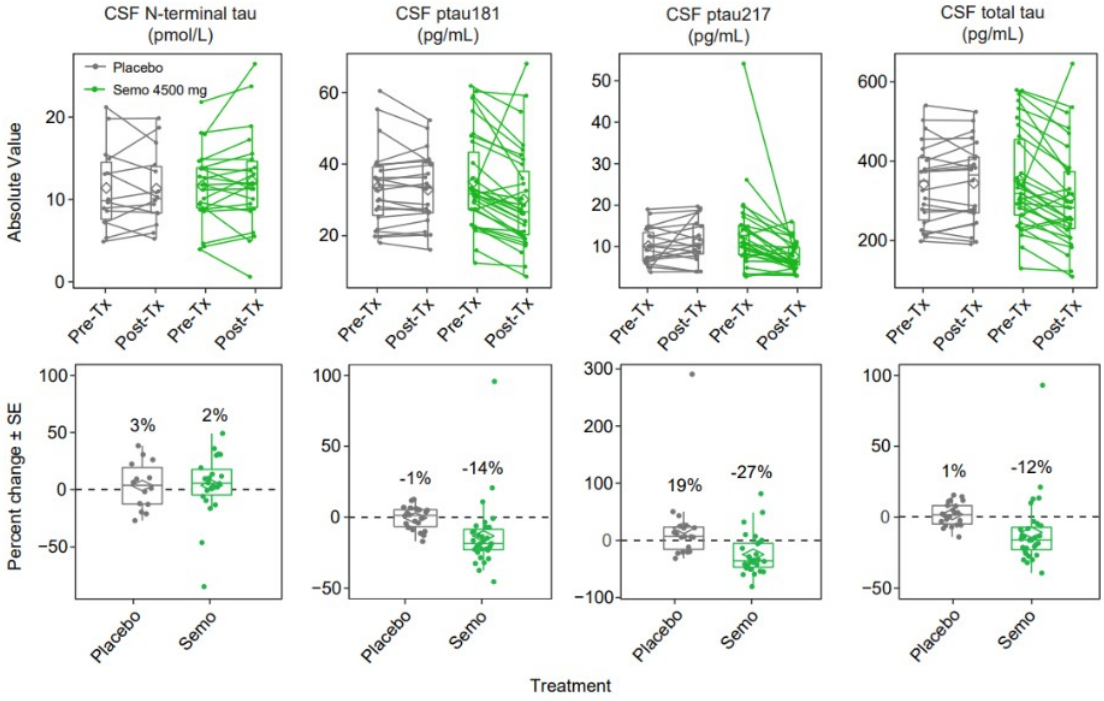
Figure 21: Plasma pharmacodynamics from all patients of the Lauriet study



Ref: Schauer *et al.*, CTAD 2022

There was no apparent effect on global or regional brain Tau load assessed by GTP-1 PET. However, CSF biomarker data were presented by Genentech at CTAD 2022 (Figure 22) and showed statistically significant reduction in pTau181, pTau217 and total Tau, but not N-terminal Tau. These results were similar to those observed in the Tauriel study.

Figure 22: CSF Tau pharmacodynamics pre- and post-treatment with semorinemab (at week 49 or week 61)



Ref: Schauer *et al.*, CTAD 2022

Safety data indicated that semorinemab was well tolerated, with no difference in the frequency of serious or non-serious adverse events or discontinuations due to adverse events. Infusion related reactions were more common in the semorinemab group compared to placebo (10.4% vs 3.8%, respectively). None were Grade 3 or higher (i.e. severe) in intensity.

Semorinemab's results provide the first positive cognitive results for an anti-Tau mAb therapy in AD.

Crenezumab

Crenezumab is a humanized, conformation-specific monoclonal antibody that targets misfolded Abeta and has a broad binding profile. Crenezumab was developed using our proprietary SupraAntigen platform. In 2006, we licensed crenezumab to Genentech, a company with a long history of developing and commercializing innovative biologics.

Mechanism of action

- Crenezumab binds to multiple forms of Abeta, particularly oligomeric forms, which it binds to with ten times higher affinity than to monomers. This is a desirable property since oligomeric forms of Abeta are believed to be principally responsible for neurotoxicity in AD.

- Crenezumab localizes to brain regions rich in oligomers, including the halo around plaques and hippocampal mossy fibers, but not to vascular Abeta (Maloney *et al.*, 2019).

- Crenezumab was designed with an IgG4 backbone to reduce effector function on microglia compared with an IgG1 backbone, and to clear Abeta from the brain while limiting inflammation by minimizing FcγR-mediated inflammatory activation of microglia (Adolfsson *et al*., J. Neurosci 2012).
- The potential for a better safety profile derived from a human IgG4 rather than a IgG1 backbone has been born out in practice by the safety findings from multiple Phase 1, 2 and 3 clinical studies of crenezumab, in which, following either single or multiple doses, no increase in ARIA-E was reported (Cummings et al., 2014 and Cummings et al., 2018).

- Due to its capacity to bind to multiple forms of Abeta, with 10-fold higher specificity for oligomers, which are thought to be the most toxic species, crenezumab also protects against oligomer-induced neurotoxicity.

- Linked to its unique epitope, crenezumab has been shown to promote disaggregation of existing Abeta aggregates and to disrupt their assembly, preventing amyloid plaque formation. The crystal structure reveals binding interactions that are consistent with this flexible binding profile and provides further explanation for crenezumab's ability to block aggregation and to promote disaggregation. (Adolfsson *et al.*, J. Neurosci 2012 and Ultsch *et al.*, Sci. Rep.,2016).

Summary of activity in patients with milder AD (MMSE 22–26) in Phase 2 clinical trials

- In the proof-of-concept Phase 2 studies of crenezumab, a positive trend in cognition was observed, with a greater effect on cognition in patients with a milder stage of AD (MMSE 22–26).

- In the ABBY cognition study, there was a statistically significant 35% reduction in the rate of cognitive decline in the non-pre-specified milder AD patient population (MMSE 22–26) for the high-dose arm.

- In the BLAZE biomarker study, the high-dose arm showed a consistent trend of reduced Abeta accumulation in the brain over time, as shown in two independent exploratory analyses of florbetapir-PET data. In addition, results have shown that crenezumab has the ability to enhance the removal of these proteins from the brain as evidenced by a significant increase in CSF Abeta, confirming target engagement by crenezumab.

Favorable safety profile allowing for higher dosing

- Phase 2 data from ABBY and BLAZE studies suggested that there were no imbalances in overall rate of AEs, and these were not dose-related, with only one case of asymptomatic ARIA-E (0.4% in ABBY, 0.3% on active pooled) in patients treated with crenezumab. AEs also included inflammation of the throat and nasal passages, urinary tract infections and upper respiratory infections. However, no patients in the studies experienced SAEs that were believed related to the administration of crenezumab.

- A Phase 1 study with higher doses of crenezumab up to 120 mg/kg showed good tolerability with no investigator assessed drug-related SAEs and no events of ARIA-E, supporting the dose of 60 mg/kg in the Phase 3 CREAD clinical trials.

- The good safety profile and lack of induction of ARIA-E was confirmed in the Phase 3 CREAD and CREAD 2 studies, as well as the API prevention study in which there was no increase in incidence of SAEs compared with placebo.

- As of 2019, two Phase 3 clinical trials, CREAD and CREAD 2, in patients with prodromal-to-mild AD were discontinued after an interim analysis of the CREAD study conducted by our collaboration partner Genentech (Ostrowitzki et al., JAMA Neurology 2022). Crenezumab has also been evaluated in a Phase 2 clinical

prevention trial in Colombia, which has enrolled 252 cognitively healthy individuals of whom 169 are genetically predisposed to develop early AD.

Clinic

Phase 2 studies

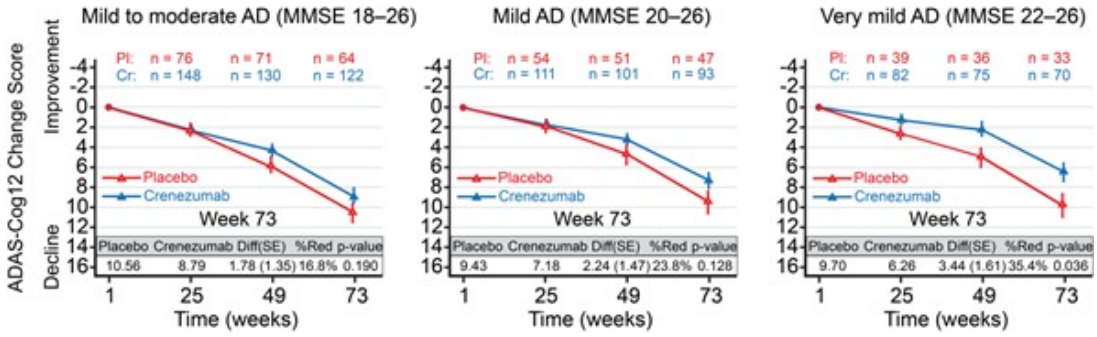
Phase 2 study design overview

Crenezumab has been studied in two Phase 2 clinical studies, the ABBY proof-of-concept study and the BLAZE biomarker study. These two studies enrolled a total of 522 patients. The purpose of these studies was to investigate whether crenezumab could delay cognitive and functional decline and reduce the accumulation of brain amyloid in patients with mild-to-moderate AD. The sample size of the studies was not expected to have adequate power to detect a modest but clinically significant difference between active medication and placebo at the 5% significance level (as is commonly the case in Phase 2 studies in AD). Instead, consistent trends across different endpoints and dose dependencies were considered indicators of a response in this learning phase of development, with confirmation to then be sought in Phase 3. Both studies had two active arms: a low-dose arm receiving 300 mg subcutaneous injection, every 2 weeks and a higher-dose arm receiving 15 mg/kg intravenously every 4 weeks. The primary analysis was conducted at 73 weeks, after 68 weeks of treatment. Safety and tolerability measures included repeated MRI scans to assess for the development of ARIA, both vasogenic edema (E) and hemorrhages (H).

ABBY study results

In the ABBY study, a positive trend in cognition was observed with a greater effect on cognition in patients with a milder stage of AD (MMSE 22–26), although the study did not meet its co-primary endpoints in patients with mild-to-moderate AD (MMSE 18–26). There was no significant change in cognition in patients who received low-dose subcutaneous crenezumab. Results of an exploratory analysis of the high-dose intravenous arm demonstrated that patients with the mildest cognitive impairment at screening (MMSE 22–26) showed a statistically significant 35% slowing of the rate of cognitive decline over 73 weeks. The effect became greater over time as shown by the increasing separation of the crenezumab (solid line) and placebo (dashed line) curves in the Figure below. The milder group was not pre-specified, meaning the group of patients with milder AD was not identified before commencing the Phase 2 clinical studies.

Figure 23: ABBY high-dose arm: Change in ADAS-Cog 12



Ref: Cummings *et al.*, AAIC 2014

An exploratory subanalysis in a non-pre-specified subgroup of patients with milder symptoms (MMSE 22–26) showed a 35.4% reduction in cognitive decline. The sample size of the study was not expected to have adequate power to detect a modest but clinically significant difference between active medication and placebo at the 5% significance level (as is commonly the case in Phase 2 studies in AD). Instead, consistent trends across different endpoints and dose

dependency are considered indicators of a response in this learning phase of development, with confirmation then sought in Phase 3. In the pre-specified subgroup analysis in patients with mild AD (MMSE 20–26), treatment with high-dose intravenous crenezumab led to a 23.8% reduction in cognitive decline. In patients with mild-to-moderate AD (MMSE 18–26) treated with high-dose intravenous crenezumab, there was a 16.8% reduction in cognitive decline. Effect sizes and p-values for exploratory analyses were not adjusted for multiplicity.

BLAZE study design

The BLAZE study was a randomized, double-blind, parallel-group, placebo-controlled study to evaluate the effects of crenezumab on brain amyloid burden as assessed by amyloid PET imaging and other biomarker endpoints in patients with mild-to-moderate AD. The primary endpoint was the change in brain amyloid load using florbetapir-PET. The terms "brain amyloid burden" and "brain amyloid load" refer to the total amount of amyloid deposited in the brain. In total, 91 patients were included in the study.

BLAZE study results

The primary endpoint of change in brain amyloid load by florbetapir-PET was not met, but the study was not powered to detect statistically significant results. However, positive trends were observed as shown below in exploratory analyses of the BLAZE amyloid PET results using a white matter reference region, which is considered a more sensitive approach for longitudinal studies. These analyses, conducted independently by two laboratories, the Banner Alzheimer's Institute and MNI Laboratories, produced analogous results, with a trend in the reduction of Abeta accumulation observed in the high-dose arm. As described below, a similar result was obtained in the Phase 3 studies.

The BLAZE biomarker study high-dose intravenous cohort showed a consistent trend of reduced Abeta accumulation in the brain over time as shown by two independent exploratory analyses of florbetapir-PET data. Using white matter rather than cerebellum as the key reference region in the brain is generally considered a more robust method of showing treatment effects of AD therapies.

In the BLAZE study, patients also showed a statistically significant increase in CSF $Abeta_{1–42}$, which we believe confirms target engagement by crenezumab. Similar results were observed in the ABBY study, which assessed CSF $Abeta_{1-42}$ level in 49 patients. These results suggest that Abeta is being eliminated from the brain when treated with crenezumab.

The BLAZE study results suggest that Abeta is being eliminated from the brain as patients showed a statistically significant increase in CSF $Abeta_{1–42}$, which confirms target engagement by crenezumab.

Safety data from ABBY and BLAZE studies

Crenezumab demonstrated favorable safety and tolerability in Phase 2 clinical studies even at high doses. Crenezumab's safety profile is especially reflected in a low incidence of ARIA-E (0.3%) in Phase 2 clinical studies. ARIA-E was observed in only one patient who received high-dose intravenous crenezumab in the ABBY study. No case of ARIA-E was reported in the placebo arm or the BLAZE study. Favorable pharmacokinetic properties coupled with a favorable safety and tolerability profile enables crenezumab to penetrate the brain more readily at therapeutically relevant doses. As dose-limiting toxicities are a potential reason for the failure of other antibodies to demonstrate efficacy, crenezumab's potential safety at high doses is a distinguishing product feature.

At AAIC in 2014, it was reported that in the combined Phase 2 study populations, SAEs occurred at similar rates in patients treated with crenezumab (16.5%) and in patients given a placebo (11.9%).

Phase 1b study to explore higher doses

To explore safety at higher doses, crenezumab was tested in a Phase 1b dose-escalation clinical study (NCT02353598) conducted in the U.S.. This randomized, placebo-controlled, double-blind, four parallel-arm study evaluated the safety and tolerability of at least four doses of intravenous crenezumab in 77 patients with mild-to-

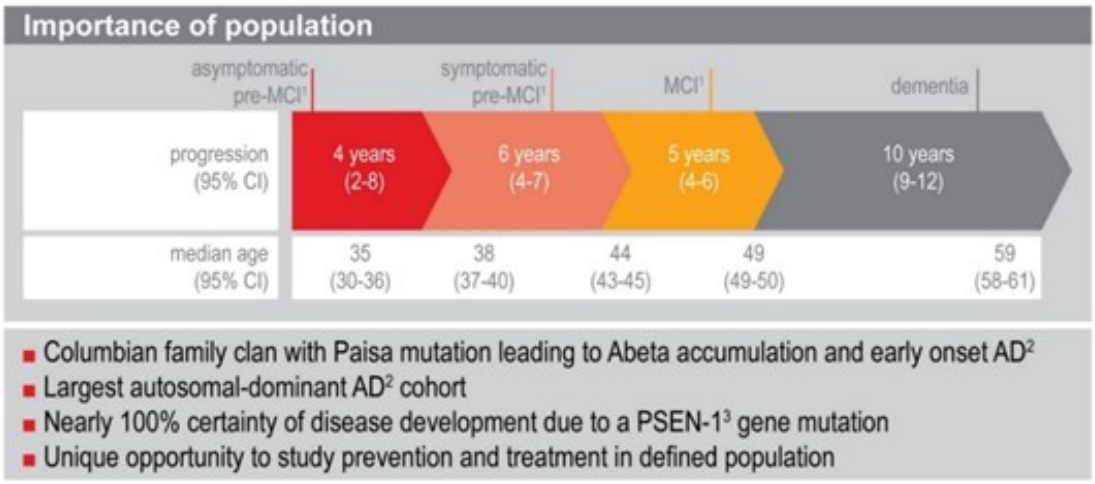
moderate AD (MMSE 18–28) between the ages of 50 and 90 years. An optional OLE stage was offered to patients after completion of the double-blind stage of the study. At the 2017 AAIC meeting, Genentech presented the results of the four cohorts with mild-to-moderate AD. No dose-limiting toxicities were observed at crenezumab doses of 30, 45, 60 and 120 mg/kg. No events of ARIA-E were observed and only few patients (6 of 75) showed asymptomatic ARIA-H. The pharmacokinetic profile of crenezumab was dose-proportional up to the 120 mg/kg dose, with the 60mg/kg dose being selected for the Phase 3 CREAD and CREAD 2 studies.

Phase 2 AD prevention study

There is increasing understanding from studies in patients at risk of AD due to genetic mutations that the accumulation of Abeta in the brain is a very early event in the condition, starting approximately 25 years before symptoms develop (McDade *et al.* 2018). To treat the underlying amyloid pathology effectively it may therefore be necessary to use anti-amyloid therapies in a preventive mode, starting in patients in whom symptoms have not yet emerged.

In 2012, crenezumab was independently selected from among 25 product candidates for use in the first-ever AD prevention study of its kind. The study, a collaboration worth USD 100 million between the NIH, Banner Alzheimer's Institute and Genentech, is the cornerstone of the global Alzheimer's Prevention Initiative (API). Family members usually develop symptoms before the 45 years of age. 252 subjects were enrolled.

Figure 24: Crenezumab AD prevention trial (Alzheimer's Prevention Initiative AD/AD): unique population to study prevention treatment



(1) Mild cognitive impairment; (2) Alzheimer's disease; (3) Presenilin-1

Ref: McDade et al., Neurology, 2018

169 carriers of the PSEN1 E280A mutation, who did not have mild cognitive impairment or dementia, were randomized to receive crenezumab (85 subjects) or placebo (84 subjects). A separate group of non-carriers (83 subjects) received a placebo. The mean age of the mutation carriers was 37 years old. This was approximately seven years before the median age for development of mild cognitive impairment.

Subjects were followed under treatment for 5-8 years, with the double-blind treatment continuing until the last subject received treatment for 5 years.

Primary endpoints were the annualized rate of change in the API autosomal dominant AD (ADAD) composite score and the Free and Cued Selective Reminding Test Cueing Index (FCRST). The latter scale was promoted to a coprimary endpoint after a blinded interim analysis had indicated less decline than expected on the composite endpoint.

Numerical differences favoring crenezumab were observed consistently across a wide range of clinical and biomarker endpoints. Plasma Abeta40 and Abeta42 rose throughout the study indicating peripheral target engagement. Only a small difference favoring crenezumab was observed in amyloid PET scan measures of fibrillary amyloid. Numerical differences favoring crenezumab compared to placebo were seen for clinical scales including both the two primary endpoints (i.e. API ADAD composite score, FCRST). Results did not reach statistical significance. However, the power to detect differences with statistical significance was low due to the lower and more variable rate of decline observed compared to that predicted at the start of the study. This effect may have been related to the younger and earlier stage of the condition in the subjects recruited compared to the population in the natural history study used to power the study.

Numerical changes favoring crenezumab were also seen for the secondary endpoints including time to MCI/dementia due to AD, CDR-SB, time to non-zero score on CDR Global Score and RBANS total score. Similarly, numerical differences favoring crenezumab were seen across all reported biomarkers including Tau and FDG measures, CSF biomarkers, including pTau 181 and t-Tau, NfL and plasma pTau 181, pTau217, NfL, GFAP, YKL-40 and sTREM2. Only plasma GFAP reached statistical significance (p=0.04, not corrected for multiplicity).

The dose of crenezumab was raised seven-fold during the study in response to emerging data from Phase 2 that higher doses may be more effective. The initial dose of 300mg subcutaneously injected every two weeks was increased to a maximum dose of 60mg/kg injected intravenously once monthly. On average, subjects were exposed to intravenous dosing for less than half of the treatment period.

Tolerability was good, with low rates of ARIA, no instances of ARIA-E and no macrohemorrhages. All mutation carriers may continue to receive crenezumab while the data are further analyzed.

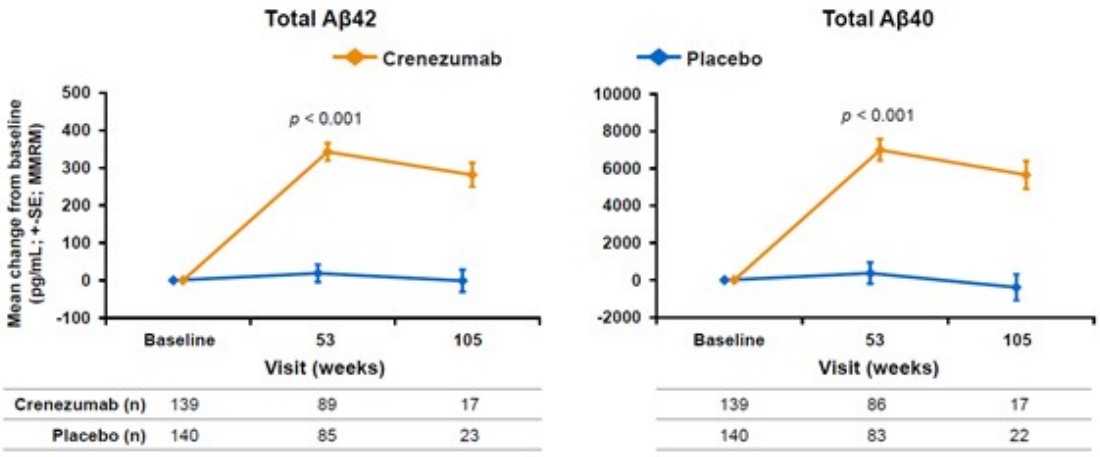
Phase 3 studies (CREAD and CREAD 2)

The randomized, double-blind, placebo-controlled, parallel-group Phase 3 CREAD study enrolled about 750 participants with prodromal or mild AD at the age of 50−85 years. A high dose of crenezumab (60 mg/kg) was administered intravenously once every 4 weeks for 100 weeks. The primary outcome measure was the change from baseline to week 105 in CDR-SB score. An exposure–response model to evaluate the best dose of crenezumab for the treatment of AD was established, which predicted an improved outcome of the Phase 3 CREAD study by using the higher dose of 60 mg/kg relative to the Phase 2 trials (Polhamus *et al.*, CTAD 2016).

In January 2019, we announced that Roche, the parent company of our collaboration partner, is discontinuing the CREAD and CREAD 2 (BN29552 and BN29553) Phase 3 studies of crenezumab in people with prodromal-to-mild sporadic AD. The decision came after an interim analysis of the first CREAD study conducted by the IDMC, which indicated that crenezumab was unlikely to meet its primary endpoint of change from baseline in CDR-SB score.

As presented at CTAD 2019, target engagement was observed with increases in levels of $Abeta_{1–42}$ in blood and CSF. As shown in the Figure below, the number of subjects available for analysis fell significantly after the baseline. Due to the early termination of the studies, data at the 2-year time point was only available for 17 of the 139 crenezumab subjects in whom CSF Abeta was analyzed at baseline.

Figure 25: CSF total Abeta42 and total Abeta change from baseline, pooled CREAD/CREAD2 results

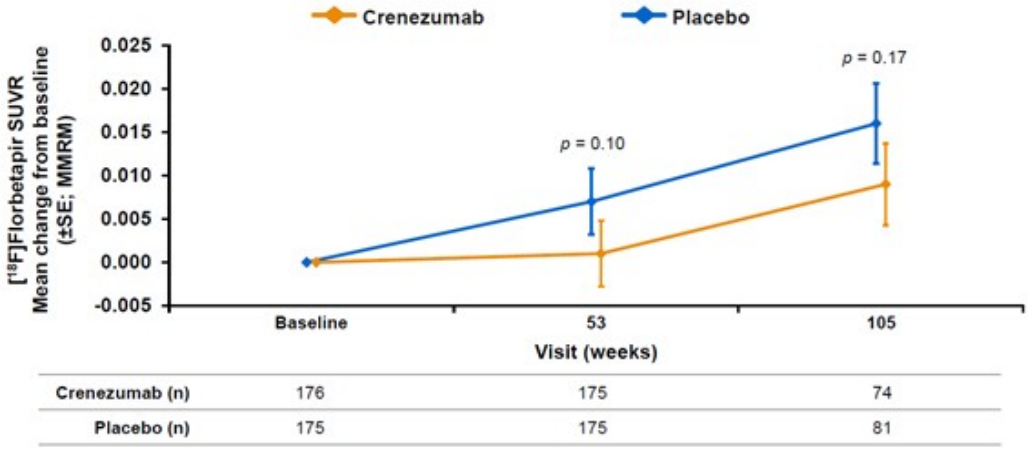


Crenezumab (n)	139	89	17
Placebo (n)	140	85	23
	139	86	17
	140	83	22

Ref: Bittner *et al.,* CTAD 2019

Reduced accumulation of Abeta in the brain on florebetapir amyloid PET scans was observed, with a pattern very similar to that observed in the Phase 2 BLAZE studies.

Figure 26: [18F] Florbetapir amyloid PET standard uptake value ratio (SUVR) change from baseline, pooled CREAD/CREAD2

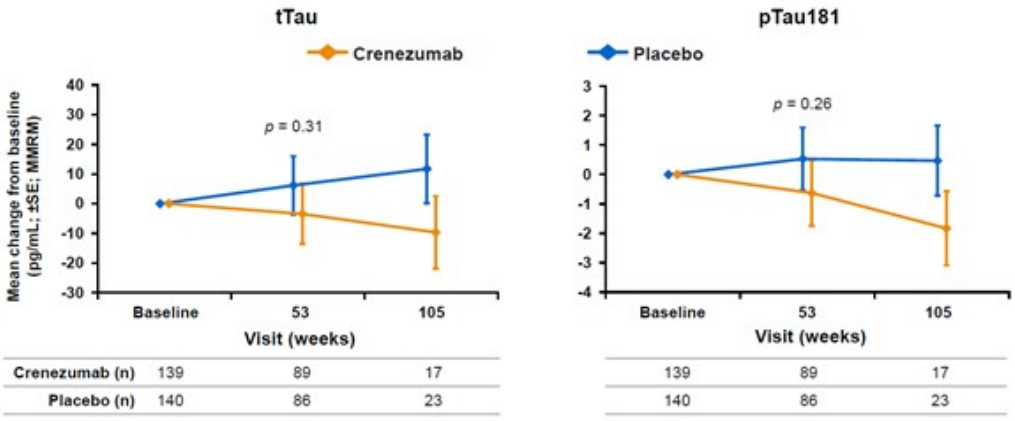


Crenezumab (n)	176	175	74
Placebo (n)	175	175	81

Ref: Bittner *et al.,* CTAD 2019

A numerical trend to reduction in level of total Tau and phospho-Tau 181 (pTau181) in the CSF in patients on crenezumab compared with placebo was observed although the small numbers in the analysis due to early termination of the studies preclude firm conclusions from being drawn.

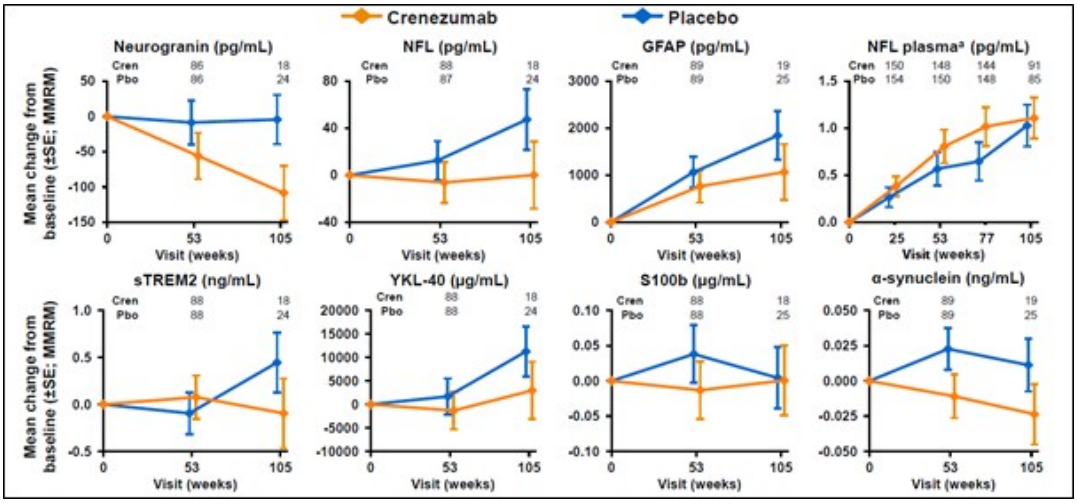
Figure 27: CFS total Tau and pTau181 change from baseline, polled CREAD/CREAD2



Ref: Bittner *et al.,* CTAD 2019

Positive trends on a range of biomarkers associated with AD in CSF including neurogranin, neurofilament light chain (NFL), Glial fibrillary acidic protein (GFAP), soluble Triggering receptor expressed on myeloid cells 2 (sTREM2), Chitinase-3-like protein 1(YKL-40) and a-syn were reported by Roche at the CTAD 2019 conference, although again the small numbers due to early termination of the studies limit interpretability of the results.

Figure 28: Exploratory biomarkers: Roche NeuroToolkit



Ref: Bittner *et al.,* CTAD 2019

Safety in the CREAD and CREAD 2 studies

The decision to terminate the CREAD and CREAD 2 was not related to safety. No safety signals for crenezumab were observed in this analysis and the overall safety profile was similar to that seen in previous trials. There was no

difference in the rate of newly developing ARIA-E (0.3%) between the active and placebo arms and the rates of ARIA-H were also similar (8.8% on crenezumab vs 6.8% on placebo).

Morphomer Tau

Approximately 2,200 compounds have been screened thus far for the Morphomer Tau program. This has allowed for the identification of several chemical series of orally bioavailable small molecules with suitable CNS properties. The lead compounds displayed selectivity for binding to pathological Tau aggregates in preference to other protein aggregates. In addition, the lead compounds were able to prevent Tau aggregation and promote its disaggregation. Further characterization using multiple orthogonal *in vitro*, *ex vivo* and *in vivo* tests addressing pharmacology absorption, distribution, metabolism, and excretion (ADME), and safety properties led to the identification of the first clinical candidate ACI-3024.

ACI-3024

ACI-3024 is a potent Tau aggregation inhibitor active against the 3R and 4R human Tau isoforms as well as the mutant forms associated with human Tauopathies, such as FTLD-Tau (e.g., PSP, Pick's disease, corticobasal degeneration). ACI-3024 selectively binds to aggregated Tau and does not bind to the monomeric forms of Tau. Moreover, the binding to Tau aggregates is selective, with no cross-reactivity to aggregates of Abeta and a-syn.

ACI-3024 showed a potent and dose-dependent reduction in spontaneous intracellular Tau aggregation and misfolding as measured by immunocytochemistry in human neuronal-like cells over-expressing Tau. Furthermore, ACI-3024 promoted *ex vivo* disaggregation of Tau neurofibrillary tangles on human AD brain sections.

The *in vivo* efficacy of ACI-3024 was evaluated in the Tg4510 mouse model (Ramsden *et al.*, 2005). *In vivo* treatment of Tg4510 transgenic mice with ACI-3024 reduced aggregated and insoluble hyper-phosphorylated Tau. Immunohistochemistry analysis of misfolded Tau using an MC1 antibody in Tg4510 brain sections of the same mice treated with ACI-3024 showed reduction of misfolded Tau. These effects were proportional to the plasma concentration of ACI-3024.

Total Tau concentration in cerebrospinal fluid (CSF) was inversely correlated with ACI-3024 exposure in plasma, suggesting the possibility of exploring CSF Tau concentrations as a biomarker of target engagement.

Preclinical safety

ACI-3024 has a good *in vitro* and *in vivo* ADME profile, including low clearance, long half-life and good CNS disposition as assessed by brain and CSF concentrations. ACI-3024 was negative in *in vitro* and *in vivo* genotoxicity assays [Ames, micronucleus test (MNT) and mouse lymphoma cell mutagenesis (MLY)] and has undergone an extensive toxicology and safety pharmacology assessment. The no observed adverse effect level has been established at 300 mg/kg in rodent and at 450 mg/kg in non-rodent animals after 4 weeks of treatment (Poli, CTAD 2018).

Effect on neuroinflammation

ACI-3024 efficacy on pathological Tau-induced neuroinflammation was assessed *in vitro* and *in vivo*. *In vitro*, ACI-3024 induced a potent reduction of Tau-induced neuroinflammation markers. *In vivo,* in Tg4510 mice, treatment with ACI-3024 overall reduced microgliosis, most likely as a downstream consequence of reducing Tau pathology, by reducing the derived pathological Tau-induced microglial activation.

Clinical development

Phase 1 study

This Phase 1 study was a first-in-human (FiH), randomized, placebo-controlled, double-blind, sequential single and multiple ascending dose study. The study assessed the safety, tolerability, pharmacokinetics, and pharmacodynamics of ACI-3024. Part I included five single ascending doses in healthy volunteers, with a food effect assessment in the fourth dose cohort. In Part II, three escalating multiple dose regimens were evaluated; regimen two was assessed in different populations of healthy volunteers. CSF samples were collected from the highest multiple dose group.

The study was executed as planned and all single and multiple dosing regimens were completed in healthy young, elderly, and Japanese subjects. ACI-3024 was administered following single or multiple oral doses and dose-dependent plasma exposure was observed. ACI-3024 showed a long half-life (47.5 to 101 h), with steady state reached after 12-13 days. Low renal clearance was shown. After multiple doses, ACI-3024 concentrations in CSF exceeded target concentrations based on animal studies.

ACI-3024 will not be further developed under the collaboration and the Companies have decided to pursue other promising Tau Morphomer candidates from AC Immune's research platform for potential clinical development in AD.

Tau diagnostics

The severity of cognitive impairment in patients with AD is correlated with the presence of Tau protein tangles, leading us to believe that an imaging agent for Tau is equally, if not more important than Abeta-PET to assess spreading of pathology in the brain. In May 2020, Eli Lilly received FDA approval for the first Tau-PET tracer TAUVID (flortaucipir F18 injection). However, TAUVID received approval only for a pathology indication (i.e., correlation with histopathology findings in Braak 5 and 6 patients), but has not received a prognostic label (i.e., prediction of cognitive deterioration based on a positive Tau-PET scan.)

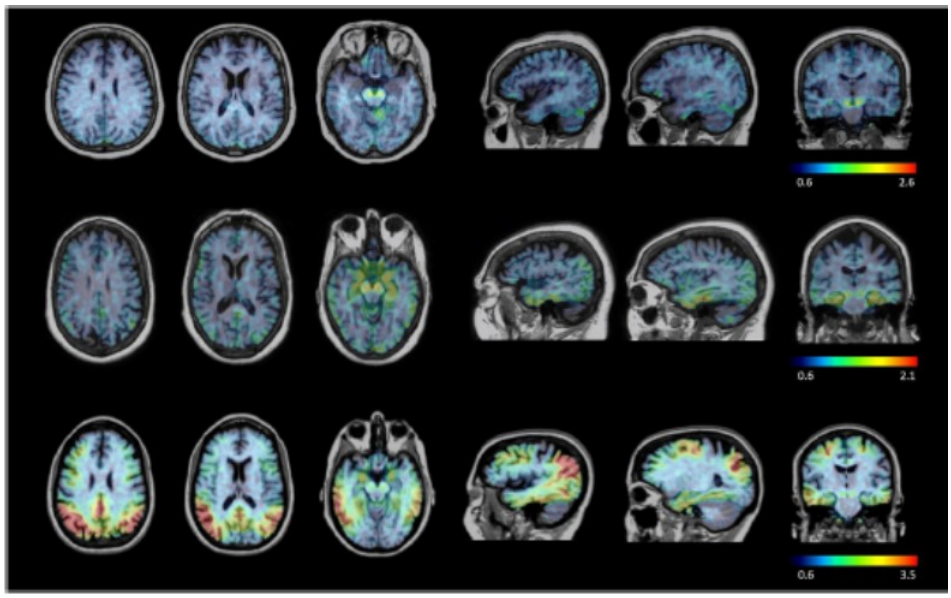
Our Tau-PET tracers are designed to bind specifically to the pathological forms of human Tau in AD and other Tauopathies. They have demonstrated an excellent PET tracer profile with their ability to cross the blood brain barrier and a high selectivity to pathological Tau even in the early-stage disease.

In May 2014, we established a license and collaboration agreement for our Tau-PET imaging program with LMI. The Phase 1 clinical study of our clinical candidate PI-2620 in AD was completed in Q1 2018. The Phase 2 longitudinal study in AD in South Korea (Asan Medical Center, NCT03903211) was completed in Q4 2021 and results presented at AAIC 2022. The pivotal ADvance Phase 3 histopathology study in AD (NCT05641688) was initiated in December with FPFV in December 2022. The first Alzheimer's patient was imaged with PI-2620 scan in January 2023.

PI-2620 is selective for Tau over Abeta and other "off-target" binding compared with current published Tau-PET agents in development, as no binding to Abeta *in vivo* and no "off-target" retention in basal ganglia or choroid plexus was observed. In addition, PI-2620 was shown to be suitable for measuring longitudinal Tau accumulation. A major differentiator for PI-2620 is its ability to bind 4-repeat (4R) Tau isoforms, which are present in varying amounts in different neurodegenerative diseases. Most Tau-PET tracers in development are not able to bind 4R Tau and are of limited use for certain diseases driven by these Tau species.

The Tau PET tracer ^{18}F-PI-2620 was included into a sub-study of the MissionAD trial of elenbecestat to evaluate Tau deposition in amyloid-beta positive subjects with a diagnosis of mild cognitive impairment (MCI) due to AD or mild AD dementia. The findings support the hypothesis that ^{18}F-PI-2620 PET imaging of neuropathologic Tau deposits may reflect underlying neurodegeneration in AD. Significant correlations were observed with hippocampal volume and CSF biomarkers, and an association between Tau and Abeta load. Quantifiable increases in ^{18}F-PI-2620 PET SUVR over 1 year were observed in regions with early Tau deposition and the results are consistent with the hypothesis that cortical Tau is associated with cognitive impairment. This study supports the utility of ^{18}F-PI-2620 PET to assess Tau load in an early AD population. Quantifiable Tau load and its corresponding increase in early AD could be a relevant target engagement marker of anti-Tau but also anti-amyloid clinical trials.

Figure 29: PI-2620 – Ability to detect Tau deposits in an early AD population



Ref: Bullich *et al.*, Alzheimer's Research & Therapy, 2022

Figure 29 shows ^{18}F-PI-2620 SUVR PET images (scalp stripped) registered to the T1-weighted MRI illustrating the tracer distribution in a Tau negative subject (upper row), a Tau-positive subject with uptake in the mesial temporal cortex (center row), and a Tau-positive subject with extensive neocortical uptake (bottom row).

A recent study (Malarte *et al.*, Mol. Psychiatry, 2022) showed that ^{3}H-PI-2620 has comparable binding affinity in AD, CBD and PSP brain tissue, although the binding site density can vary between these pathologies in the order: AD > CBD > PSP. Competitive binding studies indicate that PI-2620 can detect multiple binding sites in AD, CBD and PSP brain tissue. Importantly, in CBD and PSP brains, PI-2620 displayed high specificity which was not observed with other tracers.

Franzmeier *et al.* (Nat. Communications, 2022) compared *in vivo* Tau-PET analyses to independent post-mortem samples thereby providing further evidence that PI-2620 binds to 4R Tau. This study demonstrated a close link between 4R Tau deposition patterns and connectivity supporting the concept of trans-neuronal Tau spreading in 4R Tauopathies.

Tau diagnostics are a major market opportunity that will be driven by the growth in the aging population and the testing and availability of disease-modifying drugs. We believe a best-in-class Tau tracer has the potential to achieve a substantial global market share in this large and growing market, which includes AD as well as other important Tauopathies.

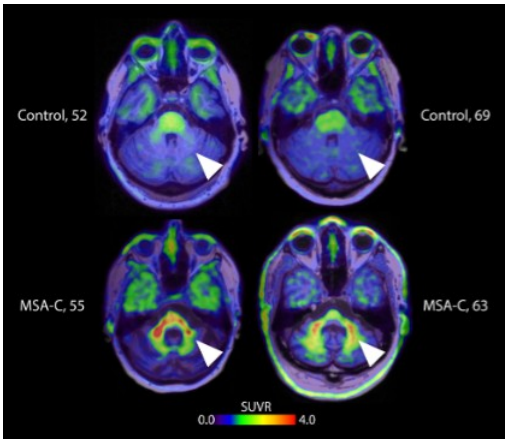
A-syn diagnostics

We are also developing PET imaging agents to detect a-syn, which progressively accumulates in the brains of PD patients and is believed to be central to the neurodegenerative process of PD, as well as several other disorders, including Lewy body dementia and MSA, making it a priority target for development of therapeutics and diagnostics. We have identified molecules leveraging our Morphomer technology that selectively bind to a-syn pathological structures from human PD brain with affinity in the low-nanomolar range.

In the same timeframe, we have also initiated the clinical development of our third-generation candidate, ACI-12589. ACI-12589 is the first molecule capable to detect pathological a-syn in the brain of patient with MSA and to differentiate those from controls, other synucleinopathies and more generally other neurodegenerative diseases (Figure 30). Additionally, ACI-12589 showed some signal retention in familial PD cases in brain areas compatible with the expected distribution of pathological a-syn. The preclinical and clinical data obtained within the program were presented at AD/PD 2022 and AAIC 2022.

The FiH clinical evaluation of ACI-12589 in PD, MSA and other a-synucleinopathies was completed in 2022. In preparation to further steps in clinical development, in Q4 2022 a dosimetry study in healthy volunteers was completed.

Figure 30: ACI-12589 PET signal in patients with MSA compared to controls



Ref: Capotosti, AAIC 2022

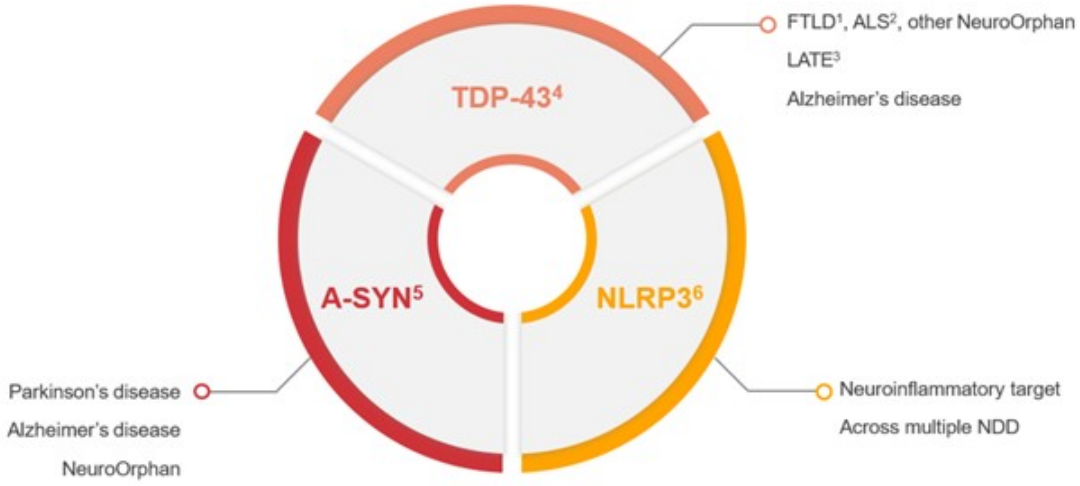
Currently there are no imaging products in the market that target a-syn. This provides us with the opportunity to become the market leader in a-syn PET imaging. We believe the ability to image a-syn deposits in the brain will enable a fundamental change in the approach toward diagnosing and treating a-syn-associated diseases.

In 2020, the Company's a-syn-PET tracer won the Ken Griffin Alpha-synuclein Imaging Competition from the MJFF. In 2022, the Company received a continuation grant from the MJFF.

Our preclinical programs

Using our SupraAntigen and Morphomer platforms, we have generated additional discovery and preclinical stage molecules targeting key pathologies that drive a range of neurodegenerative diseases, including TDP-43, a-syn, and NLRP3. We are accelerating the development of several therapeutic product candidates currently in preclinical development, including several programs focused on indications outside of AD as a critical part of our expansion strategy.

Figure 31: Key pathologies for further pipeline expansion



(1) Frontotemporal lobar degeneration; (2) Amyotrophic lateral sclerosis; (3) Limbic-predominant age-related TDP-43 encephalopathy; (4) TAR DNA-binding protein 43; (5) alpha-synuclein; (6) NOD-like receptor protein 3

Based on the data to date, our technology platforms can be applied to misfolded proteins across a broad range of indications. See our novel targets pipeline above at Figure 6.

A-syn antibody

The a-syn antibodies generated using our SupraAntigen platform have unique binding properties allowing them to bind preferentially to the pathological forms of a-syn. Leveraging the wide collection of anti-a-syn antibodies generated with diverse binding epitopes and sub-nM binding affinities to aggregated a-syn, new immunoassays are being developed for the detection of pathological a-syn in biofluids. A-syn aggregation and spreading are established targets for PD, MSA and other synucleinopathies. Antibodies that interfere with the aggregation and spreading mechanisms of a-syn provide a therapeutic option for the treatment of PD. The a-syn antibodies were able to significantly delay the seeded aggregation of pathological a-syn in an *in vitro* aggregation assay, and were able to significantly decrease pathological a-syn spreading in an *in vivo* animal model of PD. Characterization using multiple orthogonal *in vitro* and *in vivo* tests addressing binding, specificity, functionality and pharmacological properties has led to the identification of the lead candidate ACI-5755.

Lead characterization

ACI-5755 selectively binds to pathological forms of a-syn with low-nanomolar affinity and shows a significant preference over monomeric a-syn. Additionally, ACI-5755 shows strong recognition for pathological a-syn in patient-derived tissues in both PD and MSA. ACI-5755 showed a potent and dose-dependent reduction in the seeding capacity of pathological a-syn in a proprietary *in vitro* aggregation assay. Moreover, ACI-5755 substantially reduced the propagation of a-syn aggregates in a cell-based model. The *in vivo* efficacy of ACI-5755 was evaluated in the M83 propagation mouse model (Luk *et al*., 2012). Treatment of mice with ACI-5755 significantly decreased pathological a-syn spreading *in vivo*. Furthermore, a significant reduction in the rate of body weight loss compared with the vehicle-treated control group was observed for mice treated with ACI-5755.

Morphomer a-syn

Leveraging our Morphomer platform, we discovered and characterized the first biologically active small molecule inhibitors targeting intracellular a-syn aggregates. Identified compounds, from several distinct chemical series, which significantly decrease a-syn aggregate accumulation in neurons by interfering with the seeding and fibrillation processes. Iterative medicinal chemistry optimization led to the identification of orally available compounds with favorable CNS-penetrant pharmacokinetic properties, which progressed into *in vivo* proof-of-concept study in an animal model of alpha-synucleinopathies. Treatment with hit compound resulted in significant, dose-dependent decrease of pathological a-syn aggregates *in vivo*, Medicinal chemistry efforts will continue on improving properties of lead chemical series, in parallel to identifying structurally diverse compounds fulfilling the target product profile.

In December 2021, the Company received a grant from the MJFF to fund the optimization of the current compound series and declare a preclinical lead, which commenced in Q1 2022.

TDP-43 antibody

TDP-43 is a recently identified target of growing interest for NeuroOrphan indications such as frontotemporal dementia (FTD) and ALS. Interestingly, TDP-43 also plays an important role in other significant neurodegenerative indications such as AD or LATE.

Anti-TDP-43 antibodies binding to various regions of TDP-43 were generated by our SupraAntigen platform. A subset displayed conformational selectivity to misfolded TDP-43, while others recognized all TDP-43 isoforms (Figure 32A). Multiple antibodies were generated and characterized *in vitro*, from which two pan-TDP-43 antibodies (ACI-5891 and ACI-5886) were selected for the evaluation of their efficacy in mitigating TDP-43 aggregation *in vitro* and *in vivo* (Figure 32B-C). ACI-5891 showed a high binding affinity for TDP-43 and ability to reduce TDP-43 aggregation *in vitro and in vivo*. ACI-5891 was successfully humanized and clinical lead selected (ACI-5891.9). The lead molecule shows excellent pharmacokinetics in non-human primates and good developability profile.

Lead characterization

To evaluate the functional efficacy of TDP-43 antibodies *in vitro*, the ability of ACI-5891 to inhibit TDP-43 aggregation was tested. In an *in vitro* assay with recombinant TDP-43, ACI-5891 significantly inhibited TDP-43 aggregation by 98% compared with the isotype control and significantly promoted their phagocytosis by mouse primary and ALS patient-derived microglia. Using FTLD-TDP patient-derived brain extracts to induce templated TDP-43 aggregation *in vitro*, ACI-5891, which binds to the C-terminal domain of TDP-43, was able to substantially interfere with this process of seeding (Figure 32B). Moreover, ACI-5891 demonstrated functional efficacy *in vivo* by reducing pathological TDP-43 in two different mouse models of ALS and FTD (Figure 32C). Importantly, these beneficial effects are achieved while preserving physiological TDP-43 activity. Our findings demonstrate, for the first time, that a monoclonal antibody targeting the C-terminal region of TDP-43 limits pathology and neurotoxicity by enabling clearance of misfolded TDP-43 through microglia engagement and support the clinical strategy to target TDP-43 by passive immunotherapy.

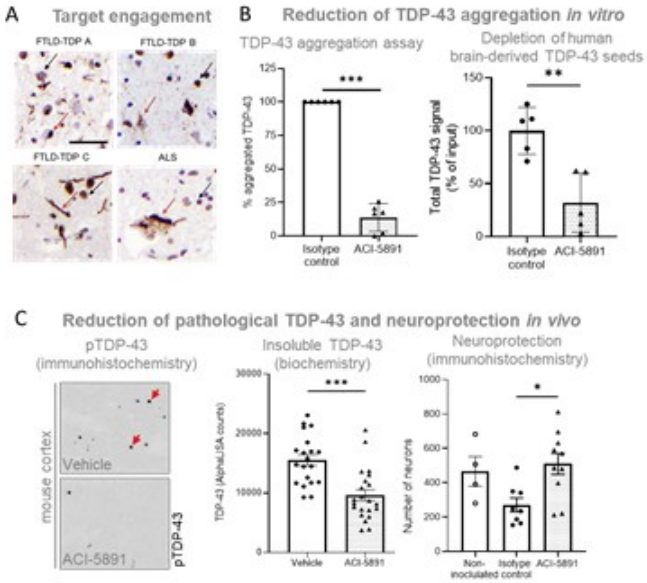
Clinical lead declaration and initiation of IND-enabling studies

ACI-5891 was successfully humanized on a human antibody framework. Several variants had a similar binding capacity for TDP-43 while retaining the potency for inhibition of TDP-43 aggregation as compared to the chimeric monoclonal antibody. The target values were achieved for the lead candidates in terms of target affinity, functional efficacy, and percentage humanness. These variants were then evaluated for pharmacokinetics in non-human primates. The selected clinical lead (ACI-5891.9) shows excellent pharmacokinetics in non-human primates. Developability of clinical lead candidates was further confirmed in manufacturability assessment studies. Dose-range finding study to evaluate safety of clinical lead in non-human primates is ongoing.

TDP-43 antibody-based biofluid assay

Since the levels of TDP-43 are low in biofluids, a real-time quaking-induced conversion (RT-QuIC) assay was developed for the detection of pathological TDP-43 seeds. Using this assay, the presence of seeding-competent TDP-43 species was confirmed in CSF of sporadic ALS donors compared to healthy controls. In addition, to evaluate target engagement of the clinical lead in vivo, novel assays to measure free TDP-43 in biofluids were established using SIMOA technology. The assay allows the measurement of free TDP-43 in serum and CSF from animals dosed with the clinical lead.

Figure 32: Key results for TDP-43 antibodies program



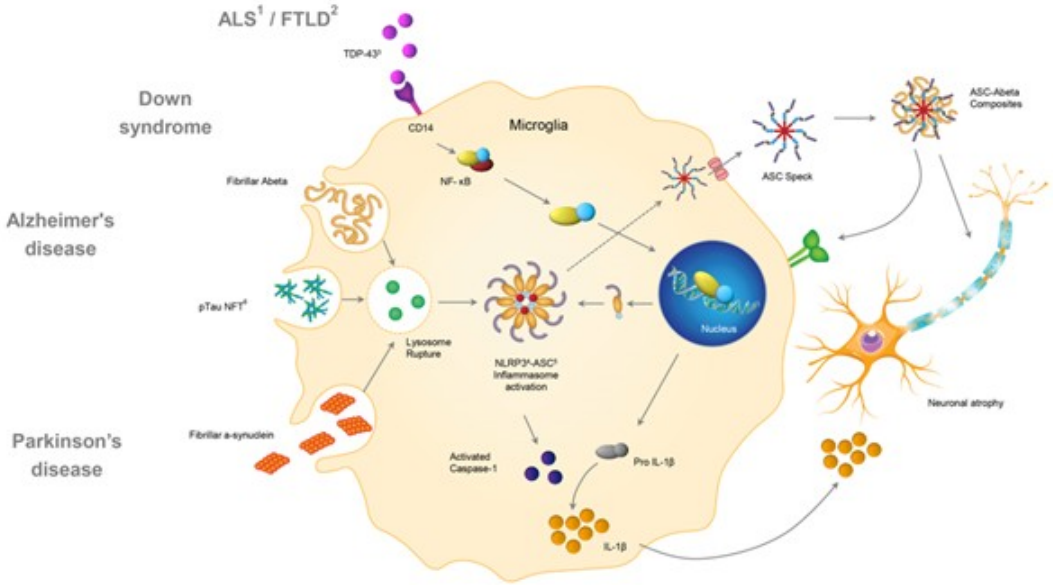
Ref: Afroz, AD/PD 2022

Neuroinflammation and the NLRP3-ASC inflammasome pathway

Microglial cells are the main resident immune cells in the brain, which maintain a healthy environment by removing damaged cells and misfolded protein aggregates. When overstimulated, microglia can drive neuroinflammation, leading to increased neuronal death and disease progression. A key molecular pathway that is activated by misfolded proteins related to neurodegenerative and other diseases, is the NLRP3 inflammasome, a multi-protein complex that forms within microglia leading to production of pro-inflammatory factors that exacerbate neuronal atrophy. A critical component of the NLRP3 pathway is ASC (apoptosis-associated speck-like protein containing a C-terminal caspase recruitment domain), which is formed and released by activated microglia. Intracellularly, ASC specks participate in the production of pro-inflammatory cytokines, whereas extracellular ASC specks cause acute inflammatory reactions. ASC specks have been identified in microglia within the CNS of patients with NDD (Venegas, 2017) as well as patients' body fluids.

As illustrated in Figure 33, pathological species of Abeta, Tau, a-syn and TDP-43 induce NLRP3 inflammasome activation and ASC speck formation. AC Immune is developing multiple small molecule and antibody-based candidates with the potential to inhibit the NLRP3 pathway. Recent *in vitro* studies and *in vivo* experiments in animal models of AD, PD and ALS have validated this approach.

Figure 33: Proteinopathies exacerbate NLRP3-driven neuronal damage and promote further neurodegeneration



(1) Amyotrophic lateral sclerosis; (2) Frontotemporal lobar dementia; (3) TAR DNA-binding protein 43; (4) NOD-like receptor protein 3; (5) Apoptosis-associated speck-like protein containing a CARD, also PYCARD; (6) Neurofibrillary tangle

Targeting NLRP3-ASC in neurodegenerative diseases

In AD, Abeta peptides, which accumulate to form the characteristic plaques in AD activate the NLRP3 inflammasome (Halle, 2008). The downstream pro-inflammatory factors, IL-1b and IL-18, are increased in cells isolated in these patients (Saresella, 2016). Further validation of these targets in AD involve crossing NLRP3 or ASC knockout mice to models of Abeta-driven pathology. In these models, neuroinflammation decreased and neuronal and memory function improved (Heneka, 2013; Demspey, 2017; Venegas, 2017). Recently, ASC speck and IL-18 levels were shown to be higher in human Mild Cognitive Impairment (MCI) and AD brain samples indicating that ASC is a promising biomarker of MCI and AD (Scott, 2020).

In Parkinson's disease, NLRP3 is activated and ASC formation is upregulated (Gordon, 2018 and Anderson, 2021). Exome sequencing analysis identified multiple single-nucleotide polymorphisms of NLRP3 including rs7525979, which was associated with a significantly reduced risk of developing PD (von Herrmann, 2018). In vitro, NLRP3 inhibition decreases a-syn-mediated inflammasome activation in mouse microglial cells and extracellular ASC release. In multiple PD animal models, targeting NLRP3 effectively mitigates motor deficits, nigrostriatal dopaminergic degeneration and accumulation of a-syn aggregates (Gordon 2018). Taken together, NLRP3 is responsible for driving neuroinflammation that results in progressive dopaminergic neuropathology, highlighting NLRP3 as a potential target for PD disease-modifying treatments.

As illustrated in Figure 33, extracellular Tau activates NLRP3 and ASC formation in microglia. In patients with frontotemporal dementia, elevated cleavage of caspase-1, increased ASC levels and mature IL-1b are observed (Ising, 2019). Furthermore, in preclinical models, injection of fibrillar Abeta induces Tau pathology in an NLRP3-dependent manner (Ising, 2019) and the absence of ASC or inhibition of NLRP3 decreases seeding by Tau *in vivo* and *in vitro* (Stancu, 2019). Finally, NLRP3 inhibition ameliorates inflammation and ER stress signaling in a model of Tau-driven pathology, as well as partially normalizes phospho-Tau levels (Hull, 2020).

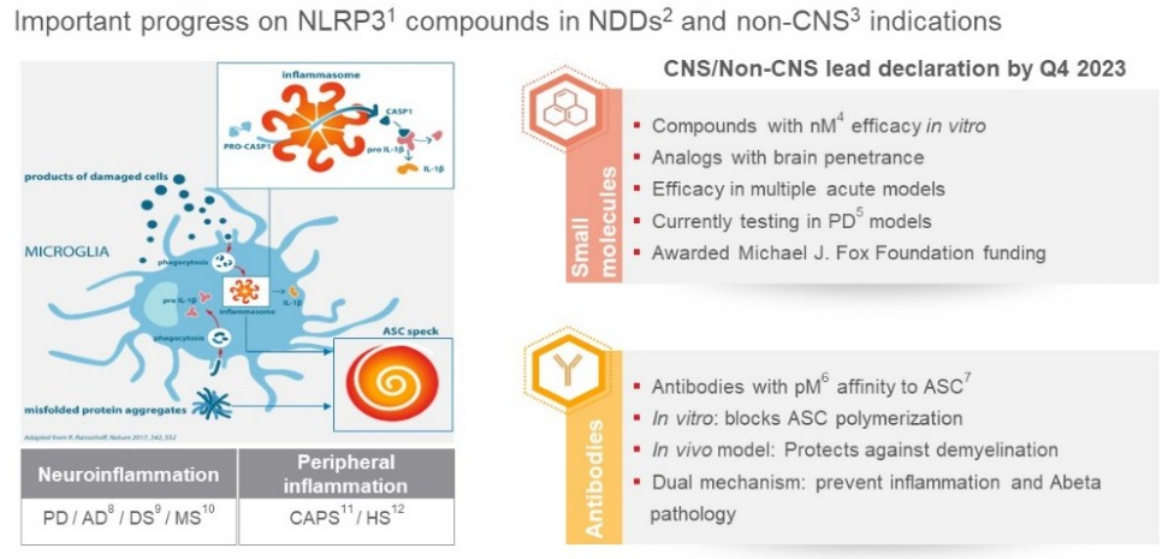
Concerning ALS, TDP-43-mediated activation of microglia causes motor neuron cell death *in vitro* (Zhao, 2015) with downstream activation of NF-kB and NLRP3 (Clark, 2020) and involves CD14. This finding is clinically relevant as increased CD14 expression by microglia is observed in postmortem spinal cord tissue from patients with ALS, a TDP-43-driven disease (Clark, 2020). Furthermore, wildtype and mutant forms of TDP-43 activate microglia to generate IL-1b, which is abolished by NLRP3 inhibition (Deora, 2019).

Microglia isolated from the ALS mouse model, SOD1G93A, express elevated levels of NLRP3 (Deora, 2019). When microglia are incubated with soluble or aggregated SOD1G93A, NLRP3 is activated, ASC specks are formed and IL-1b is secreted which is prevented by treatment with an NLRP3 inhibitor (Deora, 2019).

Our strategy for targeting the NLRP3-ASC inflammasome

AC Immune is exploring this key pathway in order to reduce the unwanted progression of inflammation in diseases and syndromes caused by the hyper-activation of the NLRP3 inflammasome. Our aim is to develop therapeutics that decrease production of pro-inflammatory factors yet maintain normal phagocytosis of debris and misfolded proteins as well as allow the function of other pathogen-sensing pathways. Currently, AC Immune is targeting the NLRP3-ASC pathway using two complementary approaches, derived from our two technology platforms (Figure 34):

Figure 34: Strategy to use our dual proprietary technology platforms to target NLRP3-ASC



(1) (NOD)-like receptor protein 3; (2) Neurodegenerative disease; (3) Central nervous system; (4) Nanomolar; (5) Parkinson's Disease; (6) picomolar affinity to human and mouse ASC; (7) Apoptosis-associated speck-like protein containing a CARD, also PYCARD; (8) Alzheimer's Disease; (9) Down syndrome; (10) Multiple sclerosis; (11) Cryopyrin-associated periodic syndrome; (12) Hidradenitis suppurativa

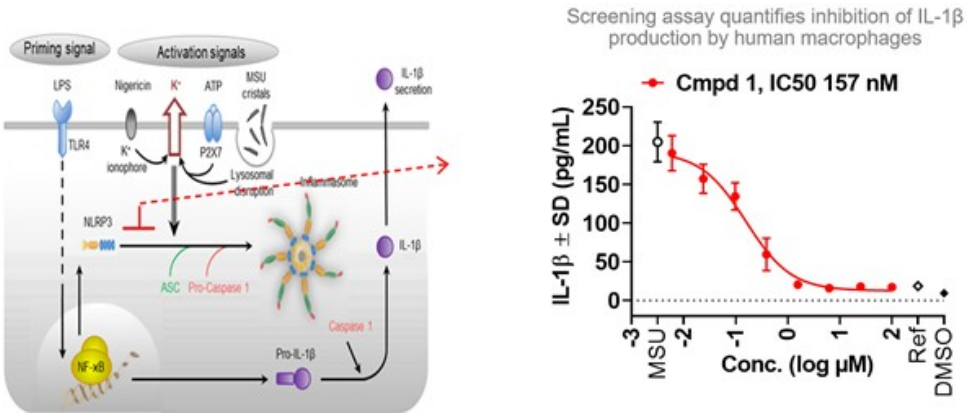
Ref: Adapted from Ransohoff, Nature, 2017

Small molecule inhibitors of NLRP3

Leveraging our proprietary Morphomer platform, the Company has successfully identified various chemical series of potent small molecule NLRP3 inhibitors. The Company has established biological activity for these compounds in multiple functional assays (Figures 35 and 36), and initial animal studies show highly potent target inhibition in a model of peripheral inflammation (Figure 37), providing the first evidence of *in vivo* activity. AC Immune is currently evaluating potential lead compounds for further *in vivo* efficacy and optimization for CNS delivery.

In December 2021, the Company received a grant from the MJFF to fund the development of novel brain penetrant NLRP3 inflammasome inhibitors as potential therapeutics for Parkinson's disease, which commenced in Q1 2022.

Figure 35: Screening assay to quantify the compound-mediated inhibition of IL-1β production *in vitro* using human microglia

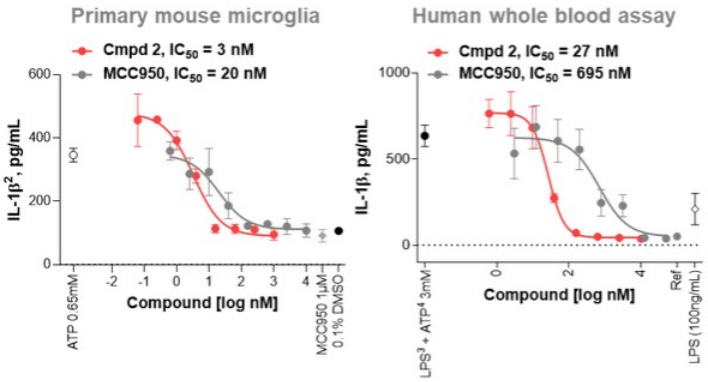


(1) NOD-like receptor protein 3; (2) Interleukin 1 beta

Ref: Adapted from Choi *et al.,* Mol Cell 2014

In the Figure above, the left panel illustrates the signal transduction pathway leading to NLRP3 inflammasome activation. The right panel shows the dose dependent inhibition by a small molecule candidate (cmpd 1) and reference molecule (MCC950) of the NLRP3 pathway post stimulation with monosodium urate (MSU) crystal that induced interleukin-1β production by human macrophages. IC50 (inhibition concentration at 50%); DMSO (negative vehicle control).

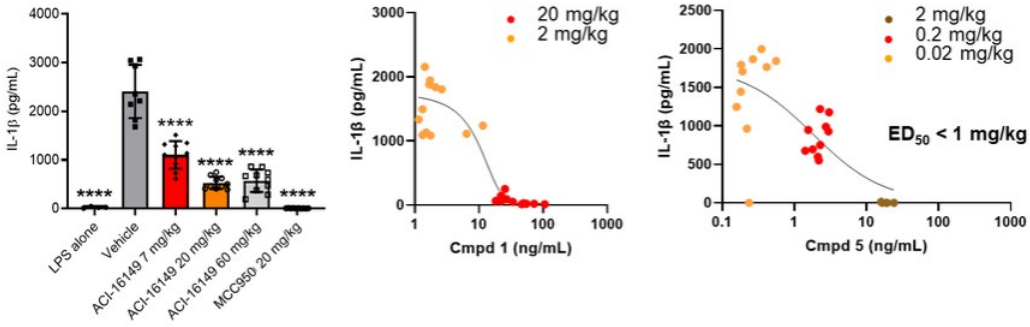
Figure 36: Secondary assays involving NLRP3[1] inhibition in primary mouse microglia and human whole blood demonstrate potent hit compounds active *in vitro*



(1) NOD-like receptor protein 3; (2) Interleukin 1 beta; (3) lipopolysaccharide; (4) adenosine triphosphate

Ref: AC Immune unpublished data

Figure 37: In a mouse model of peritonitis, several of the initial hits targeting NLRP3[1] show significant inhibition of IL-1β[2] production *in vivo*



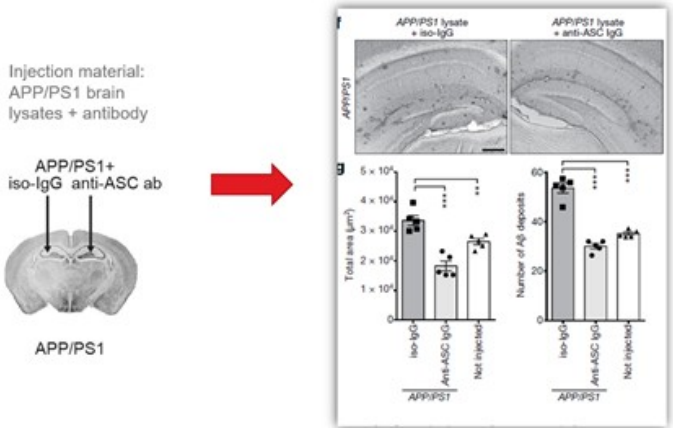
(1) NOD-like receptor protein 3; (2) Interleukin 1 beta

Ref: AC Immune unpublished data

Therapeutic monoclonal antibodies for neuroinflammation (mAb-ASC)

Apoptosis associated speck like protein containing CARD (ASC) is widely researched and recognized as an adaptor protein participating in inflammasome assembly and pyroptosis. It contains a bipartite structure comprising of a pyrin (PYD) and a caspase recruitment domain (CARD) domain. These two domains help ASC function as an adaptor molecule. ASC plays pivotal role in various inflammatory diseases in the CNS as well as peripherally. Thus, the use of antibodies against ASC is an attractive therapeutic approach. It has been shown in the APP/PSI mouse model of AD, intracellular and extracellular ASC specks are present. Treatment using an anti-ASC antibody, which targets extracellular ASC specks, decreases the Abeta load in these mice (Figure 38).

Figure 38: ASC[1] specks in AD patients and mouse model of AD



(1) Apoptosis-associated speck-like protein containing a CARD; (2) Amyloid precursor protein/presenilin 1

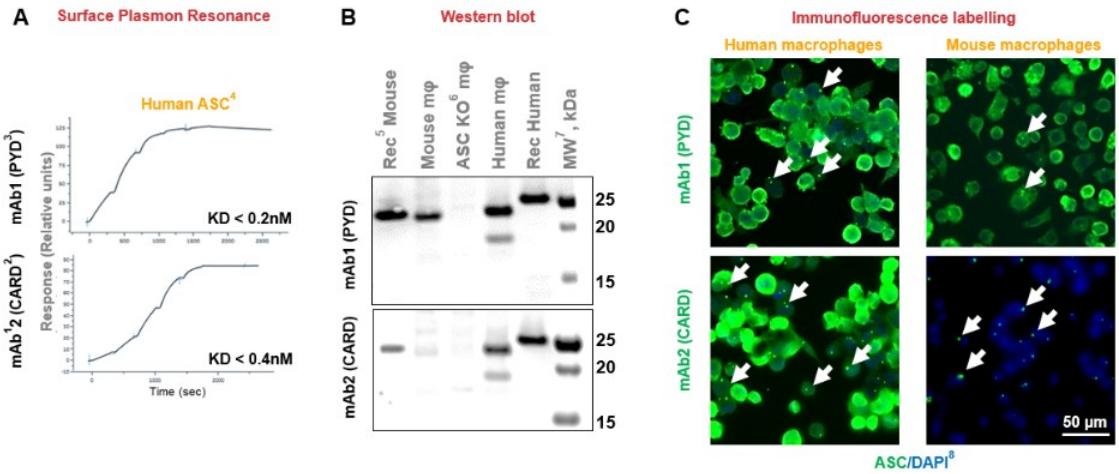
Ref: Venegas *et al.,* Nature, 2017

Using our SupraAntigen platform, AC Immune generated and characterized a novel class of anti-ASC monoclonal antibodies. ASC mAbs recognize either the PYD or the CARD domain of the protein, and show picomolar affinity (Figure 39A). Specificity of ASC detection was assessed in cell lysates of human and mouse macrophages by western blot experiment and confirmed the absence of signal in human macrophages lacking ASC proteins (Figure 39B). Furthermore, immunofluorescence analysis revealed the ability of our ASC mAbs to recognize ASC proteins in both free cytosolic form and aggregated as specks (arrows in the immunofluorescence images, Figure 39C).

Efficacy of selected antibodies was evaluated *in vivo* using mouse models of neuroinflammation and demyelination. ASC mAbs significantly slowed down the progression of the disease (decreases clinical score on Figure 40A), decreased demyelination (black arrows; Figure 40B) and infiltration of T-cells in the spinal cord (black arrows in Figure 40C).

The efficacy of ASC mAbs will be further tested in other relevant mouse models of CNS and non-CNS disease for lead declaration. These innovative, potentially disease-modifying antibodies are designed to have the highest potential to prevent inflammation and modify the downstream exacerbation of various proteinopathies.

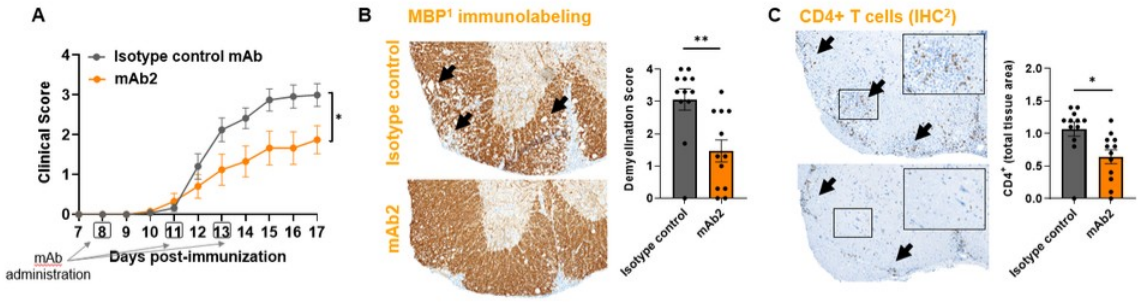
Figure 39: Binding affinity and target engagement of neutralizing anti-ASC antibodies recognizing murine and human ASC



(1) monoclonal antibody; (2) caspase activation and recruitment domain; (3) Pyrin domain (4) Apoptosis-associated speck-like protein; (5) recombinant: (6) knock-out; (7) molecular weight, (8) 4',6-diamidino-2-phenylindole

Ref: Seredenina, 4th Inflammasome Therapeutics Summit, 2022

Figure 40: Anti-ASC mAb shows functional improvement in the model of neuroinflammation



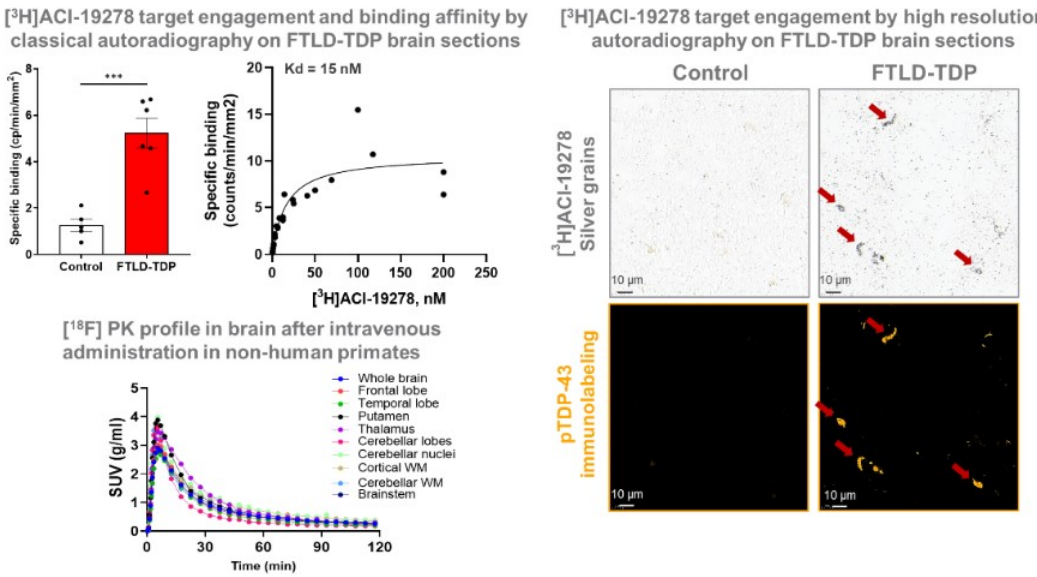
(1) Myelin basic protein; (2) Immunohistochemistry

Ref: Seredenina, 4th Inflammasome Therapeutics Summit, 2022

TDP-43 imaging diagnostics

To complement our pipeline of PET imaging tracers, we also selected TDP-43 as a third target (after Tau and a-syn). Using proprietary assays, a set of small molecular weight compounds from four chemically distinct series were identified. These bind to patient-derived pathological TDP-43. Several of these compounds demonstrated favorable pharmacokinetic profiles in rodents suggesting suitable properties for further development as PET ligands. We identified candidates showing nanomolar affinities on TDP-43 aggregates enriched from patients with TDP-43 proteinopathies. A selected compound is able to differentiate FTLD-TDP pathology from control cases by classical autoradiography and shows target engagement on TDP-43 inclusions in FTLD-TDP brain sections by high resolution autoradiography. This compound is selective over Abeta and a-syn in AD and PD brain homogenates respectively. Pharmacokinetic profile of this compound in non-human primate brain is suitable for FiH evaluation. Medicinal chemistry optimization is ongoing to explore SAR and enrich our TDP-43 PET tracer library with additional candidates to deliver a potential first-in-class PET tracer for TDP-43.

Figure 41: TDP-43 PET imaging tracer demonstrates target engagement in FTLD-TDP brain sections and promising PK profile



Ref: Seredenina, ISFDT Conference, 2022

There are no imaging products in the market today targeting TDP-43. This provides us with a unique opportunity to become the first company to provide a TDP-43-PET tracer to the market. We believe the ability to image TDP-43 deposits in the brain will enable fundamental change in the approach toward treating primary and secondary TDP-43 proteinopathies including improved design for AD clinical trials to provide better outcomes for patients.

In February 2023, the Company announced that it had been awarded USD 500 thousand in new grants from the MJFF to support the development of its TDP-43 PET tracer program.

License agreements and collaborations

Our SupraAntigen and Morphomer platforms have generated large numbers of clinical assets that address multiple diseases related to protein misfolding. Selected key assets in the product pipeline have been licensed for upfront payments, milestones and royalties to help offset the cost of our research and internal product development. We have signed a number of licensing agreements with leading pharmaceutical companies to assist and accelerate the development of our product pipeline, including:

- a worldwide licensing agreement with Genentech signed in November 2006 (and amended in March 2009, January 2013, May 2014 and May 2015) for anti-Abeta antibodies for AD and potentially other indications, under which we may become eligible to receive payments potentially greater than USD 340 (CHF 317) million, excluding royalties;

- a worldwide licensing agreement with Genentech signed in June 2012 (and amended in December 2015) for anti-Tau antibodies to treat AD and potentially other indications, under which we may become eligible to receive payments potentially greater than CHF 400 million, excluding royalties;

- a worldwide licensing agreement with Janssen signed in December 2014 (and amended in April 2016, July 2017, January 2019, November 2019 and December 2022) for therapeutic anti-Tau vaccines for AD, and

potentially other Tauopathies, under which we may become eligible to receive payments totaling up to CHF 500 million, excluding royalties;

- a worldwide licensing and collaboration agreement (LCA) with LMI (formerly Piramal Imaging SA) signed in May 2014 (and amended in June 2022) for small-molecule Tau ligands for use as PET tracers under which we may become eligible to receive payments totaling up to EUR 160 (CHF 159) million, excluding royalties; and

- a worldwide license agreement with Lilly to research and develop Morphomer Tau small molecules for the treatment of AD and other neurodegenerative diseases, which was entered into in December 2018 (and amended in September 2019 and March 2020). The agreement was deemed effective on January 23, 2019. Under this agreement, we may become eligible to receive payments up to approximately CHF 1.9 billion, excluding royalties.

Further information concerning details of our agreements and collaborations can be found under "Item 5: Operating and financial review and prospects."

Competition

The pharmaceutical and biopharmaceutical industries are highly competitive across all therapeutic fields. In the field of neurodegenerative diseases, there are many public and private companies or institutions that are actively engaged in the discovery and development of therapeutic and diagnostic products. Some of these products may have a similar target to our product candidates or address similar markets. The industry is still in its infancy in terms of defining the pathology of neurodegenerative diseases. As disease understanding progresses, the number of novel product candidates may well increase and broaden the therapeutic and diagnostic options in our product markets.

Currently, there are two approved disease-modifying products for AD. Most currently approved therapies seek to treat the symptoms of AD, such as cognitive decline, but do not slow or stop the progression of the disease. In addition, commonly, there is off-label prescription of antidepressant and antipsychotic agents for more patients with advanced AD who may have agitation, aggressive behaviors, psychosis and depression.

We expect there to be several classes of disease-modifying agents that will enter the AD market. Among our monoclonal antibodies, semorinemab targets extracellular Tau and crenezumab targets pathologic Abeta oligomers. Therapeutic vaccines are another class of potentially disease-modifying immunotherapies targeting pathologic protein species, and include our candidate products ACI-35.030, which targets aggregated, phosphorylated Tau protein and ACI-24.060, which targets oligomeric and pyroglutamate Abeta. A further class of disease-modifying therapies, small molecules, include our Morphomer Tau program, which inhibits Tau aggregates.

The availability of novel diagnostic agents to visualize the disease development in patients with AD is critical for successful clinical development of disease-modifying products in AD. At the forefront of this new diagnostic effort are PET agents for imaging of disease pathology, and in particular, Tau-targeting PET agents, which we believe will allow precise assessment of disease in patients with AD. A similar situation is developing in other NDD, such as PD, where PET imaging is becoming available.

ACI-35.030. ACI-35.030, if approved, would potentially compete with other Tau-targeting therapeutic vaccines currently being developed. This could include, for example, the AADvac1 vaccine being developed by Axon Neuroscience, which completed a Phase 2 study in 2019 and AV-1980R (Nuravax) which is expected to enter phase 1 clinical development in the near future.

ACI-24.060 for AD. ACI-24.060, if approved, would potentially compete with other anti-Abeta-targeting therapeutic vaccines currently being developed. This includes the ABvac 40 (Araclon Biotech), which is currently being evaluated in a Phase 2 study and UB-311(Vaxxinity), which has completed a Phase 2a study. In addition, ABvac 42 (Araclon Biotech) has completed a Phase 1 study and ALZ-101 (Alzinova) is currently being evaluated in a Phase 1b study and AV-1959D (Nuravax) in Phase 1 clinical development.

ACI-24.060 for DS. ACI-24.060 is the first disease-modifying vaccine candidate addressing DS-related AD, with a potential preventive and therapeutic application. Although there are symptomatic treatments of DS in clinical development, to our knowledge there are currently no other disease-modifying treatments in clinical development for AD in DS.

ACI-7104.056. ACI-7104.056, if approved, would potentially compete with other a-syn-targeting therapeutic vaccines. This includes the UB-312 vaccine developed by Vaxxinity, which is being evaluated in a Phase 1b study.

Semorinemab. Semorinemab is one of several Tau-targeting monoclonal antibodies in development to potentially act as disease-modifying agents. Bepranemab (UCB/Roche) and JNJ-63733657 (Janssen) are being evaluated in Phase 2 studies. E-2814 (Eisai) is being evaluated in a Phase 2/3 prevention study. Lu AF87908 (Lundbeck), APNmAb005 (Aprinoia Therapeutics), MK-2214 (Merck/Teijin Pharma) and PRX005 (Prothena/BMS) are being evaluated in Phase 1 studies.

Crenezumab. Crenezumab is the first monoclonal antibody candidate that targets Abeta in cognitively healthy individuals at risk of developing familial AD. However, Lilly's solanezumab and donanemab (Eli Lilly) are being evaluated in studies of presymptomatic AD. ADUHELM (Biogen) and Leqembi (BioArctic/Eisai/Biogen) have been approved by FDA under the accelerated approval pathway for the treatment of patients with mild cognitive impairment and mild dementia.

Morphomer Tau. In collaboration with Lilly, we are researching and developing small molecule Tau aggregation inhibitors with plans to evaluate candidates in AD and NeuroOrphan tauopathies. We completed a Phase 1 study in healthy volunteers with ACI-3024 in Q2 2020. Continued candidate characterization across the research program also identified new and highly differentiated candidates with excellent cerebrospinal fluid exposure and selectivity for pathological aggregated Tau.

Tau-PET tracer. Tauvid (previously known as Flortaucipir) was developed by Eli Lilly and approved by FDA in May 2020. However, should the Company's PI-2620 be approved, it would also compete with (i) 18F-florzolotau (previously known as APN-1607), a product candidate in a Phase 3 study and being advanced by Aprinoia; (ii) 18F-MK-6240, which is being evaluated by Cerveau/Merck in a Phase 2 clinical trial in patients with ADAD; (iii) 18F-GTP1, which is being developed by Genentech and has completed a Phase 2 study in subjects at risk of developing ADAD, (iv) 18F-RO6958948, for which Roche has completed a Phase 1 study in patients with AD and (v)18F-JNJ-067, for which Janssen has completed a Phase 1 study in patients with AD.

ACI-12589. ACI-12589, if approved, would potentially compete with other a-syn-targeting PET tracers. This includes the 18F-UCB-2897 tracer developed by UCB, which is being evaluated in a Phase 1 study.

A-syn antibody. Several a-syn antibodies are currently in development. Roche/Prothena entered a Phase 2 with prasinezumab in June 2017 and in May 2021, began a Phase 2b study in PD patients with more advanced symptoms; AstraZeneca/Takeda started a Phase 1 study in patients with PDf with MEDI1341 in August 2020 and a Phase 2 study in MSA in November, 2022; Lundbeck/Genmab entered a Phase 2 in MSA with Lu AF82422 in November 2021; and UCB7853 (UCB/Novartis) entered a Phase 1 study in December 2020.

TDP-43 antibodies. To our knowledge, there are no TDP-43 antibodies in the clinic.

Many of our competitors have significantly greater financial, technical and human resources than we have. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunities and our success will be based in part on our ability to identify, develop and manage a portfolio of product candidates that are safer and more effective than competing products. However, this opportunity could be eroded or even eliminated if our competitors develop and/or market products that are novel and have superior safety and efficacy profiles, that may be brought to the market more rapidly due to greater available resources, or that are less costly than our current or future product candidates.

Commercialization strategy

Our strategy to date has been to focus on identifying partnerships for our early-stage product candidates as both a way to secure non-dilutive capital to fund our other research and development programs and also as a way to accelerate the development of these partnered products by leveraging our partners' extensive knowledge in clinical studies, drug development, manufacturing and commercialization.

With greater financial resources at our disposal and the significant knowledge acquired by our scientists and scientific leadership, we intend to retain selected promising product candidates in-house for a longer period of time and fund their development from our own resources. This will allow us to generate greater value from these product candidates, allowing us to demand more significant terms from a prospective partner. For example, while we ultimately plan to seek a strategic partner for our Abeta vaccine program in AD, we currently plan to retain full control of this asset for development in the DS population. We have commenced a Phase 1b/2 study for AD in advance of potentially partnering this program and intend to fund further clinical development in DS with our own financial resources. In the field of diagnostics, the parallel development of therapeutic compounds and companion diagnostics is of growing importance to the pharmaceutical and biopharmaceutical industries. The development timeframe of a PET diagnostic agent is significantly shorter than for a therapeutic product, providing the prospect for potential diagnostic product revenues to be realized quicker than potential therapeutic product revenues. Our Morphomer platform is particularly well suited to generate molecules for use in the development of diagnostics for NDDs which provides additional partnering opportunities.

Given our current stage of product development, we currently do not have a commercialization infrastructure. If any of our product candidates is granted marketing approval, we intend to focus our initial commercial efforts in the U.S. and select European markets, which we believe represent the largest market opportunities for us. In those markets, we expect our commercial operations to potentially include our own specialty sales force that will target Neurologists and Gerontologists, both in hospitals and in private practice. In other markets, we expect to seek partnerships that would maximize our products' commercial potential.

Intellectual property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining U.S. and foreign patents intended to cover our products and compositions, their methods of use and processes for their manufacture, and our proprietary technology platforms, diagnostic candidates and any other inventions that are commercially important to the development of our business. We also rely on trade secrets and know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will significantly depend on our and our collaboration and licensing partners' ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, to defend and enforce patents, to preserve the confidentiality of our trade secrets and to operate our business without infringing any patents and other intellectual property or proprietary rights of third parties. See the section titled "Risk factors— Risks related to intellectual property" for additional information.

As of December 31, 2022, we owned or co-owned with our collaboration and licensing partners, approximately 48 issued U.S. patents and 399 issued patents in other jurisdictions, as well as 34 pending U.S. patent applications and 565 pending foreign patent applications. As of December 31, 2022, we licensed approximately 32 issued U.S. patents and 282 issued patents in other jurisdictions, as well as 16 pending U.S. patent applications and 317 pending foreign patent applications.

The patent portfolios for our most advanced product candidates as of December 31, 2022 are summarized below:

Anti-Tau vaccines

Our patent portfolio for anti-Tau vaccines includes a patent family with composition-of-matter claims (including claims directed to the ACI-35 antigenic peptide and a pharmaceutical composition comprising such an antigenic peptide), claims directed to treating certain indications using ACI-35 including AD, and claims directed to using ACI-35 to induce an immune response. This patent family currently contains approximately 28 issued patents and two pending patent applications in 27 countries. The issued patents in this patent family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2030, excluding any additional term for patent term adjustments or patent term extensions.

Our patent portfolio for anti-Tau vaccines also includes a patent family relating to therapeutic Tau vaccine claims (including claims directed to a pharmaceutical composition comprising an antigenic Tau peptide), claims directed to using such vaccines to induce an immune response in a subject, and claims directed to methods for preventing or treating a neurodegenerative disease or disorder, including AD, among others. This patent family currently contains 1 issued patent and approximately 46 pending patent applications in 38 countries. The issued patent and any patents issuing in this patent family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2038, excluding any additional term for patent term adjustments or patent term extensions.

ACI-24

Our patent portfolio for ACI-24 includes a patent family with composition-of-matter claims (including claims directed to the ACI-24 antigenic construct), claims directed to treating certain indications using ACI-24 including AD, and claims directed to using ACI-24 to induce an immune response. As of December 31, 2022, in this patent family, we owned approximately 27 issued patents and 6 pending patent applications in 30 countries. With respect to the U.S., we owned two issued U.S. patents. The issued patents in this patent family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2026, excluding any additional term for patent term adjustments or patent term extensions.

Our patent portfolio for ACI-24 also includes a patent family directed to the use of the ACI-24 vaccine in the treatment and/or prevention of memory and/or cognitive impairments or abnormalities in the DS population, among others. As of December 31, 2022, in this patent family, we owned approximately 14 issued patents and 4 pending patent applications in 18 countries. Issued patents in this patent family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2032, excluding any additional term for patent term adjustments or patent term extensions.

Our patent portfolio for ACI-24 also includes a patent family relating to therapeutic anti-Abeta vaccine claims (including claims directed to a pharmaceutical composition comprising an antigenic peptide), and claims directed to using such vaccines in treating, preventing, inducing a protective immune response against or alleviating the symptoms associated with an Abeta-associated disease in a subject, among others. As of December 31, 2022, in this patent family, we owned one issued U.S. patent and approximately 33 pending patent applications in 32 countries. Any issued patents in this patent family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2039, excluding any additional term for patent term adjustments or patent term extensions.

ACI-7104

Our patent portfolio relating to ACI-7104 includes patents and patent applications with composition-of-matter claims (including claims directed to the peptide, as well as pharmaceutical formulations comprising the peptide), and claims directed to the use of compounds comprising the peptide in treating or preventing synucleinopathies including PD and MSA.

Our patent portfolio relating to ACI-7104 includes patents and patent applications that we own in two different patent families. As of December 31, 2022, in these patent families, we owned approximately 13 issued patents and 17

pending patent applications, in 11 countries. With respect to the U.S., we owned two issued U.S. patents. Issued patents in the basic patent family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2029, excluding any additional term for patent term adjustments or patent term extensions.

Semorinemab

Our global patent portfolio relating to semorinemab includes patents and patent applications with claims directed to compositions of matter, methods of treatment for certain indications including AD, and methods of use, among others.

Crenezumab

Our patent portfolio relating to crenezumab includes patents and patent applications with claims directed to composition of matter (including claims directed to the crenezumab antibody or a fragment thereof, a polynucleotide encoding the crenezumab antibody or a fragment thereof, a cell line used to produce the crenezumab antibody as well as pharmaceutical compositions comprising the crenezumab antibody), claims directed to treating certain indications using the crenezumab antibody including AD, claims directed to a method of manufacturing the crenezumab antibody and claims directed to diagnostic and prognostic uses of the crenezumab antibody.

Our patent portfolio relating to crenezumab includes patents and patent applications that we own or co-own in four different patent families. As of December 31, 2022, we owned or co-owned approximately 50 patents (not including the patents in the individual countries where the issued European patent was validated) and 12 patent applications in 34 countries in our main patent family directed to the crenezumab antibody and methods of using the crenezumab antibody to treat certain indications, including AD. This patent portfolio includes three issued U.S. patents and one pending U.S. patent applications, which, if the appropriate maintenance or other governmental fees are paid, are expected to expire in 2027, excluding any additional term for patent term adjustments or patent term extensions. This patent portfolio also includes a PCT patent application that was filed on July 13, 2007. If the appropriate maintenance, renewal, annuity, or other governmental fees are paid, national-stage applications claiming priority from this PCT patent application, if issued, are expected to expire in 2027, excluding any additional term for patent term adjustments or patent term extensions, as applicable.

Morphomer Tau

Our patent portfolio relating to Morphomer Tau therapeutics includes patent applications with claims directed to composition of matter (including claims directed to the molecule, a pharmaceutical composition comprising such molecule and a mixture comprising such molecule), and claims directed to prevention and treatment of certain indications using such molecules including AD and PSP, among others.

Our patent portfolio relating to the Morphomer Tau therapeutic program includes patent applications that we own or co-own in four different patent families. As of December 31, 2022, we owned or co-owned approximately 48 pending patent applications and 4 issued patents, including one U.S. issued patent in our main patent family directed to the ACI-3024 small molecule Tau aggregation inhibitor. If the appropriate maintenance, renewal, annuity, or other governmental fees are paid, national-stage applications claiming priority from this PCT patent application, if issued, are expected to expire in 2039, excluding any additional term for patent term adjustments or patent term extensions, as applicable.

PI-2620

Our patent portfolio relating to PI-2620 includes patent applications with claims directed to composition of matter (including claims directed to the molecule, its precursor and a diagnostic composition comprising such molecule), claims directed to diagnosis of certain indications using PI-2620 including AD and PSP, and claims directed to a method of manufacturing PI-2620, among others.

Our patent portfolio relating to PI-2620 includes patent applications that we own or co-own in three different patent families. As of December 31, 2022, we owned or co-owned 6 patents and approximately 12 patent applications in 16

countries in our main patent family directed to the PI-2620 molecule, its precursor and methods of using the PI-2620 to diagnose certain indications, including AD and PSP. This main patent family includes one issued U.S. patent. If the appropriate maintenance, renewal, annuity, or other governmental fees are paid, national-stage applications claiming priority from this PCT patent application, if issued, are expected to expire in 2037, excluding any additional term for patent term adjustments or patent term extensions, as applicable.

ACI-12589

Our patent portfolio relating to a-syn diagnostics includes composition of matter claims (including claims directed to the ACI-12589 molecule, its precursor, and diagnostic compositions comprising the molecule), and claims directed to use of the molecule in imaging and in diagnostics of a-synucleinopathies including PD and MSA.

Our patent portfolio relating to a-syn diagnostics includes patents and patent applications that we own in three different patent families. As of December 31, 2022, we owned or co-owned approximately 17 patent applications in 17 countries in our main patent family directed to the ACI 12589 molecule, its precursor, diagnostic compositions, and methods of using ACI-12589 for imaging and diagnostics of a-synucleinopathies including PD and MSA. If the appropriate maintenance, renewal, annuity or other governmental fees are paid, any issued patents are expected to provide protection up to 2041, excluding any additional term for patent term adjustments or patent term extensions, as applicable.

Manufacturing and supply

We do not own or operate facilities for the manufacture, testing, packaging, labeling, storage or distribution of preclinical or clinical supplies of any of our product candidates. We instead contract with and rely on third-party CMOs to manufacture, package, label, store, test and distribute all preclinical and clinical supplies of our product candidates, and we plan to continue to do so for the foreseeable future. We have established relationships with CMOs such as WuXi AppTec (WuXi STA), WuXi Biologics, Avecia, Almac Clinical Services, Bachem AG, Evonik Industries AG, Polymun Scientific Immunbiologische Forschung GmbH, piCHEM Forschungs-und Entwicklungs GmbH, Baccinex SA, Solvias AG and Pfenex Inc. among others.

Compliance with governing rules and quality requirements

The facilities used by our collaboration partners and CMOs to manufacture our product candidates are systematically audited by local authorities and occasionally inspected by competent authorities where the clinical studies are ongoing. The facilities where the commercial productions are performed will have to be approved by the FDA or other relevant regulatory authorities, pursuant to inspections that are conducted after we submit our NDA or comparable marketing applications. We perform periodic quality audits of the manufacturing facilities and CMOs to monitor their compliance with the regional laws, regulations and applicable cGMP standards and other laws and regulations, such as those related to environmental health and safety matters. The scope of our audits also involves monitoring the ability of our providers to maintain adequate QCs and QA systems including personnel qualification.

After manufacturing, our products are submitted to extensive characterization and QC testing plans performed by using properly developed analytical methods that are qualified or validated; this ensures the accuracy of the results generated and provides evidence of the quality of our products. In addition, our products are submitted to detailed and standardized stability programs aimed at demonstrating product stability during the storage period; this, in addition to guaranteeing the safety of the products, supports the definition of a suitable supply chain that may encompass the distribution of the products in different continents.

Contractual framework

We have established, with CMOs supplying and testing active pharmaceutical ingredients, drug substances or drug products under cGMP, quality agreements and master service agreements. Quality agreements define the quality standards required to develop, produce and supply the product, and also define the responsibilities related to the collaboration with regards to the quality related aspects. Manufacturing service agreements define the commercial and

financial framework under which product manufacturing and testing under cGMP is performed. Any failure to achieve and maintain compliance with the laws, regulations and standards, suspension of the manufacturing of our product candidates or withdrawals of cGMP permissions, which would adversely affect our business and reputation, are defined in the master service agreements and quality agreements. The risk that any third-party providers may breach the agreements they have with us because of factors beyond our control and the possibility that they may also terminate or refuse to renew their agreements because of their own financial difficulties or business priorities, potentially at a time that is costly or otherwise inconvenient for us, is managed by us with constant investments toward maintaining reserve stocks and in-depth process know-how. The latter is supported by continuous in-house process development and production activities of small-scale/research grade materials, which may offer the chance to rapidly identify alternative contract manufacturers to whom the manufacturing process could be transferred providing continuity for the clinical study. Finally, our contracts may also offer us limited remedies.

Interaction with CMOs

Finally, our partnerships with CMOs are managed through an efficient project management platform in which teams are formed with the representatives of each key function from both parties. Meetings occur either through telephone conferences aimed at updating short-term actions or face-to-face conferences when mid- to long-term development plans are discussed.

Government regulation and our regulatory department

Our regulatory department has a strong culture of regulatory compliance, operating under three guiding principles, to:

- provide constructive regulatory input for development products;
- ensure smooth regulatory approvals by anticipating hurdles; and
- build confidence with regulators by continuous communication.

The QA group is included within the regulatory department with the mission to:

- create and maintain a corporate quality management system; and
- ensure cGCP, cGMP, cGLP and current Good Distribution Practice (cGDP) compliance.

A science-driven approach is the cornerstone of our interactions and this has helped us to build and maintain a high level of trust with regulators. Besides informal conversations with the authorities, our regulatory department has conducted several pre-Investigational New Drug (pre-IND), Type B and Type C meetings with the FDA (ACI-24.060 for AD and DS, ACI-7104.056 and PI-2620) and Scientific Advice meetings, which are the European equivalent of pre-IND meetings (with the German Paul-Ehrlich-Institut, Swedish Medical Products Agency; UK Medicine & Healthcare Products Regulatory Agency, Finnish Medicines Agency, the Spanish Agency of Medicines and Medical Devices and the EMA). Since 2008, our regulatory department has filed a total of 24 clinical trial applications in the EU (one each in Austria, Denmark, the Netherlands and Poland, two in Spain, three in Germany, three in Sweden, four in Finland and eight in the UK) and 4 INDs in the U.S.. Given the seriousness of AD and public pressure for new therapeutics, we consider regulatory agencies to be important stakeholders in our product development strategies. We are committed to working closely with global regulatory authorities to adhere to and achieve the highest levels of safety and quality of our product candidates in the most timely and efficient manner. The transparency we have achieved and our goal of a close working relationship with the regulatory agencies, in particular the FDA and the EMA, are intended to facilitate expeditious execution through the regulatory approval process.

Our regulatory department contains a QA group. As every quality issue ultimately requires regulatory involvement and input, this approach is intended to lead to rapid resolution of issues and ensure full compliance to satisfy both the

reviewers and the inspectors at the government health authorities. Our regulatory department is charged with keeping our entire organization, directly or indirectly involved in the clinical study application process, in a state of "inspection readiness." To that end, we ensure that the Trial Master Files are complete and regularly updated. Our regulatory department is also tasked with generating our annual quality plan. The personnel tasked with QA have issued a set of approximately 109 standard operating procedures and working instructions and continuously train the relevant staff. Our QA personnel conduct regular audits, including in-person audits of the contract manufacturers, contract research organizations and laboratories conducting primary endpoint analysis. In addition, we have a full-time QA documentation assistant to ensure good documentation practice and archiving.

Product approval process

The clinical studies, manufacturing, labeling, storage, distribution, record-keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the U.S. and other countries. The U.S. FDA, under the Federal Food, Drug, and Cosmetic Act (FDCA), regulates pharmaceutical products in the U.S.. The steps required before a drug may be approved for marketing in the U.S. generally include:

- the completion of preclinical laboratory tests and animal tests conducted under cGLP regulations;
- the submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical studies commence;
- obtaining a positive opinion from the ethics committee (Europe)/institutional review board (U.S.) to commence study on human subjects;
- the performance of adequate and well-controlled human clinical studies to establish the safety and efficacy of the product candidate for each proposed indication and conducted in accordance with cGCP requirements;
- pre-NDA submission meeting with FDA (highly recommended);
- the submission to the FDA of an NDA;
- the FDA's acceptance of the NDA;
- satisfactory completion of an FDA Pre-Approval Inspection (PAI) of the manufacturing facilities at which the product is made to assess compliance with cGMP requirements;
- the FDA's review and approval of an NDA prior to any commercial marketing or sale of the drug in the U.S.; and
- having parallel scientific advice from the EMA or Health Technology Assessment body whereby the payors are involved at the outset (Phase 2), which is intended to facilitate the design of clinical studies to target primarily populations with a high chance of obtaining reimbursement and accelerate the process of time to reimbursement.

The FDA has various programs, including Fast Track, Priority review, Accelerated Approval and Breakthrough Therapy designation, which are intended to increase agency interactions, expedite or facilitate the process for reviewing product candidates, and/or provide for initial approval based on surrogate endpoints. We believe that one or more of our product candidates may qualify for some of these expedited development and review programs. However, even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product candidate no longer meets the conditions for qualification.

The Fast Track program is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are designed to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug may request the FDA to designate the drug as a Fast Track product at any time during the clinical development of the product. AD, for example, meets both pre-requisites—it is life-threatening and constitutes an unmet medical need. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program may be eligible for other types of FDA programs intended to expedite development and review, such as Priority Review and Accelerated Approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or it provides a significant improvement in the treatment, diagnosis or prevention of a disease compared with marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for Priority Review to facilitate the review. Additionally, a product may be eligible for the Accelerated Approval program. Product candidates that are studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive Accelerated Approval, which means that they may be approved on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving Accelerated Approval perform adequate and well-controlled post-marketing clinical studies. Failure to conduct required post-approval trials, or the inability to confirm a clinical benefit during post-marketing trials, may allow the FDA to withdraw the drug from the market on an expedited basis. In addition, as a condition for Accelerated Approval the FDA currently requires pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. The Fast Track, Priority Review and Accelerated Approval programs do not change the standards for approval but may expedite the development or approval process.

The Food and Drug Administration Safety and Innovation Act of 2012 also amended the FDCA to require the FDA to expedite the development and review of a breakthrough therapy. A drug can be designated as a breakthrough therapy if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies in one or more clinically significant endpoints. A sponsor may request that a drug be designated as a breakthrough therapy at any time during the clinical development of the product. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather nonclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor, and taking steps to ensure that the design of the clinical trials is as efficient as practicable.

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. Given this paradigm, AD has been given Life-Threatening Disease status by the FDA and therefore AD therapies are eligible for the expanded access program for investigational drugs and other pathways such as Breakthrough Therapy, Accelerated Approval and Priority Review. Additionally, a single well-designed, well-conducted, pivotal clinical study could be sufficient to trigger market approval pending a successful PAI.

Preclinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which must become effective before clinical studies may be commenced. The IND will automatically become effective 30 days after receipt by the FDA,

unless the FDA raises concerns or questions about the conduct of the studies as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical studies can proceed.

Clinical studies involve the administration of the product candidates to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator. Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Further, each clinical study must be reviewed and approved by an independent IRB, either centrally or individually at each institution at which the clinical study will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries. The FDA, the IRB or the clinical study sponsor may suspend or terminate clinical studies at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a Data Safety Monitoring Board/Committee. This group provides authorization for whether or not a study may move forward at designated checkpoints based on access to certain data from the study. We may also suspend or terminate a clinical study based on evolving business objectives and/or competitive climate.

Clinical studies are typically conducted in three sequential phases prior to approval, but the phases may overlap. These phases generally include the following:

Phase 1. Phase 1 clinical studies represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and pharmacodynamics.

Phase 2. Phase 2 clinical studies usually involve studies in a limited patient population to (i) evaluate the efficacy of the product candidate for specific indications, (ii) determine dosage tolerance and optimal dosage, and (iii) identify possible adverse effects and safety risks.

Phase 3. If a product candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 studies, the clinical study program will be expanded to Phase 3 clinical studies to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical study sites.

Phase 4. Phase 4 clinical studies are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under Accelerated Approval regulations, or when otherwise requested by the FDA in the form of post-marketing requirements or commitments. Failure to conduct any required Phase 4 clinical studies promptly could result in withdrawal of approval.

The results of preclinical studies and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information on the manufacture, composition and quality of the product, are submitted to the FDA in the form of an NDA requesting approval to market the product. The NDA must be accompanied by a significant user-fee payment. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

We estimate that it generally takes 10 to 15 years, or possibly longer, to discover, develop and bring to market a new pharmaceutical or biopharmaceutical product in the U.S.. Several years may be needed to complete each phase, including discovery, preclinical, Phase 1, 2 or 3, or marketing authorization.

In addition, under the Pediatric Research Equity Act, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Recently, the Food and Drug Administration Safety and Innovation Act (FDASIA), which was signed into law on July 9, 2012, amended the FDCA. The FDASIA requires that a sponsor who is planning to submit a marketing application for a drug

or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan within 60 days of an end-of-Phase-2 meeting or as may be agreed between the sponsor and the FDA. The initial Pediatric Study Plan must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the Pediatric Study Plan. A sponsor can submit amendments to an agreed-upon initial Pediatric Study Plan at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early-phase clinical trials, and/or other clinical development programs.

The cost of preparing and submitting an NDA is substantial. Under federal law, NDAs are subject to substantial application user fees and the sponsor of an approved NDA is also subject to annual product and establishment user fees. Under the Prescription Drug User Fee Act (PDUFA), as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA VI eliminates fees for supplements as well as for establishments, although applicants will be assessed for annual prescription drug program fees for prescription drug products, rather than the prescription drug product fee assessed under the previous iteration of PDUFA. According to the FDA's fee schedule for the 2022 FY, the user fee for each NDA application requiring clinical data is USD 3,242,026 and the annual program fee is USD 393,933. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Once the NDA submission has been submitted, the FDA has 60 days after submission of the NDA to conduct an initial review to determine whether it is sufficient to accept for filing. Under the PDUFA, the FDA sets a goal date by which it plans to complete its review. This is typically 12 months from the date of submission of the NDA application. The review process is often extended by FDA requests for additional information or clarification. Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMP regulations and may also inspect clinical study sites for integrity of the data supporting safety and efficacy. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical study data. The FDA is not bound by the recommendations of an advisory committee, but generally follows such recommendations in making its decisions. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product.

After the FDA evaluates the NDA and conducts inspections of the manufacturing facilities where the drug product and/or its API will be produced, it may issue an Approval Letter or a Complete Response Letter. An Approval Letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical study or studies, and/or other significant, expensive and time-consuming requirements related to clinical studies, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy (REMS), plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-marketing studies or clinical studies. Such post-marketing testing may include Phase 4 clinical studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Special protocol assessment

The FDA and an IND sponsor may agree in writing on the design and size of clinical studies intended to form the primary basis of a claim of effectiveness in an NDA. This process is known as a special protocol assessment (SPA). Upon a specific request for a SPA by an IND sponsor, the FDA will evaluate the protocol. If an SPA agreement is reached, however, it is not a guarantee of product approval by the FDA or approval of any permissible claims about the product. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement. In particular, the SPA agreement is not binding on the FDA if previously unrecognized public health concerns later come to light, other new scientific concerns regarding product safety or efficacy arise, the IND sponsor fails to comply with the agreed-upon protocol, or the relevant data, assumptions, or information provided by the IND sponsor when requesting a SPA agreement change, are found to be false statements or misstatements, or are found to omit relevant facts. An SPA agreement may not be changed by the sponsor or the FDA after the study begins except with the written agreement of the sponsor and the FDA, or if the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began.

Orphan-drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is a disease or condition that either affects fewer than 200,000 individuals in the U.S., or affects more than 200,000 individuals in the U.S. but there is no reasonable expectation that the cost of developing and making a drug product available in the U.S. for this type of disease or condition will be recovered from sales of the product in the U.S.. Orphan-product designation must be requested before submitting an NDA. After the FDA grants orphan-product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan-product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan-product exclusivity, which means that the FDA cannot approve any other applications to market the same drug or biological product for the same indication for 7 years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding toward clinical study costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan-product exclusivity also could block the approval of one of our products for 7 years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan-product exclusivity. Orphan-drug status in the EU has similar but not identical benefits in that jurisdiction.

Disclosure of clinical trial information

Sponsors of clinical trials (other than Phase 1 trials) of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, comparator, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of certain trials may be delayed until the new product or new indication being studied has been approved. However, there are evolving rules and increasing requirements for publication of trial-related information, and it is possible that data and other information from trials involving drugs that never garner approval could be required to be disclosed in the future. In addition, publication policies of major medical journals mandate certain registration and disclosures as a pre-condition for potential publication, even when this is not presently mandated as a matter of law. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Post-approval requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user-fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and QC to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-marketing studies or clinical studies to assess new safety risks, or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Patent term restoration and marketing exclusivity

Depending upon the timing, duration, and specifics of FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term to be extended up to 5 years as compensation for patent term effectively lost due to the FDA's pre-market approval requirements. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half of the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to

exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension. Extensions are not granted as a matter of right and the extension must be applied for prior to expiration of the patent and within a 60-day period from the date the product is first approved for commercial marketing. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. Where a product contains multiple active ingredients, if any one active ingredient has not been previously approved, it can form the basis of an extension of patent term provided the patent claims that ingredient or the combination containing it.

In the future, we may apply for patent term restoration for some of our presently owned patents to add patent life beyond their current expiration date, depending on the expected length of clinical studies and other factors involved in the submission of the relevant NDA; however, there can be no assurance that any such extension will be granted to us.

The Biologics Price Competition and Innovation Act of 2009 provides up to 12 years of non-patent data exclusivity within the U.S. to the first applicant to gain approval of a Biologics License Application for a new biologic product that has not previously been approved by the FDA, which we refer to as a reference product. This 12-year data exclusivity does prohibit the FDA from approving a biosimilar or interchangeable product of such reference product until 12 years after the licensure of such reference product. In addition, the FDA will not accept a biosimilar or interchangeable product application for review until 4 years after the date of first licensure of such reference product. Under 21CFR314.108, 5 years' exclusivity is also granted to new chemical entities that contain no active moiety that has been approved by the FDA under section 505(b). This market exclusivity bars the FDA from accepting for review any ANDA or 505(b)(2) application for a drug containing the same active moiety for (i) 5 years if an ANDA or 505(b)(2) application does not contain a paragraph IV certification to a listed patent, or (ii) 4 years if an ANDA or 505(b)(2) is submitted containing a paragraph IV certification to a listed patent. Moreover, pediatric exclusivity, if granted, may add 6 months of exclusivity if the reference product has been studied with respect to a pediatric indication in accordance with certain regulatory requirements. A reference product may also be granted 7 years of orphan-drug exclusivity for the treatment of a rare disease or condition under section 527(a) of FDCA, which would run in parallel with the 12 years of data exclusivity of the reference product, if applicable.

Non-U.S. regulation

In order to market any product outside of the U.S., we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy, and governing, among other things, clinical studies, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical studies or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the U.S. apply similarly in the context of the EU, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods, as described in greater detail below. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

EU drug review approval

In the EEA, which is comprised of the 27 Member States of the EU plus Norway, Iceland and Liechtenstein medicinal products can only be commercialized after obtaining a marketing authorization. There are two types of marketing authorization: the Community Marketing Authorization, which is issued by the EC through the Centralized Procedure based on the opinion of the Committee for Medicinal Products for Human Use (CHMP), a body of the EMA, and which is valid throughout the entire territory of the EEA; and the National Marketing Authorization, which is issued by the competent authorities of the Member States of the EEA and authorizes marketing only in that Member State's national territory and not the EEA as a whole.

The Centralized Procedure is compulsory for human medicines for the treatment of human immunodeficiency virus or acquired immune deficiency syndrome (AIDS), cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions, and viral diseases; for veterinary medicines for use as growth or yield enhancers; for medicines

derived from biotechnology processes, such as genetic engineering; for advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines; and for officially designated ‘orphan medicines’ (medicines used for rare human diseases). The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation, or for products that are in the interest of public health in the EU. The National Marketing Authorization is for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National Marketing Authorization can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National Marketing Authorization in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure, an identical dossier is submitted to the competent authorities of each of the Member States in which the marketing authorization is sought, one of which is selected by the applicant as the Reference Member State (RMS). If the RMS proposes to authorize the product, and the other Member States do not raise objections, the product is granted a National Marketing Authorization in all the Member States in which the authorization was sought. Before granting the marketing authorization, the EMA or the competent authorities of the Member States of the EEA assesses the risk–benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Regulation in the EU

Product development, the regulatory approval process, and safety monitoring of medicinal products and their manufacturers in the EU proceed in much the same manner as they do in the U.S.. Therefore, many of the issues discussed above apply similarly in the context of the EU. In addition, drugs are subject to the extensive price and reimbursement regulations of the various EU Member States.

Clinical studies

As is the case in the U.S., the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls. The new Clinical Trials Regulation (Regulation (EU) No 536/2014) came into force on 31 January 2022. The new Regulation repealed the Clinical Trials Directive (EC) No. 2001/20/EC and national implementing legislation in the EU Member States, which regulated clinical trials in the EU until the Regulation's entry into application. A transition period applies to new clinical trial submissions under the Regulation. New clinical trial applications may be submitted under the Clinical Trials Directive until 30 January 2023, after which all new clinical trial applications will need to be submitted under the Regulation. Ongoing clinical trials under the Clinical Trials Directive have until 30 January 2025 to transition to the Regulation. The Regulation, provides a system for the approval of clinical studies in the European Union via a single online platform known as the Clinical Trials Information System (CTIS) for approval to run a clinical trial in several European countries, making it more efficient to carry out such multinational trials. Under this system, a single application dossier is submitted through CTIS to all Concerned Member States (CMS) where it is intended to conduct the trial. Using a harmonized format, the dossier consists of two parts, Part I contains the more scientific documents, whereas Part II contains the national documents. The review and evaluation is coordinated by one of the Member States, referred to as the Reference Member State (RMS). The Reference Member State is responsible for the evaluation of Part I whereas Part II assessment will be conducted separately by each individual CMS for its own country, including the review by the Ethics Committee. A clinical trial may only be started after the positive assessment by the RMS, and the approval by each CMS. A clinical trial may only be undertaken if provision has been made for insurance or indemnity to cover the liability of the investigator or sponsor. In certain countries, the sponsor of a clinical trial has a strict (faultless) liability for any (direct or indirect) damage suffered by trial subjects. The sponsor of a clinical trial, or its legal representative, must be based in the EEA. European regulators and ethics committees also require the submission of AE reports during a study and a copy of the final study report.

Marketing approval

Marketing approvals under the EU regulatory system may be obtained through a centralized or decentralized procedure. The centralized procedure results in the grant of a single marketing authorization, which is valid for all (currently 27) EU Member States and the three European Free Trade Association (EFTA) members (Norway, Iceland and Liechtenstein).

Pursuant to Regulation (EC) No. 726/2004, as amended, the centralized procedure is mandatory for drugs developed by means of specified biotechnological processes, advanced-therapy medicinal products, drugs for human use containing a new active substance for which the therapeutic indication is the treatment of specified diseases, including but not limited to AIDS, neurodegenerative disorders, auto-immune diseases and other immune dysfunctions, as well as drugs designated as orphan drugs. The CHMP also has the discretion to permit other products to use the centralized procedure if it considers them sufficiently innovative or they contain a new active substance.

In the marketing authorization application, the applicant must properly and sufficiently demonstrate the quality, safety and efficacy of the drug. Under the centralized approval procedure, the CHMP, possibly in conjunction with other committees, is responsible for drawing up the opinion of the EMA on any matter concerning the admissibility of the files submitted in accordance with the centralized procedure, such as an opinion on the granting, variation, suspension or revocation of a marketing authorization, and pharmacovigilance.

The CHMP and other committees are also responsible for providing guidelines and have published numerous guidelines that may apply to our product candidates. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of drug products and may include, among other things, the preclinical studies required in specific cases, the manufacturing and control information that should be submitted in a marketing authorization application, and the post-approval measures required to monitor patients and evaluate the long-term efficacy and potential adverse reactions. Although these guidelines are not legally binding, we believe that our compliance with them is likely to be necessary to gain approval for any of our product candidates.

The maximum timeframe for the evaluation of a marketing authorization application by the CHMP under the centralized procedure is 210 days after receipt of a valid application. This period will be suspended until such time as the supplementary information requested by the CHMP has been provided by the applicant. Likewise, this time limit will be suspended for the time allowed for the applicant to prepare oral or written explanations. When an application is submitted for a marketing authorization in respect of a drug that is of major interest from the viewpoint of public health and in particular therapeutic innovation, the applicant may request an accelerated assessment procedure. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

If the CHMP concludes that the quality, safety and efficacy of the product are sufficiently proven, it adopts a positive opinion. This is sent to the EC, which drafts a decision within approximately 67 days following the CHMP opinion. After consulting with the Member States, the EC adopts a decision and grants a marketing authorization, which is valid for the whole of the EEA. The marketing authorization may be subject to certain conditions, which may include, without limitation, the performance of post-authorization safety and/or efficacy studies.

The EMA has various programs, including accelerated assessment, conditional approval and PRIority MEdicines (PRIME), which are intended to increase agency interactions, expedite or facilitate the process for reviewing product candidates, and/or provide for initial approval on the basis of surrogate endpoints. One or more of our product candidates may qualify for some of these expedited development and review programs. However, even if a product candidate qualifies for one or more of these programs, the EMA may later decide that the product candidate no longer meets the conditions for qualification. Eligibility to the PRIME scheme is limited to products considered to offer a major therapeutic advantage in populations with high unmet need. PRIME is a voluntary scheme aimed at enhancing interaction and early dialogue with developers of promising medicines through achieving the early appointment of the Rapporteur for the product, optimizing development plans and speeding up evaluation so these medicines can reach patients earlier. Products benefiting from PRIME can expect to be eligible for accelerated assessment at the time of application for a marketing authorization application.

EU legislation also provides for a system of regulatory data and market exclusivity. According to Article 14(11) of Regulation (EC) No. 726/2004, as amended, and Article 10(1) of Directive 2001/83/EC, as amended, upon receiving marketing authorization, new chemical entities approved on the basis of a complete independent data package benefit from 8 years of data exclusivity and an additional 2 years of market exclusivity. Data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic (abbreviated) application. During the

additional 2-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall 10-year period will be extended to a maximum of 11 years if, during the first 8 years of those 10 years, the marketing authorization holder (MAH) obtains an authorization for one or more new therapeutic indications that, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator can gain the period of data exclusivity, another company nevertheless could also market another version of the drug if such company obtained marketing authorization based on a marketing authorization application with a completely independent data package of pharmaceutical test, preclinical tests and clinical studies. However, products designated as orphan medicinal products enjoy, upon receiving marketing authorization, a period of 10 years of orphan market exclusivity. See also "—Orphan drug regulation" below. Depending upon the timing and duration of the EU marketing authorization process, products may be eligible for an SPC of up to 5 years', pursuant to Regulation (EC) No. 469/2009. Such SPCs extend the rights under the basic patent for the drug.

In the EU, the pediatric regulation [Regulation (EC) No 1901/2006 as amended] requires sponsors to submit a pediatric investigation plan at the end of Phase 1. This plan will provide the details of the quality, non-clinical and clinical studies required to support the authorization of a pediatric indication. Additional rules apply to medicinal products for pediatric use under Regulation (EC) No. 1901/2006. Potential incentives include a six-month extension of any supplementary protection certificate granted pursuant to Regulation (EC) No. 469/2009, but not in cases in which the relevant product is designated as an orphan medicinal product pursuant to Regulation (EC) No. 141/2000, as amended. Instead, a medicinal product designated as an orphan medicinal product may enjoy an extension of the 10-year market exclusivity period granted under Regulation (EC) No. 141/2000 to 12 years subject to the conditions applicable to orphan drugs.

Orphan drug regulation

In the EU, Regulation (EC) No. 141/2000, as amended, states that a drug will be designated as an orphan drug if its sponsor can establish:

- that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the EU when the application is made, or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment; and

- that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, that the drug will be of significant benefit to those affected by that condition.

Regulation (EC) No. 847/2000 sets out further provisions for implementation of the criteria for designation of a drug as an orphan drug. An application for the designation of a drug as an orphan drug must be submitted at any stage of development of the drug before filing of a marketing authorization application.

If an EU-wide community marketing authorization in respect of an orphan drug is granted or if all the EU Member States have granted marketing authorizations in accordance with the procedures for mutual recognition, the EU and the Member States will not, for a period of 10 years, accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect of a similar drug. This period may, however, be reduced to 6 years if, at the end of the fifth year, it is established, with respect to the drug concerned, that the criteria for orphan-drug designation are no longer met; in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify

maintenance of market exclusivity. Notwithstanding the foregoing, a marketing authorization may be granted, for the same therapeutic indication, to a similar drug if:

- the holder of the marketing authorization for the original orphan drug has given its consent to the second applicant;
- the holder of the marketing authorization for the original orphan drug is unable to supply sufficient quantities of the drug; or
- the second applicant can establish in the application that the second drug, although similar to the orphan drug already authorized, is safer, more effective or otherwise clinically superior.

Other incentives available to orphan drugs in the EU include financial incentives such as a reduction of fees or fee waivers and protocol assistance. Orphan-drug designation does not shorten the duration of the regulatory review and approval process.

Manufacturing and manufacturers' license

Pursuant to Directive 2003/94/EC, as transposed into the national laws of the Member States, the manufacturing of investigational medicinal products and approved drugs is subject to a separate manufacturer's license and must be conducted in strict compliance with cGMP requirements, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Manufacturers must have at least one qualified person permanently and continuously at their disposal. The qualified person is ultimately responsible for certifying that each batch of finished product released onto the market has been manufactured in accordance with cGMP and the specifications set out in the marketing authorization or investigational medicinal product dossier. cGMP requirements are enforced through mandatory registration of facilities and inspections of those facilities. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action, or possible civil and criminal penalties.

Wholesale distribution and license

Pursuant to Directive 2001/83/EC, the wholesale distribution of medicinal products is subject to the possession of an authorization to engage in activity as a wholesaler in medicinal products. Possession of a manufacturing authorization includes authorization to distribute by wholesale the medicinal products covered by that authorization. The distribution of medicinal products must comply with the principles and guidelines of cGDP.

Advertising

In the EU, the promotion of prescription medicines is subject to intense regulation and control, including EU and national legislation as well as self-regulatory codes (industry codes). Advertising legislation *inter alia* includes a prohibition on direct-to-consumer advertising. All advertising of prescription medicines must be consistent with the product's approved Summary of Product Characteristics, and must be factual, accurate, balanced and not misleading. Advertising of prescription medicines pre-approval or off-label is not allowed. Some jurisdictions require that all promotional materials for prescription medicines be subjected to prior review and approval, either internal or regulatory.

Other regulatory requirements

An MAH for a medicinal product is legally obliged to fulfill a number of obligations by virtue of its status as an MAH. The MAH can delegate the performance of related tasks to third parties, such as distributors or marketing partners, provided that this delegation is appropriately documented and the MAH maintains legal responsibility and liability.

The obligations of an MAH include the following:

- *Manufacturing and batch release*—MAHs should guarantee that all manufacturing operations comply with relevant laws and regulations, applicable GMPs, and the product specifications and manufacturing conditions set out in the marketing authorization, and that each batch of product is subject to appropriate release formalities.

- *Availability and continuous supply*—Pursuant to Directive 2001/83/EC, as transposed into the national laws of the Member States, the MAH for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medical product to pharmacies and persons authorized to supply medicinal products so that the needs of patients in the Member State in question are covered.

- *Pharmacovigilance*—MAHs are obliged to establish and maintain a pharmacovigilance system, including a qualified person responsible for oversight, to submit safety reports to the regulators and to comply with the good pharmacovigilance practice guidelines adopted by the EMA.

- *Advertising and promotion*—MAHs remain responsible for all advertising and promotion of their products, including promotional activities by other companies or individuals on their behalf, and in some cases must conduct internal or regulatory pre-approval of promotional materials. Regulation in this area also covers interactions with healthcare practitioners and/or patient groups, and in some jurisdictions legal or self-regulatory obligations to disclose such interactions exist.

- *Medical affairs/scientific service*—MAHs are required to disseminate scientific and medical information on their medicinal products to healthcare professionals, regulators and patients.

- *Legal representation and distributor issues*—MAHs are responsible for regulatory actions or inactions of their distributors and agents.

- *Preparation, filing and maintenance of the application and subsequent marketing authorization*— MAHs must maintain appropriate records, comply with the marketing authorization's terms and conditions, fulfill reporting obligations to regulators, submit renewal applications and pay all appropriate fees to the authorities. We may hold any future marketing authorizations granted for our product candidates in our own name, or appoint an affiliate or a collaboration partner to hold marketing authorizations on our behalf. Any failure by an MAH to comply with these obligations may result in regulatory action against an MAH and ultimately threaten our ability to commercialize our products.

Pricing and reimbursement

In the EU, the pricing and reimbursement mechanisms by private and public health insurers vary largely by country and even within countries. The public systems reimbursement for standard drugs is determined by guidelines established by the legislator or responsible national authority. The approach taken varies by Member State. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. Other Member States allow companies to fix their own prices for medicines, but monitor and control company profits and may limit or restrict reimbursement. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers to the entry of new products are being erected and some EU countries require the completion of studies that compare the cost-effectiveness of a particular product candidate with that of currently available therapies in order to obtain reimbursement or pricing approval. Special pricing and reimbursement rules may apply to orphan drugs. Inclusion of orphan drugs in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any drug. Acceptance of any medicinal product for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. In addition, results based rules of reimbursement may apply.

Other U.S. healthcare laws

In addition to FDA restrictions on marketing of pharmaceutical or biopharmaceutical products, federal and state healthcare laws restrict certain business practices in the pharmaceutical and biopharmaceutical industries. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The U.S. federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical and biopharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all the criteria for a statutory exception or safe harbor protection. Practices involving remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct *per se* illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare-covered business, the statute has been violated. The Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act (collectively, the Health Care Reform Law), amended the intent requirement under the Anti-Kickback Statute and criminal healthcare fraud statutes (discussed below) such that a person or entity no longer needs to have actual knowledge of the statute or the specific intent to violate it in order to have committed a violation. In addition, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below). Further, the Civil Monetary Penalties Law imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-covered, uses. The federal HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services.

Additionally, the Health Care Reform Law also included the federal Physician Payments Sunshine Act, which requires that certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Additionally, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Certain states require the posting of information relating to clinical studies, and require pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals and to track and report gifts and other payments made to physicians and other healthcare providers. If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Data privacy and security laws

In addition, we may be subject to international, federal and state data privacy and security laws, regulations, rules and standards. Internationally, laws, regulations and standards in many jurisdictions, such as the GDPR, the Swiss Federal Data Protection Act and the UK GDPR, apply broadly to the collection, use, retention, security, disclosure, transfer and other processing of personal information. At the federal level, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates—independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and to seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws, (such as the CCPA and the CPRA,) govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Non-compliance with these laws, regulations, rules and standards could result in significant penalties or legal liability. Although we take steps to comply with applicable laws, rules and regulations, we cannot ensure that we will not be subject to regulatory or private actions, investigations, disputes and litigation, which may include substantial fines or other legal liability for noncompliance of data privacy and security laws, rules and regulations, including in the event of a cybersecurity breach or other security incident. We could be adversely affected if legislation or regulations are expanded to require changes in our or our third-party service providers' business practices or if governing jurisdictions interpret or implement their legislation or regulations in ways that negatively affect our business, results of operations or financial condition. See "Risk Factors—*Changes in laws, rules or regulations relating to data privacy and security, or any actual or perceived failure by us to comply with such laws, rules, regulations and standards, or contractual or other obligations relating to data privacy and security, could have a material adverse effect on our reputation, results of operations, financial condition and cash flows.*"

Pharmaceutical coverage, pricing and reimbursement

In both domestic and foreign markets, our or our collaboration partners' sales of any approved products will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products, if approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of our products will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by third-party payors. These third-party payors are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services.

In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare product candidates. The market for our product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical or biopharmaceutical companies. Additionally, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or another alternative is available. Because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that our product candidates will be considered cost-effective. Because coverage and reimbursement determinations are made on a payor-by-payor basis, obtaining acceptable coverage and reimbursement from one payor does not guarantee we will obtain similar acceptable coverage or reimbursement from another payor. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success.

Furthermore, in many foreign countries, particularly the countries of the EU, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical or biopharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare reform

In the U.S., EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to commercialize our products directly.

In particular, there have been and continue to be a number of initiatives at the U.S. federal and state level that seek to reduce healthcare costs. Initiatives to reduce the federal deficit and to reform healthcare delivery are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability.

We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing approval testing and other requirements.

In addition, there has been heightened governmental scrutiny in the U.S. of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to

product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At both the federal and state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. One significant example of recent legislative action is the IRA, which has been considered a scaled-back version of the Build Back Better Act. The IRA was signed into law on August 16, 2022. While the IRA is still subject to rulemaking (with more information to come via guidance documents from the responsible federal agencies), the IRA, as written, will, among other changes, give HHS the ability and authority to directly negotiate with manufacturers the price that Medicare will pay for certain high-priced drugs. The IRA will also require manufacturers of certain Part B and Part D drugs to issue to HHS rebates based on certain calculations and triggers (i.e., when drug prices increase and outpace the rate of inflation). At this time, we cannot predict the implications the IRA provisions will have on our business.

In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our products candidates, or the amounts of reimbursement available for our product candidates. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost-containment and healthcare-reform measures. Such policy actions could have a material adverse impact on our profitability.

Moreover, the federal Drug Supply Chain Security Act imposes new obligations on manufacturers of pharmaceutical or biopharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new federal legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition and notification responsibilities related to counterfeit, diverted, stolen and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or that are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Physician Payment Sunshine Act and transparency

The Physician Payment Sunshine Act requires most pharmaceutical and biopharmaceutical manufacturers to report annually to the Secretary of Health and Human Services any and all financial arrangements, payments, or other transfers of value made by that entity to physicians and teaching hospitals. The payment information is made publicly available in a searchable format on a content management system website. Once we have an approved product, we will need to dedicate significant resources to establish and maintain systems and processes in order to comply with these regulations. Failure to comply with the reporting requirements can result in significant civil monetary penalties. Similar laws have been enacted or are under consideration in foreign jurisdictions, including France, which has adopted the Loi Bertrand, or French Sunshine Act, which became effective in 2013. In addition, the Code of Ethics from the EFPIA requires certain disclosures of interactions with institutions and healthcare professionals, depending on the jurisdictions in which we operate.

Environmental, health and safety laws and regulations

We are subject to numerous environmental, health and safety laws and regulations and permitting requirements, including those governing laboratory procedures, decontamination activities, and the handling, transportation, use, remediation, storage, treatment, and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, and the risk of injury, contamination or noncompliance with environmental, health

and safety requirements cannot be eliminated. Although compliance with such laws and regulations and permitting requirements has not had a material effect on our capital expenditures, earnings or competitive position, environmental, health and safety laws, and regulations and permitting requirements have tended to become increasingly stringent and, to the extent that legal or regulatory changes may occur in the future, they could result in, among other things, increased costs to us or the impairment of our research, development or production efforts.

C. Organizational structure

We are a Swiss stock corporation (*société anonyme*) organized under the laws of Switzerland. We were formed as a Swiss limited liability company (*société à responsabilité limitée*) on February 13, 2003 with our registered office and domicile in Basel, Switzerland. We converted to a Swiss stock corporation (*société anonyme*) under the laws of Switzerland on August 25, 2003. Our Swiss enterprise identification number is CHE-109.878.825. Our domicile and registered office is in Ecublens, at the École Polytechnique Fédérale Lausanne (EPFL) Innovation Park Building B, 1015 Lausanne, Vaud, Switzerland. Our common shares were admitted to trading on Nasdaq Global Market on September 23, 2016, and trade under the symbol ACIU.

Our general telephone number is (41) 21 345 91 21 and our internet address is www.acimmune.com. References to our website address do not constitute incorporation by reference of the information contained on the website, and the information contained on the website is not part of this document or any other document that we file with or furnish to the SEC. The SEC maintains an internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, which can be found at http://www.sec.gov. Our agent for service of process in the United States is Cogency Global Inc. located at 122 East 42nd Street, 18th Floor, New York, New York 10168.

The Company controls a fully-owned subsidiary, AC Immune USA, Inc. (“AC Immune USA” or “Subsidiary”), which was registered and organized under the laws of Delaware, USA in Q2 2021. The Company and its Subsidiary form the Group.

D. Property, plant and equipment

The Company’s capital expenditures were CHF 0.9 million in 2022 with CHF 0.8 million for laboratory equipment, additional laboratory space and leasehold improvements. These investments were made to enhance our research facilities.

Facilities

We do not own any real property. The table below details the sizes and uses of our leased facilities as of December 31, 2022:

Location	Primary Function	Approximate Size
École Polytechnique Fédérale Lausanne (EPFL) Innovation Park Building B, 1015 Lausanne, Vaud, Switzerland	Headquarters Research, discovery, preclinical and clinical development Chemistry manufacturing and control	27,000 square feet
1230 Avenue of the Americas Suite 1634 New York, New York 10020	U.S. operations	1,600 square feet

The Innovation Park of the EPFL serves as our corporate headquarters, our research facility and laboratories. We believe that using the EPFL facilities instead of building our own infrastructure helps us to maximize the value of our research and development capital and make efficient use of our funds as we continue to build and develop our pipeline. We believe that the space of our existing facilities is sufficient to meet our current needs.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements, including the notes thereto, included in this Annual Report. The following discussion is based on our financial information prepared in accordance with IFRS as issued by the IASB, which might differ in material respects from generally accepted accounting principles in other jurisdictions. The following discussion includes forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those described under "Item 3. Key information—D. Risk factors" and elsewhere in this Annual Report.

A. Operating results

Overview

To date, we have primarily financed our operations through the proceeds from our public offerings, share issuances, contract revenues from license and collaboration agreements and grants. We have no products approved for commercialization and have never generated any revenues from product sales. Pharmaceutical and biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. It may be several years, if ever, before we or our collaboration partners complete pivotal clinical studies and have a product candidate approved for commercialization, and we begin to generate revenue and royalties from product sales. Since our inception, we have received upfront and milestone payments from our collaboration partners and certain other revenue. However, we have also incurred significant operating losses. We incurred net losses of CHF 70.8 million for the fiscal year ended December 31, 2022 and have an accumulated losses balance of CHF 264.0 million as of December 31, 2022.

Strategic collaborations and licensing agreements

Since our inception, we have entered into strategic collaboration agreements with a range of partners covering a number of our product candidates. We entered into a strategic collaboration with Genentech in November 2006 (as amended in March 2009, January 2013, May 2014 and May 2015) regarding the development, manufacture and commercialization of anti-Abeta antibodies including crenezumab, and we refer to this agreement as the 2006 Agreement.

In June 2012, we entered into an additional strategic collaboration agreement with Genentech regarding the development, manufacture and commercialization of anti-Tau antibodies, which covers semorinemab, and we refer to this agreement as the 2012 Agreement. We expect to capitalize on Genentech's drug development and regulatory expertise and commercial capabilities to bring our partnered therapeutic products to market.

In May 2014 (as amended in June 2022), we entered into a license and collaboration agreement with LMI (formerly Piramal Imaging SA) covering our Tau-PET Imaging tracers.

In December 2014 (as amended in April 2016, July 2017, January 2019, November 2019 and December 2022), we entered into a strategic collaboration agreement with Janssen regarding the development, manufacture and commercialization of anti-Tau vaccines, which covers ACI-35. We expect to capitalize on Janssen and Johnson &

Johnson's extensive regulatory expertise and experience in developing, manufacturing and, if approved, commercializing vaccines to bring ACI-35 to market.

We entered into a license agreement with Lilly in December 2018 (as amended in September 2019 and March 2020) to research and develop Morphomer Tau small molecules for the treatment of AD and other neurodegenerative diseases. Under the terms of this agreement, we have completed a Phase 1 clinical study with ACI-3024. Lilly is responsible for leading and funding further clinical development for small molecule Tau aggregation inhibitors with plans to evaluate candidates in AD and NeuroOrphan tauopathies. Lilly will also retain global commercialization rights for all indications.

Genentech, a member of the Roche Group

We have two partnership agreements with Genentech, a company with a reputation for scientific excellence and a history of bringing innovative protein therapeutics to market.

Anti-Abeta antibody in AD – 2006 agreement

In November 2006, we signed an exclusive, worldwide licensing agreement for crenezumab, our humanized monoclonal therapeutic antibody targeting misfolded Abeta. The agreement was amended March 2009, January 2013, May 2014 and May 2015. The agreement also provides for the development of a second therapeutic product for a non-AD indication based on the same intellectual property and anti-Abeta antibody compound. The value of this partnership is potentially greater than USD 340 (CHF 317) million. The structure of the collaboration agreement is as follows:

- A right-of-use license;
- *Clinical milestone payments*: payable upon commencement of each of Phase 1 and Phase 2 of clinical developments, and upon the earlier of Genentech's decision to authorize Phase 3 or the commencement of Phase 3 of clinical developments. In addition, for a second indication, clinical milestone payments would be payable upon commencement of Phase 2 of clinical developments and upon the earlier of Genentech's decision to authorize Phase 3 or the commencement of Phase 3 of clinical developments;
- *Regulatory milestone payments*: payable upon making regulatory filings in the U.S. and Europe, respectively, and milestone payments upon obtaining marketing approval in each of the U.S. and Europe. In addition, for a second indication, additional regulatory and approval milestones would be payable.
- *Royalties*: payable on sales, with different royalty rates applicable in the U.S. and Europe. Royalty levels are tied to annual sales volumes. We may receive royalties on sales of crenezumab with the percentage rates ranging from the mid-single digits to mid-teens.

To date, we have received total milestone payments of USD 65 (CHF 70.1) million comprised of an upfront payment of USD 25 (CHF 31.6) million and of USD 40 (CHF 38.2) million for clinical development milestones achieved, all prior to January 1, 2017.

Under the terms of the agreement, Genentech bears all the costs of developing crenezumab through the clinical phases. In addition, Genentech is responsible for the costs associated with seeking and obtaining regulatory and marketing approvals, along with manufacturing sales and marketing costs. The agreement will terminate by its terms on the date on which all obligations between the parties with respect to the payment of milestones or royalties for licensed products have passed or expired. Either party may terminate the agreement for any material breach by the other Party, provided a cure period of 90 days from the date when that notice is given.

In January 2019, we announced that Roche, the parent of Genentech, is discontinuing the CREAD and CREAD 2 (BN29552 and BN29553) Phase 3 studies of crenezumab in people with prodromal-to-mild sporadic AD.

In August 2022, the Company provided an update on its Alzheimer's Prevention Initiative study evaluating crenezumab in autosomal dominant Alzheimer's disease. Crenezumab did not statistically significantly slow or prevent cognitive decline in people with a specific genetic mutation which causes early-onset Alzheimer's disease. However, numerical differences favoring crenezumab over placebo were observed across the co-primary, multiple secondary and exploratory endpoints. Initial data was presented at the Alzheimer's Association International Conference (AAIC) on August 2, 2022. All participants in the study were offered up to one year of continued treatment (crenezumab for all carriers and placebo for all non-carrier) following the end of the double-blind period while primary results and additional analyses were pending. Final efficacy visits have begun.

Anti-Tau antibody in AD – 2012 agreement

In June 2012, we entered into a second agreement with Genentech to research, develop and commercialize our anti-Tau antibodies for use as immunotherapeutics and diagnostics. The agreement was amended in December 2015. The value of this exclusive, worldwide alliance is potentially greater than CHF 400 million and includes upfront and clinical, regulatory and commercial milestone payments. In addition to milestones, we will be eligible to receive royalties on sales at a percentage rate ranging from the mid-single digits to low-double digits. The agreement also provides for collaboration on at least one additional therapeutic indication outside of AD built on the same anti-Tau antibody program as well an anti-Tau diagnostic product.

To date, we have received payments totaling CHF 59 million, including a milestone payment of CHF 14 million received and recognized in Q4 2017 associated with the first patient dosing in a Phase 2 clinical trial for AD with an anti-Tau monoclonal body known as semorinemab, a milestone payment of CHF 14 million recognized in Q2 2016 and received in July 2016, associated with the announcement of the commencement of the Phase 1 clinical study of semorinemab, and a milestone payment of CHF 14 million received in 2015 in connection with the ED-GO decision.

The structure of the collaboration agreement is as follows.

- A right-of-use license.
- *Preclinical and clinical milestone payments*: payable upon selection of a lead candidate and commencement of each of Phase 1, 2 and 3 of clinical development. In addition, for a second indication, clinical milestone payments would be payable upon commencement of each of Phase 2 and 3 of clinical development.
- *Regulatory milestone payments*: payable upon making regulatory filings for marketing approvals in each of the U.S., Europe and Japan. In addition, for a second indication, similar regulatory milestones would be payable.
- *Commercialization milestones*: payable upon making a first commercial sale in each of the U.S., Europe and Japan. For a second indication, commercialization milestones exist for each of the U.S., Europe and Japan, which are triggered by the first commercial sale for the second indication in each of those jurisdictions.
- *Royalties*: payable on sales with royalty rates differing based on the source of the intellectual property underlying the commercial product. We may receive royalties on sales at a percentage rate ranging from the mid-single digits to low-double digits.

Under the terms of the agreement, Genentech bears all the costs of developing semorinemab through the clinical phases. In addition, Genentech is responsible for the costs associated with seeking and obtaining regulatory and marketing approvals, along with manufacturing, sales and marketing costs. The agreement will terminate by its terms on the date on which all obligations between the parties with respect to the payment of milestones or royalties for licensed products have passed or expired. Either party may terminate the agreement for any material breach by the other Party, provided a cure period of 90 days from the date when that notice is given.

In September 2020, the Company reported that Genentech informed us of top line results from a Phase 2 trial of the anti-Tau antibody, semorinemab, in early (prodromal to mild) Alzheimer's disease (AD) which show that semorinemab

did not meet its primary efficacy endpoint of reducing decline on Clinical Dementia Rating-Sum of Boxes (CDR-SB) compared to placebo. The primary safety endpoint was however met. Two secondary endpoints, ADAS-Cog13 and ADCS-ADL, were not met.

In August 2021, the Company reported that Genentech had informed the Company that the Lauriet study had met one of its co-primary endpoints, ADAS-Cog 11. The second co-primary endpoint, ADCS-ADL, was not met. Safety data showed that semorinemab was well tolerated with an acceptable safety profile and no unanticipated safety signals. In November 2021, the Company reported that Genentech had presented the full top-line data from the Lauriet study during a late-breaking session at the 14th Clinical Trials on Alzheimer's Disease conference.

Janssen Pharmaceuticals, Inc.

Tau Vaccine in AD – 2014 agreement

In December 2014, we entered into an agreement with Janssen Pharmaceuticals, Inc. (Janssen), part of the Janssen Pharmaceutical Companies of Johnson & Johnson, to develop and commercialize therapeutic anti-Tau vaccines for the treatment of AD and potentially other Tauopathies. The value of this collaboration is potentially up to CHF 500 million and includes upfront and clinical, regulatory and commercial milestones. In addition to milestones, we will be eligible to receive royalties on sales at a percentage rate ranging from the high-single digits to the mid-teens for the phospho-Tau vaccine program. In April 2016, July 2017, January 2019, November 2019 and December 2022, the companies entered into the first, second, third, fourth and fifth amendments, respectively. These amendments allow for the alignment of certain payment and activity provisions with the Development Plan and Research Plan activities. We and Janssen have completed the co-development of the second-generation lead therapeutic vaccines, ACI-35.030 and JACI-35.054, through Phase 1b/2a. In November 2022, it was announced that ACI-35.030 was selected to advance into further development based on interim data from the ongoing Phase 1b/2a trial. AC Immune and Janssen will jointly share research and development costs until the completion of the first Phase 2b (AC Immune's contribution to the first Phase 2b trial is capped). From Phase 2b and onwards, Janssen will assume responsibility for the clinical development, manufacturing and commercialization of ACI-35.030.

The Company received an upfront, non-refundable license fee of CHF 25.9 million, which we recognized as revenue in 2014. In May 2016, we received a payment of CHF 4.9 million for reaching a clinical milestone in the Phase 1b study. As we met all performance obligations on reaching the milestone, we recognized this milestone as revenue.

The structure of the collaboration agreement is as follows:

- A right-of-use license.
- *Clinical milestone payments*: payable upon reaching certain milestones in the Phase 1b study, commencement of the first Phase 2b or 2b/3 of clinical development, upon reaching enrollment thresholds in the first Phase 2b or Phase 2b part of the first Phase 2b/3, commencement of the first Phase 3 or Phase 3 part of a Phase 2b/3 study. In addition, for a second indication, clinical milestone payments would be payable upon commencement of a Phase 3 clinical study, which would be payable concurrently with the first regulatory milestone, if Janssen were to file for regulatory approval based on Phase 2 clinical data.
- *Regulatory milestone payments*: payable upon making regulatory filings in the U.S., Europe, and Japan, respectively. In addition, for a second indication, similar regulatory milestones would be payable. For a second indication, additional regulatory milestone payments are payable by Janssen to us upon receipt of each of the regulatory approvals in the U.S., Europe and Japan.
- *Commercialization milestones*: payable upon making a first commercial sale in each of the U.S., Europe and Japan, and upon achieving certain commercial milestones.

- *Royalties*: payable on sales, with royalty rates differing based on the level of annual sales. We may receive royalties on sales at a percentage rate ranging from the high-single digits to the mid-teens for the phospho-Tau vaccine program.

Under the terms of the agreement, Janssen may terminate the agreement at any time after completion of the first Phase 1b clinical study in 2016 by providing 90 days' notice to us. If not otherwise terminated, the agreement shall continue until the expiration of all royalty obligations as outlined in the contract.

LMI (formerly Piramal Imaging SA)

Tau-PET imaging agent – 2014 agreement

In May 2014 (as amended in June 2022), we entered into an agreement, our first diagnostic partnership, with LMI, the former Piramal Imaging SA. The partnership with LMI is an exclusive, worldwide licensing agreement for the research, development and commercialization of the Company's Tau protein PET tracers supporting the early diagnosis and clinical management of AD and other Tau-related disorders and includes upfront and sales milestone payments totaling up to EUR 160 (CHF 159) million, plus royalties on sales at a percentage rate ranging from mid-single digits to low-teens. LMI may terminate the LCA at any time by providing 3 months' notice to us.

The structure of the collaboration agreement is as follows:

- A right-of-use license.
- *Clinical milestone payments*: payable upon the commencement of the Phase 1, 2 and 3 studies for generation of data intended to support a regulatory submission in the U.S. or the EU. We would be entitled to further clinical milestone payments for the commencement of a Phase 2 and 3 study for a second indication.
- *Regulatory milestone payments*: payable upon acceptance of Regulatory filing (NDA) and Regulatory approval for Commercialization in the U.S. or the EU.
- *Commercialization milestones*: tied to specific annual net sales amounts.
- *Royalties:* payable on sales, with royalty rates differing based on the level of annual sales. We may receive royalties on sales at a percentage rate ranging from the mid-single digits to the low-teens.

Eli Lilly and Company

Morphomer Tau small molecule – 2018 license agreement

In December 2018, we entered into an exclusive, worldwide licensing agreement with Eli Lilly and Company (Lilly) to research and develop Morphomer Tau small molecules for the treatment of AD and other neurodegenerative diseases. Per the terms of the agreement, the Company received an initial upfront payment of CHF 80 million in Q1 2019 for the rights granted by the Company to Lilly. To date, the Company has completed a Phase 1 clinical study with ACI-3024.

Additionally, the Company and Lilly have continued candidate characterization across the research program, identifying new and highly differentiated candidates with desired cerebrospinal fluid exposure and selectivity for pathological aggregated Tau. These will be broadly developed in Tau-dependent neurodegenerative diseases by Lilly. Lilly is responsible for leading and funding further clinical development and will retain global commercialization rights for all indications.

Per the terms of the agreement, the Company may become eligible to receive additional milestone payments totaling up to approximately CHF 1.9 billion. In addition to milestones, we will be eligible to receive royalties on sales at a percentage rate ranging from the low double-digits to the mid-teens. The agreement became effective in January 2019

when the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, expired. In Q3 2019, the Company and Lilly entered into the first amendment to divide the first discretionary milestone payment under the agreement of CHF 60 million into two installments with the first CHF 30 million paid in Q3 2019 and the second CHF 30 million to be paid on or before March 31, 2020 unless Lilly terminated the agreement earlier. In Q1 2020, the Company and Lilly entered into a second amendment to replace the second CHF 30 million to be paid on or before March 31, 2020 with two milestone payments, one of CHF 10 million to be paid on or before March 31, 2020 and the other of CHF 60 million following the first patient dosed in a Phase 2 clinical study of a licensed product in the U.S. or the EU.

The Company received an initial upfront payment of CHF 80 million in February 2019. We used the residual approach to estimate the selling price for the right-of-use license and an expected cost plus margin approach for estimating the research and development activities. The right-of-use license was delivered on the effective date. The research and development activities were delivered over time as the services were performed. For these services, revenue was recognized over time using the input method, based on costs incurred to perform the services, as the level of costs incurred over time is thought to best reflect the transfer of services to Lilly.

The structure of the collaboration agreement is as follows.

- *An exclusive license:* granted by us to Lilly under certain of our intellectual property to develop, manufacture and commercialize products containing Morphomer Tau small molecules for the treatment of AD and other neurodegenerative diseases throughout the world in any indication.

- *Clinical milestone payments*: payable upon completion of the Lilly preclinical activities period and following the first patient dosed in a Phase 2 and Phase 3 clinical study of a licensed product in the U.S. or the EU.

- *Regulatory milestone payments*: payable within 60 days after obtaining regulatory approval for any licensed product in the first indication and any licensed product in certain additional indications in the U.S., Europe and Japan, respectively.

- *Commercialization milestones*: payable upon achieving certain commercial sales milestones.

- *Royalties*: payable on sales with royalty rates differing based on the level of annual sales of licensed products. We may receive royalties on sales at a percentage rate ranging from the low double-digits to the mid-teens.

The agreement will terminate by the date of expiration of the last royalty term for the last licensed product. However, under the terms of the agreement, Lilly may terminate the agreement at any time after March 31, 2020 by providing 3 months' notice to us.

We and Lilly also entered into a convertible note agreement that became effective in January 2019 for USD 50 (CHF 50.3) million from Lilly. In Q2 2019, the Convertible Note Agreement with Lilly automatically converted in line with the terms of the agreement. As a result of this conversion, 3,615,328 of our common shares were issued to Lilly. This note is now fully settled and there is no further equity or cash consideration due to Lilly thereunder.

Grants

Michael J. Fox Foundation for Parkinson's Research

In May 2020, the Company, as part of a joint arrangement with Skåne University Hospital (Skåne) in Sweden, was awarded a USD 3.2 (CHF 3.0) million grant from the MJFF's Ken Griffin Alpha-synuclein Imaging Competition. As part of this grant, AC Immune is eligible to receive USD 2.5 (CHF 2.3) million directly from the MJFF. Skåne will receive USD 0.7 (CHF 0.7) million of the total grant directly from the MJFF over two years to conduct and support the clinical arm of the project. In August 2022, the Company received follow-on grant funding as part of its joint arrangement with Skåne totaling USD 0.5 (CHF 0.5) million for the continued development of its alpha-synuclein PET

imaging diagnostic agent. As part of this grant, the Company received USD 0.4 (CHF 0.4) million directly from the MJFF. Skåne will receive USD 0.1 (CHF 0.1) million of the total grant directly from the MJFF over the duration of the grant period.

In December 2021, the Company announced that it had been awarded two grants totaling USD 1.5 (CHF 1.4) million to advance small molecule PD programs. One award will support an existing early-stage program to develop small molecules that can prevent intracellular aggregation and spreading of a-syn. The other award will fund research on the therapeutic potential of chemically and mechanistically novel, brain penetrant small molecule inhibitors of NLRP3 inflammasome activation for the treatment of PD.

Grant from the Target ALS Foundation

In Q1 2021, AC Immune was awarded a USD 0.3 (CHF 0.2) million grant from Target ALS. This grant funds a collaboration between the Company and the Investigators at the Healey Center for ALS at Massachusetts General Hospital (MGH) to accelerate the development of the Company's proprietary immunoassays to detect disease-associated forms of TDP-43 in CSF and blood samples. The Company was awarded an additional one-year grant in December 2022 for USD 0.1 (CHF 0.1) million to continue the project.

Critical accounting policies and significant judgments and estimates

Revenue recognition

In May 2014, the IASB issued IFRS 15 *Revenue from Contracts with Customers,* which amends the guidance for accounting for revenues from contracts with customers. This IFRS replaces all current revenue standards in IFRS including IAS 11 *Construction Contracts*, IAS 18 *Revenue* and various interpretations.

This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under IFRS 15, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of IFRS 15, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company applies the five-step model to contracts only when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of IFRS 15, the Company assesses the goods or services promised within each contract, and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Contract revenue. The Company enters into LCAs, which are within the scope of IFRS 15, under which it licenses certain proprietary rights to its product candidates and intellectual property to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, upfront license fees, development, regulatory and/or commercial milestone payments, payments for research and clinical services the Company provides through either its full-time employees or third-party vendors, and royalties on net sales of licensed commercialized products depending on the Company's intellectual property. Each of these payments results in license, collaboration and other revenues, which are classified as contract revenue on the consolidated statements of income/(loss).

Licenses of intellectual property. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are sold in conjunction with a related service, the Company uses

judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the performance obligation is settled over time, the Company determines the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments. At the inception of each arrangement that includes development, regulatory and/or commercial milestone payments, the Company evaluates whether the milestones are considered highly probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is highly probable that a significant cumulative revenue reversal would not occur in future periods, the associated milestone value is included in the transaction price. These amounts for the performance obligations under the contract are recognized as they are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments recorded would affect contract revenues and earnings in the period of adjustment.

Research and development services. The Company has certain arrangements with our collaboration partners that include contracting our employees for research and development programs. The Company assesses if these services are considered distinct in the context of each contract and, if so, they are accounted for as separate performance obligations. These revenues are recorded in contract revenue as the services are performed.

Sublicense revenues. The Company has certain arrangements with our collaboration partners that include provisions for sublicensing. The Company recognizes any sublicense revenues at the point in time it is highly probable to obtain and not subject to reversal in the future.

Contract balances: The Company receives payments and determines credit terms from its customers for its various performance obligations based on billing schedules established in each contract. The timing of revenue recognition, billings and cash collections results in billed other current receivables, accrued income (contract assets), and deferred income (contract liabilities) on the consolidated balance sheets. Amounts are recorded as other current receivables when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be 1 year or less.

Accrued research and development costs

We record accrued expenses for estimated costs of our research and development activities conducted by third-party service providers, which include among others the conduct of preclinical studies and clinical studies and contract manufacturing activities. We record accrued expenses for estimated costs of our research and development activities based upon the estimated amount of services provided but not yet invoiced, and we include these costs in accrued expenses on the consolidated balance sheets and within research and development expenses in the consolidated statements of income/(loss). These costs are a significant component of our research and development expenses.

We record accrued expenses for these costs based on the estimated amount of work completed in accordance with agreements established with these third parties, which involves the following process:

- communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs;

- estimating and accruing expenses in our consolidated financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and

- periodically confirming the accuracy of our estimates with selected providers and adjusting, if necessary.

Examples of estimated research and development expenses that we accrue include:

- fees paid to CROs in connection with preclinical and toxicology studies and clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to CMOs in connection with the production of our product candidates prior to qualifying for capitalization as inventory; and
- professional service fees for consulting and related services.

We base our expense accruals related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and clinical CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical study milestones. Our service providers predominantly invoice us monthly in arrears for services performed. In accruing service fees, we estimate the time period over which the services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

To date, we have not experienced significant changes in our estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, we may be required to make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies and other research activities.

Share-based compensation

Options

The Company operates an equity-settled, share-based compensation plan. The fair value of the employee services received in exchange for the grant of equity-based awards is recognized as an expense. The total amount to be expensed over the vesting period is determined by reference to the fair value of the instruments granted, excluding the impact of any non-market vesting conditions. Non-market vesting conditions are included in assumptions about the number of instruments that are expected to become exercisable. At each balance sheet date, the Company revises its estimates of the number of instruments that are expected to become exercisable. It recognizes the impact of the revision of original estimates, if any, prospectively in the consolidated statements of income/(loss), and a corresponding adjustment to equity over the remaining vesting period.

We estimate the fair value of all time-vested options as of the date of grant using the Black-Scholes option-pricing model. Key assumptions in determining the fair value of share options granted utilizing the Black-Scholes valuation method include the following:

Assumption	Method of estimation
● Estimated expected term of options	● Simplified method
● Expected volatility	● The Company's actual volatility for the period congruent with the expected term of the underlying option
● Risk-free interest rate	● Yields of long-dated U.S. Treasury notes
● Expected dividends	● Zero percent as dividends have not been paid
● Forfeiture rates	● Historical and expected forfeiture data

Restricted share units

We estimate the fair value of restricted share units using a reasonable estimate of market value of the common shares on the date of the award. We classify our share-based payments as equity-classified awards as they are settled in our common shares. We measure equity-classified awards at their grant date fair value and do not subsequently re-measure them. Compensation costs related to equity-classified awards are equal to the fair value of the award at grant date amortized over the vesting period of the award using the graded method. We reclassify that portion of vested awards to share premium as the awards vested.

Right-of-use assets and lease liabilities

The Company applies IFRS 16 *Leases*, which provides the model for lessee accounting in which all leases, other than short-term and low-value leases, are accounted for by the recognition on the consolidated balance sheet of a right-of-use asset and a lease liability, and the subsequent amortization of the right-of-use asset over the earlier of the end of the useful life or the lease term. In accordance with IFRS 16, the Company (i) does not recognize right-of-use assets and lease liabilities for leases of low value (i.e. approximate fair value of USD 5,000). For a complete discussion of accounting, see "Note 5. Right-of-use assets, long-term financial assets and lease liabilities."

In-process research and development (IPR&D) asset

The Company's acquired IPR&D asset is stated at cost less any impairments. Our IPR&D asset is subject to impairment testing at least annually or when there are indications that the carrying value may not be recoverable until the completion of the development process. At that point, the capitalized amounts are amortized over their estimated useful life. The determination of the recoverable amounts include key estimates which are highly sensitive to, and depend upon, key assumptions.

The Company will not capitalize future development costs in respect to this IPR&D asset until they meet the criteria for capitalization of research and development costs in accordance with IAS 38 *Intangible Assets*.

Net employee defined benefit liabilities

The Company operates the mandatory pension schemes for its employees in Switzerland. The schemes are generally funded through payments to insurance companies. The Company has a pension plan designed to pay pensions based on accumulated contributions on individual savings accounts. However, this plan is classified as a defined benefit plan under IAS 19.

The net defined benefit liability is the present value of the defined benefit obligation at the balance sheet date minus the fair value of plan assets. Significant estimates are used in determining the assumptions incorporated in the calculation of the pension obligations, which is supported by input from independent actuaries. The defined benefit obligation is calculated annually with the assistance of an independent actuary using the projected unit credit method, which reflects services rendered by employees to the date of valuation, incorporates assumptions concerning employees' projected salaries and pension increases as well as discount rates of highly liquid corporate bonds that have terms to maturity approximating the terms of the related liability.

To the extent that the fair value of the plan assets is greater than the present value of the defined benefit obligation as calculated by our independent actuary, the Company accounts for the effect of the asset ceiling test under IAS 19.

Re-measurements of the net defined benefit liability, which comprise actuarial gains and losses and the return on plan assets (excluding interest) are recognized immediately in the consolidated statements of other comprehensive income/(loss). Past service costs, including curtailment gains or losses, are recognized immediately as a split in research and development and general and administrative expenses within the operating results. Settlement gains or losses are recognized in either research and development and/or general and administrative expenses within the operating results. The Company determines the net interest expense/(income) on the net defined benefit liability for the period by applying the discount rate used to measure the defined benefit obligation at the beginning of the annual period or in case of any

significant events between measurement dates to the then-net defined benefit liability, considering any changes in the net defined benefit liability during the period as a result of contributions and benefit payments. Net interest expense/(income) and other expenses related to defined benefit plans are recognized in the consolidated statements of income/(loss).

Results of operations

The Covid-19 global pandemic has impacted various countries in which AC Immune currently operates clinical trials and business operations. The extent to which Covid-19 may impact us will depend on future developments, which are currently uncertain and cannot be predicted with confidence, such as the duration of the outbreak, the severity of Covid-19, or the effectiveness of actions to contain and treat Covid-19.

The Company continues to effect its business continuity plan and adapt as the situation evolves. Since 2021, we have resumed normal operations at full capacity, with minimal disruption to our business. We are continuously assessing and adapting our working practices and business operations to ensure compliance with official guidance and orders related to the pandemic and are working proactively with our partners and other stakeholders to take steps intended to mitigate and minimize any negative impact to our research, clinical programs and other business operations.

The Company does not currently have or project material impacts to the ongoing key trials. Additionally, the Company has drug supplies that are expected to be sufficient to complete ongoing trials as well as additional drug substance supplies expected to be sufficient to support ongoing cohorts of clinical trials for a period of at least three to six months. The Company will refrain from starting new clinical trials if a minimum of a six-month supply on hand cannot be secured. Finally, the Company currently does not expect delays to its clinical trials due to manufacturing or supply-chain issues.

Financial operations overview

Contract revenues

Given our stage of development, we have not generated any revenue from product sales. Our contract revenues to date have been derived primarily from separate license and collaboration agreements on some of our product candidates in various stages of preclinical and clinical development.

Our contract revenues have experienced fluctuations over the past three years as a result of the timing of milestone achievement and the size of each milestone payment. We expect that any revenue we generate from our collaboration agreements with each of Lilly, Genentech, Janssen and LMI and/or from any other current or future collaboration partners will fluctuate from year to year as a result of the timing and amount of milestones and other payments.

Research and development expenses

Research and development costs are expensed as incurred, and consist of salaries and benefits, laboratory supplies, materials, intellectual property, facility and information technology (IT) costs, as well as fees paid to other non-employees and entities that conduct certain research and development activities on our behalf and all other allocated expenses. Amounts incurred in connection with license and collaboration agreements are also included in research and development expense. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until those goods or services are received.

Clinical trial costs are a component of research and development expenses. We accrue and expense clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with clinical CROs and clinical sites. We determine the actual costs through monitoring patient enrollment and discussions with internal personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Manufacturing start-up costs are a component of research and development expenses. Additionally, manufacturing costs incurred after regulatory approval but in connection with significant changes and/or enhancements to the approved manufacturing process are recorded as research and development expenses. We accrue and expense the manufacturing activities performed by third parties based upon actual work completed in accordance with agreements established with contract manufacturers.

Our investment in research and development activities, including the clinical development of our product candidates has historically been and is projected to be more than 75% of our total annual operating costs. Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our product candidates, as well as development of new product candidates from our SupraAntigen and Morphomer platforms and the development of product candidates pursuant to our collaboration agreements with Lilly, Genentech, Janssen and LMI. We recognize all research and development costs as they are incurred. Clinical study costs, contract manufacturing and other development costs incurred by third parties are expensed as the contracted work is performed. At present, most of our research activities comprise three major areas:

- AD;
- focused non-AD NDD including Parkinson's disease, ALS and NeuroOrphan indications; and
- diagnostics.

We expect our research and development expenses to continue to increase in the future and expect to fund a broader number of projects, which will impact our research strategy in four key ways:

(i) we expect to undertake later-stage research and development for certain of our product candidates and, if approved, to take some of those product candidates into commercialization;

(ii) we will allocate more funding to existing programs to advance the development of these programs;

(iii) we will increase our research and development efforts on non-AD indications including NeuroOrphans and diagnostics; and

(iv) we will initiate a number of new research initiatives that are complementary to our existing and planned research initiatives.

We expect that our total future research and development costs will increase over current levels in line with our three-pillar strategy that focuses on (i) AD, (ii) focused non-AD NDD including Parkinson's disease, ALS and NeuroOrphan indications and (iii) diagnostics.

General and administrative expenses

General and administrative expenses include personnel costs, expenses for outside professional services and all other allocated expenses. Personnel costs consist of salaries, cash bonuses, benefits and share-based compensation. Outside professional services consist of legal, accounting and audit services, IT and other consulting fees. Allocated expenses consist of certain IT, facilities and depreciation expenses. We continue to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC, and those of any national securities exchange on which our securities are traded (Nasdaq), additional insurance expenses, investor relations activities and other administrative and professional services.

Other operating income/(expense), net

Other operating income/(expense) consists primarily of income associated with foundation grants such as those from the MJFF or Target ALS.

Finance result, net

Financial income and expenses include bank fees associated with charges levied by banks on foreign payments, interest income and expense associated with our cash balances and interest expense associated with lease liabilities. For the year ended December 31, 2021, we recognized a gain on the change in fair value of derivative financial assets associated with two convertible notes sold to certain Affiris affiliated entities that did not occur in the current or comparable prior period.

Exchange differences consist of foreign exchange transactions and re-measurement gains and losses that arise from our cash being held in currency other than Swiss Francs, certain collaboration agreements such as the collaboration agreements with Genentech and LMI being denominated in currencies other than Swiss Francs, and selected purchases, which we effect in foreign currencies.

Taxation

AC Immune is subject to corporate Swiss federal, cantonal and communal taxation, respectively, in Switzerland, Canton of Vaud, Commune of Ecublens, near Lausanne. We are also subject to taxation in other jurisdictions in which we operate, in particular, the United States where our wholly-owned subsidiary is incorporated.

We are entitled under Swiss laws to carry forward any losses incurred for a period of 7 years and can offset our losses carried forward against future taxes. As of December 31, 2022, we had tax loss carry-forwards totaling CHF 264.1 million (provisional amount; tax loss is definitively recognized by Swiss tax authorities once set-off against taxable income). There is no certainty that we will make sufficient profits to be able to utilize these tax loss carry-forwards in full.

The effective corporate income tax rate (federal, cantonal and communal) where we are domiciled is currently 13.6%.

As of January 1, 2020, the Company may request for 2020 and future tax years a tax relief of 60%, which would be applied to income from patents and similar rights at the communal and cantonal levels. This relief would first require the reintegration of all expensed and deducted research and development costs related to the concerned patents and similar rights for consideration in our taxable results from the prior ten years. The Company has not currently made any decision to enter this patent box system. Additionally, a “super-deduction” may be granted for payroll and other expenses of research and development of Swiss origins.

However, the aforementioned tax relief based on the patent box and deductions for research and development may not exceed 50% of the overall taxable profit before these tax relief and deductions.

Notwithstanding the corporate income tax, the corporate capital is taxed at a rate of 0.1305% (cantonal and communal tax only, as there is no federal tax on capital).

Value added tax (VAT) is charged on all qualifying goods and services supplied by VAT-registered businesses. Rates vary based on category, but the Company applies a standard rate of 7.7% (the standard rate will increase to 8.1% as of January 1, 2024) on the value of the goods or services to all sales invoices, which is payable to the Swiss tax authorities. Similarly, VAT paid on purchase invoices is reclaimable from the Swiss tax authorities.

Results of operations

The numbers below have been derived from our audited consolidated financial statements included elsewhere in this Annual Report. The discussion below should be read along with these consolidated financial statements and it is qualified in its entirety by reference to them.

Comparison of the years ended December 31, 2022 and 2021

Contract revenue

For the year ended December 31, 2022, AC Immune generated CHF 3.9 million in contract revenues compared with nil for the comparable period in 2021. This represents an increase of CHF 3.9 million. The following table summarizes our contract revenues during the years ended December 31, 2022 and 2021:

	For the Year Ended December 31,		
In CHF thousands	2022	2021	Change
Contract revenue	3,935	—	3,935
Total revenue	3,935	—	3,935

Our contract revenues experience fluctuations as a result of securing new collaboration agreements, the timing of milestone achievements and the size of each milestone payment. For the year ended December 31, 2022, our contract revenues were wholly related to the progression of the Tau-PET Tracer PI-2620 into late-stage development in AD per our agreement with LMI.

Research and development expenses

Research and development activities are essential to our business and represent the majority of our costs incurred. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using information from the clinical sites and our vendors. Our collaboration arrangements have different arrangements to share costs for the development of our product candidates.

We have completed our R&D spending in both of our Genentech collaborations. Additionally, we have completed our co-development costs with Janssen for the Phase 1b/2a studies for our therapeutic vaccines, ACI-35.030 and JACI-35.054. AC Immune and Janssen will jointly share research and development costs until the completion of the first Phase 2b (AC Immune's contribution to the first Phase 2b trial is capped). From Phase 2b and onwards, Janssen will assume responsibility for the clinical development, manufacturing and commercialization of the second-generation vaccines.

We intend to increase our R&D costs associated with the advancement of ACI-7104.056 in Parkinson's disease and our ACI-24.060 vaccine through mid- and late-stage clinical development. Finally, we expect to incur additional R&D expenditures associated with the expansion of our Morphomer Tau program into AD and potentially NeuroOrphan indications, as well as, investments in our diagnostic programs.

Finally, we intend to further characterize our other clinical and preclinical candidates. In addition to these arrangements and proprietarily held assets, we expect that our total future R&D costs will increase over current levels, in line with our three-pillar strategy that focuses on (i) AD, (ii) focused non-AD NDD including Parkinson's disease, ALS and NeuroOrphan indications and (iii) diagnostics.

The table below provides a breakdown of our research and development costs, including direct research and development costs, manufacturing costs related to research and development and other research and development costs not allocated directly to programs for the periods covered by this Annual Report. The research and development costs not allocated to specific programs include employment costs, regulatory, QA and intellectual property costs. We do not assign our internal costs, such as salary and benefits, share-based compensation expenses, laboratory supplies, and other direct expenses and infrastructure costs to individual R&D projects, because the employees within our R&D groups are typically deployed across multiple research and development programs.

For the year ended December 31, 2022, research and development expenses totaled CHF 60.3 million compared with CHF 62.3 million for the comparable period in 2021. This represents a decrease of CHF 2.0 million. The following table presents the research and development expenses during the years ended December 31, 2022 and 2021:

Detailed research and development expenditures by major development category

In CHF thousands	For the Year Ended December 31, 2022	2021	Change
Discovery and preclinical expenses	16,889	19,963	(3,074)
Clinical expenses	13,089	14,872	(1,783)
Group function expenses	1,574	929	645
Total direct R&D expenses	31,552	35,764	(4,212)
Payroll expenses	17,548	16,465	1,083
Share-based compensation	1,622	1,528	94
Other non-allocated	9,614	8,525	1,089
Total R&D expenses	60,336	62,282	(1,946)

In CHF thousands	For the Year Ended December 31, 2022	2021	Change
Operating expenses[1]	41,166	44,289	(3,123)
Salaries and related costs[2]	19,170	17,993	1,177
Total R&D expenses	60,336	62,282	(1,946)

[1]Includes depreciation expenses

[2]Includes share-based compensation

For the year ended December 31, 2022:

Discovery and preclinical expenses decreased CHF 3.1 million, primarily due to:

- a decrease in ACI-24.060 for DS of CHF 2.3 million for the development costs due to the completion of the vaccine formulation which has been advanced into clinical studies and CHF 0.6 million for our anti-TDP-43 antibody due to the completion of *in vivo* efficacy studies in the prior year and CHF 1.3 million for certain other discovery programs,

partially offset by:

- an increase of CHF 1.1 million associated with investments in our ACI-7104.056 vaccine, our alpha-synuclein vaccine for Parkinson's disease acquired in Q4 2021.

Clinical expenses decreased by CHF 1.8 million, primarily due to:

- a decrease of CHF 5.9 million for the clinical development of ACI-35.030 driven by timing of activities across various cohorts started in prior years and expenses associated with the R&D cost sharing, CHF 1.1 million for ACI-24.060 for AD as the prior clinical trial completed and CHF 0.6 million for Morphomer Tau program as we expand the development of other preclinical candidates,

partially offset by:

- an increase of CHF 3.2 million for the clinical development of ACI-7104.056, which were largely not incurred in the prior period as the asset was acquired in H2 2021 and CHF 2.6 million for the initiation of our Phase 1b/2a ABATE study for our ACI-24.060 vaccine.

The variances in Group function expenses relate to regulatory and quality assurance, intellectual property and other non-allocated costs.

Total salaries and related costs increased by CHF 1.2 million, primarily due to:

- an increase in salary- and benefit-related costs of CHF 1.1 million primarily related to new hires during the year and annualization of 2021 hires.

The CHF 1.1 million increase in other non-allocated expenses relate to certain non-allocated functional expenses, primarily due to:

- an increase of CHF 0.8 million associated with targeted IT investments such as our electronic laboratory notebook implementation and maintenance as well as R&D consultants; and

- CHF 0.3 million in other items.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs, including share-based compensation, professional fees such as legal and accounting related services, infrastructure expenses, and other operating expenses.

For the year ended December 31, 2022, general and administrative expenses totaled CHF 15.8 million compared with CHF 17.9 million for the comparable period in 2021. This represents a decrease of CHF 2.1 million. The following table presents the general and administrative expenses during the years ended December 31, 2022 and 2021:

	For the Year Ended December 31,		
In CHF thousands	**2022**	**2021**	**Change**
Operating expenses[1]	6,207	7,031	(824)
Salaries and related costs[2]	9,582	10,879	(1,297)
Total general and administrative expenses	15,789	17,910	(2,121)

[1]Includes depreciation expenses

[2]Includes share-based compensation

For the year ended December 31, 2022, this decrease is primarily due to:

- CHF 1.1 million for transaction costs associated with our asset acquisition in the prior year for a portfolio of therapeutics targeting alpha-synuclein from Affiris which did not repeat in 2022; and
- a decrease of CHF 1.3 million in personnel expenses, largely driven by a CHF 0.9 million decrease in share-based compensation expense associated with the forfeiture of awards to a former member of management,

partially offset by:

- a CHF 0.3 million increase driven largely by increased audit and reporting fees as well as professional services.

Other operating income/(expense), net

For the year ended December 31, 2022, other operating income/(expense) totaled CHF 1.3 million in income compared with CHF 1.2 million in income for the comparable period in 2021. This represents an increase of CHF 0.1 million. The following table presents the other operating income/(expense) during the years ended December 31, 2022 and 2021:

	For the Year Ended December 31,		
In CHF thousands	2022	2021	Change
Other operating income/(expense), net	1,343	1,182	161
Total other operating income/(expense), net	1,343	1,182	161

For the year ended December 31, 2022, this increase is primarily due to:

- an increase of CHF 0.1 million associated with ongoing grants from the MJFF.

Finance result, net

For the year ended December 31, 2022, finance result was a CHF 0.1 million gain compared with a CHF 6.0 million gain for the comparable period in 2021. This represents a decrease of CHF 5.9 million. The following table presents the finance result during the years ended December 31, 2022 and 2021:

	For the Year Ended December 31,		
In CHF thousands	2022	2021	Change
Financial income	69	6,485	(6,416)
Financial expense	(355)	(581)	226
Exchange differences	393	113	280
Finance result, net	107	6,017	(5,910)

Net finance result was a gain, which primarily decreased related to:

- a decrease of CHF 6.4 million in financial income, predominantly related to a CHF 6.5 million gain associated in the change of fair value of derivative financial assets associated with two convertible notes sold to certain Affiris affiliated entities in the prior period which did not repeat in the current period,

partially offset by:

- a CHF 0.2 million decrease in financial expense due to the transition from negative to positive interest rates during the year for our interest-bearing deposit accounts; and
- a CHF 0.3 million increase in favorable foreign currency exchange differences related to movement in the CHF versus foreign currencies, predominantly the US Dollar and Euro.

Non-IFRS financial measures

In addition to our operating results, as calculated in accordance with IFRS, as adopted by the IASB, we use adjusted loss and adjusted loss per share when monitoring and evaluating our operational performance. Adjusted loss is defined as loss for the relevant period, as adjusted for certain items that we believe are not indicative of our ongoing operating performance. Adjusted loss per share is defined as adjusted loss for the relevant period divided by the weighted-average number of shares for such period.

We believe that these measures assist our shareholders because they enhance the comparability of our results each period and provide more useful insight into operational results for the period. The Company's executive management uses these non-IFRS measures to evaluate our operational performance. These non-IFRS financial measures are not meant to be considered alone or as substitutes for our IFRS financial measures, and should be read in conjunction with our consolidated financial statements prepared in accordance with IFRS. The most directly comparable IFRS measure to these non-IFRS measures is net loss. The following table reconciles net loss to adjusted loss and adjusted loss per share for the periods presented:

Reconciliation of loss to adjusted loss and loss per share to adjusted loss per share

	For the Year Ended December 31,		
In CHF thousands, except for share and per share data	**2022**	**2021**	**2020**
Loss	**(70,753)**	**(72,996)**	**(61,921)**
Adjustments:			
Non-cash share-based payments[1]	3,330	4,126	4,088
Foreign currency (gains)/losses[2]	(521)	70	703
Change in fair value of derivative financial assets[3]	—	(6,459)	—
Transaction costs[4]	—	1,144	—
Adjusted loss	**(67,944)**	**(74,115)**	**(57,130)**
Loss per share – basic and diluted	(0.85)	(0.97)	(0.86)
Adjustment to loss per share – basic and diluted	0.04	(0.02)	0.07
Adjusted loss per share – basic and diluted	**(0.81)**	**(0.99)**	**(0.79)**
Weighted-average number of shares outstanding Adjusted loss – basic and diluted	83,554,412	74,951,833	71,900,212

[1]Reflects non-cash expenses associated with share-based compensation for equity awards issued to directors, management and employees of the Company. This expense reflects the awards' fair value recognized for the portion of the equity award which is vesting over the period.
[2]Reflects foreign currency re-measurement gains and losses for the period, predominantly impacted by the change in the exchange rate between the U.S. Dollar and the Swiss Franc.
[3]Reflects the change in the fair value of the derivative financial instruments associated with two convertible notes sold to certain Affiris affiliated entities.
[4]Reflects transaction costs associated with our asset acquisition for a portfolio of therapeutics targeting alpha-synuclein.

The Company also discloses liquidity, which is defined as a financial indicator comprised of cash and cash equivalents and short-term financial assets. See "Note 3. Summary of significant accounting policies" to our consolidated financial statements for further definition.

B. Liquidity and capital resources

Cash flows

Comparison of the years ended December 31, 2022 and 2021

The following table summarizes our cash flows for the periods indicated:

In CHF thousands	For the Year Ended December 31, 2022	2021	Change
Net cash provided by/ (used in):			
Operating activities	(73,568)	(65,689)	(7,879)
Investing activities	23,763	(53,664)	77,427
Financing activities	(1,346)	40,746	(42,092)
Net decrease in cash and cash equivalents	(51,151)	(78,607)	27,456

Operating activities

Net cash used in operating activities was CHF 73.6 million for the year ended December 31, 2022 compared with net cash used in operating activities of CHF 65.7 million for the year ended December 31, 2021. The change in cash used in operating activities for the year ended December 31, 2022 was due to the Company incurring a net loss of CHF 70.8 million for the year ended December 31, 2022 compared with net loss of CHF 73.0 million for the same period in 2021, which was driven by (i) an increase of CHF 1.7 million in prepaid expenses (ii) a CHF 6.1 million decrease in accrued expenses, offset by (i) a CHF 6.5 million gain on the change in fair value of derivative financial assets associated with two convertible notes sold to certain Affiris affiliated entities in 2021 which did not repeat in the current period.

Investing activities

Net cash provided by investing activities was CHF 23.8 million for the year ended December 31, 2022 compared with net cash used in by investing activities of CHF 53.7 million for the year ended December 31, 2021. CHF 25.0 million of short-term financial assets matured for the year ended December 31, 2022, compared to a net investment of CHF 51.0 million of short-term financial assets in the prior period. Additionally, the Company spent CHF 1.2 million on property, plant and equipment, predominantly to enhance its laboratory and facilities.

Financing activities

Net cash used in financing activities was CHF 1.3 million for the year ended December 31, 2022, compared with net cash provided by financing activities of CHF 40.7 million for the year ended December 31, 2021. The decrease of CHF 42.0 million is predominantly related to prior year's (i) CHF 23.5 million received from two convertible notes sold to certain Affiris affiliated entities, (ii) CHF 4.6 million for the issuance of shares as part of the Company' acquisition with Affiris for the program portfolio of therapeutics targeting a-syn, notably ACI-7104 (see "Note 6. Asset acquisition.") and (iii) CHF 12.1 million received from proceeds from the sale of treasury shares in public offerings, net of underwriting fees and transaction costs, which did not repeat in the current period.

Operating capital requirements and plan of operations

We do not expect to generate revenues from royalties based on product sales unless and until our partners obtain regulatory approval of, and successfully commercialize, our current or any future product candidates. As of December 31, 2022, we had cash and cash equivalents of CHF 31.6 million and short-term financial assets of CHF 91.0 million, resulting in CHF 122.6 million of liquidity. The decrease relative to December 31, 2021 was predominantly related to R&D spending on our major discovery and R&D programs, and the strengthening of the Company's

infrastructure, systems and organization. This was offset by the receipt of CHF 3.9 million in contract revenue from LMI linked to the progression of the Tau-PET Tracer PI-2620 into late-stage development in AD. There can be no certainty as to the exact timing of future milestone payments, or in fact, whether any of these will ever be made, given that they are contingent on clear milestones being reached. Accordingly, assuming that we do not receive potential milestone payments and based upon our currently contemplated R&D strategy, we believe that our existing capital resources will be sufficient to meet our projected operating requirements into Q3 2024.

We expect to generate losses for the foreseeable future, and these losses could increase as we continue product development until we successfully achieve regulatory approvals for our product candidates and begin to commercialize any approved products. We are subject to all the risks pertinent to the development of new products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may harm our business. We expect to incur additional costs associated with operating a public company and we anticipate that we will need substantial additional funding in connection with our continuing operations. If we need to raise additional capital to fund our operations and complete our ongoing and planned clinical studies, funding may not be available to us on acceptable terms, or at all.

Our future funding requirements will depend on many factors, including but not limited to the following:

- The scope, rate of progress, results and cost of our preclinical and clinical studies and other related activities, according to our long-term strategic plan;
- The cost of manufacturing clinical supplies and establishing commercial supplies of our product candidates and any other products we may develop;
- The cost, timing and outcomes of regulatory approvals;
- The costs and timing of establishing sales, marketing and distribution capabilities;
- The terms and timing of any collaborative, licensing and other arrangements that we may establish, including any required milestone and royalty payments thereunder;
- The emergence of competing technologies or other adverse market developments; and
- The potential cost and timing of managing, protecting, defending and enforcing our portfolio of intellectual property.

Contractual obligations

In addition, the Company has been a tenant at our current location in the EPFL Innovation Park since shortly after our inception in 2003. We have entered into long-term rental lease agreements with respect to these facilities. However, our lease agreements are structured such that we can exit these lease agreements without penalty provided we give the owner of our premises sufficient notice. We have capitalized a portion of our lease liabilities in accordance with IFRS 16. See “Note 5. Right-of-use assets, long-term financial assets and lease liabilities.”

The Company currently projects CHF 1.0 million in undiscounted short-term lease obligations and CHF 2.4 million in undiscounted long-term lease obligations. Additionally, the Company projects CHF 23.0 million in short-term purchase commitments and CHF 29.2 million in long-term purchase commitments predominantly driven by R&D activities.

ATM program

Commencing in September 2020, the Company established an “at the market offering” (ATM) for the sale of up to USD 80.0 (CHF 74.6) million worth of our common shares from time to time by entering into an Open Market Sale

Agreement (Sales Agreement) with Jefferies LLC (Jefferies). In Q2 2021, we filed a new registration statement on Form F-3 and entered into a new Sales Agreement in Q2 2021 to replace and extend the ATM program. To date, the Company has sold 1,179,139 common shares previously held as treasury shares pursuant to the new Sales Agreement, raising USD 13.3 (CHF 12.1) million, net of underwriting fees and transaction costs.

Comparison of the years ended December 31, 2021 and 2020

For a discussion of the financial results and condition for the fiscal year ended December 31, 2020, please refer to "Item 5. Operating and financial review and prospects—A. Operating results—Comparison of the years ended December 31, 2021 and 2020" of our Annual Report on Form 20-F for the year ended December 31, 2021 filed on March 22, 2022.

C. Research and development, patents and licenses, etc.

See "Item 4. Information on the Company—B. Business overview" and "Item 5. Operating and financial review and prospects—A. Operating results—results of operations."

D. Trend information

See "Item 5. Operating and financial review and prospects."

E. Critical Accounting Estimates

We prepare our consolidated financial statements in accordance with IFRS as issued by the IASB. See "Note 3. Summary of significant accounting policies" to our consolidated financial statements for a description of the most significant accounting policies applied in the preparation of our consolidated financial statements.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and senior management

Executive Officers, other key employees and board of directors

The following table presents information about our executive officers, other key employees, and directors and director nominees, including their ages, as of March 1, 2023. The term of each of our directors is 1 year and, accordingly, will expire at our 2023 annual shareholder meeting to be held in June 2023.

Name	Position	Age	Initial year of appointment
Executive Officers			
Andrea Pfeifer, Ph.D.	Chief Executive Officer and Director	65	2003
Marie Kosco-Vilbois, Ph.D.	Chief Scientific Officer	65	2019
Johannes Rolf Streffer, M.D.	Chief Medical Officer	54	2020
Piergiorgio Donati	Chief Technical Operations Officer	52	2019
Christopher Roberts	VP Finance, Interim Chief Financial Officer	34	2022
Howard Donovan	Chief Human Resources Officer	48	2022
Jean-Fabien Monin	Chief Administrative Officer	52	2009
Other Key Employees			
Julien Rongère, Ph.D.	SVP Regulatory Affairs and Quality Assurance	45	2017
Olivier Sol, M.D.	VP Head of Clinical Development	56	2016
Alexandre Caratsch	General Counsel	57	2018

Name	Position	Age	Initial year of appointment
Bojana Portmann, Ph.D.	VP IP and Business Development	43	2011
Julian Gray, M.D., Ph.D.	Clinical Advisor	65	2007
Mark Danton	VP Information Systems, Security and Digital Technologies	59	2019
Non-Executive Directors			
Douglas Williams, Ph.D.	Chair and Director	64	2018
Thomas Graney	Director	58	2016
Werner Lanthaler, Ph.D.	Director	54	2018
Roy Twyman, M.D.	Director	66	2019
Carl June, M.D.	Director	68	2020
Alan Colowick, M.D.	Director	60	2021
Monika Bütler, Ph.D.	Director	61	2021
Monica Shaw, M.D.	Director	44	2021

The current business addresses for our executive officers, other key employees, directors and director nominee is AC Immune SA, EPFL Innovation Park, Building B, 1015 Lausanne, Switzerland.

Executive Officers

Andrea Pfeifer, Ph.D., Co-Founder, Chief Executive Officer and Director: Andrea Pfeifer co-founded AC Immune SA in 2003, successfully leading it to an IPO in 2016, since when she has served as a Director on the Board. Under her leadership, multiple transformative partnerships have been established with leading pharmaceutical companies, yielding a potential value of up to CHF 3.3 billion plus additional royalties. Before founding the Company, she was the Head of Nestlé Research Centre in Lausanne, Switzerland where she played a major role in connecting science and business. Whilst at Nestlé she led the scientific development of a number of highly innovative, critically acclaimed products from laboratory to market, established the microbiome as a major cross-category product development platform and co-founded the Life Science focused Nestlé Venture Capital Fund. Prior to this she was a Visiting Fellow at the Human Carcinogenesis Branch of The National Institute of Health, Bethesda, USA. She currently serves as the Chair of Investment Fund BioMedInvest, Basel and AB2 Bio SA, Lausanne, and is a member of the Supervisory Board of Symrise AG, Holzminden, Germany. She is also a key member of the CEOi initiative on Alzheimer's Disease and the Davos Alzheimer's Collaborative (DAC).

Prof. Pfeifer holds a Ph.D. in Toxicology (Cancer Research) from the University of Würzburg, Germany and is a registered Toxicologist and Pharmacist. She received her Habilitation from the University of Lausanne, Switzerland and is an Honorary Professor at the Ecole Polytechnique Fédérale de Lausanne (EPFL).

Marie Kosco-Vilbois, Ph.D., Chief Scientific Officer: A U.S. citizen, Marie Kosco-Vilbois has extensive experience in the biopharmaceutical industry and served as Chief Scientific Officer of Novimmune since 2005. Prior to joining Novimmune in 2002, Dr. Kosco-Vilbois was Head of Immunology and Preclinical Pharmacology at the Serono Pharmaceutical Research Institute, a Senior Scientist and then Head of Immunology at the Glaxo Wellcome Research Institute in Geneva, and a Scientific Member of the Basel Institute for Immunology. During her career, she has taken numerous biologicals from discovery into preclinical studies and clinical development, most notably filing market applications of a biological for an orphan indication. Dr. Kosco-Vilbois gained her Bachelor's Degree in Biology from Rutgers University, New Jersey, U.S., and a PhD in Anatomy and Immunology from the Medical College of Virginia/Virginia Commonwealth University School of Medicine, U.S..

Johannes Rolf Streffer, M.D., Chief Medical Officer: Johannes Streffer joined AC Immune in January 2021 as Chief Medical Officer from UCB Biopharma SPRL where he was VP, Head of Translational Medicine Neuroscience. Prior to this he was a member of the Alzheimer Disease Area Leadership Team at Janssen R&D and the industrial lead for EMIF-AD, where 14 countries are combined to foster understanding of early biomarkers and change in the predementia AD spectrum. His recognized expertise and standing in the scientific and medical community provide an

invaluable asset as we work to develop innovative treatments for neurodegenerative diseases based on our proprietary technology platforms.

Prof. Streffer graduated from the University of Tübingen, Germany with a medical degree. He completed graduate studies on neuro-oncology and is Board certified in Psychiatry and Neurology. Currently he is a visiting Professor in the Department of Biomedical Sciences, University of Antwerp.

Piergiorgio Donati, Chief Technical Operations Officer: Piergiorgio Donati joined AC Immune in June 2018 as Director, Global Program Management, having previously worked for AC Immune from 2011 to 2015 as Head of Manufacturing and Project Management. Between 2015 and 2018, Mr. Donati was Head of CMC program development at Glenmark Pharmaceuticals and Biotech CMC Lead at Merck KGaA. Prior to 2011, he held R&D positions at Abiogen, Merck Group and Serono. Mr. Donati holds a degree in Analytical Chemistry from the Technical Institute G.L. Bernini.

Christopher Roberts, Vice President Finance, Interim Chief Financial Officer: Christopher Roberts joined AC Immune in 2019 serving in various roles within the Company's finance leadership team prior to his promotion in 2022. Previously, Mr. Roberts worked as a Senior Manager for Ernst & Young for more than 10 years and supported the AC Immune IPO. During that time, he served high-growth life science companies in Switzerland, the San Francisco Bay Area, and the UK, focusing on initial and follow-on offerings, SEC reporting, and SOX 404 implementation projects. Mr. Roberts is a Trustee and Treasurer of Msizi Africa, a charity dedicated to sustainably improving the lives of children in Lesotho.

Mr. Roberts is a Chartered Accountant with the Institute of Chartered Accountants in Scotland (ICAS) and holds a Bachelor of Science in Accounting, Auditing and Finance with first class honours from Lancaster University.

Howard Donovan, Chief Human Resources Officer: Howard Donovan joined AC Immune in 2022 and is an internationally experienced, commercially focused leader who has competencies in all aspects of employee services, well-being, benefit design, international mobility, talent management, operations and HR business partnering. He has been at the World Economic Forum since 2015, where he led People Services and was responsible for global reward, employee experience, people insights, strategic sourcing, new office launches, and business partnering with the Board of Directors across its locations in Switzerland, United States, China, Japan and India. Howard previously worked as the inhouse Global Head of Reward for Puma Energy and prior to that he held senior HR leadership roles with a strong reward focus with multinational companies, including SGS Group and Xerox Corporation.

Jean-Fabien Monin, Chief Administrative Officer: Jean-Fabien Monin was nominated Chief Administrative Officer in July 2015 following his role as our Chief Financial Officer from March 2009 to July 2015. Prior to AC Immune, he held several positions during his tenure of 14 years at bioMérieux, a leading international *in vitro* diagnostics group, culminating in his nomination as Chief Financial Officer. His last position was CFO of bioMérieux Central Europe based in Vienna, Austria from December 2006 to March 2009. Mr. Monin holds a Masters in Finance and International Business from the University of Paris-Dauphine, France.

Other key employees

Julien Rongère, Ph.D., SVP Regulatory Affairs and Quality Assurance: Julien Rongère joined AC Immune in July 2017 as Head of European Regulatory Affairs and Quality Assurance. Prior to joining AC Immune, Dr. Rongère held positions of increasing responsibility at Celgene in Switzerland. Most recently, he served as Director, Regulatory Affairs, leading the development of regulatory strategies for small molecules and CAR-T cell therapies and contributed to the development and approval of Revlimid in multiple myeloma and mantle cell lymphoma. Prior to Celgene, Dr. Rongère served as a Regulatory Expert at Apoxis, SA in Switzerland. During his career, Dr. Rongère gained specific expertise in the development of regulatory strategies for taking products from Phase 1 through to commercialization in the field of hematology/oncology and immunology/inflammation, including fast-to-market approaches, orphan drugs and pediatric development. Dr. Rongère gained his Master's Degree in Medical Genetics from the University of Aberdeen, UK, and holds a Ph.D. in Molecular Biology from the University of Lausanne, Switzerland.

Oliver Sol, M.D., VP Head of Clinical Development: Prior to joining AC Immune, Olivier Sol was Clinical Director of Exonhit (Paris) and thereafter Medical & Regulatory Affairs Director for Diaxonhit, where he was responsible for the development and medical validation of *in vitro* diagnostic products in cancer, infectious diseases and Alzheimer's disease. Dr. Sol spent his over 20-year career as a Medical Expert in several therapeutic areas with a strong focus on central nervous system diseases, within pharmaceutical companies as Janssen, UCB-Pharma, GlaxoSmithKline and Sanofi. He contributed to the clinical development of currently marketed drugs in epilepsy (topiramate and levetiracetam) and galantamine in Alzheimer's disease. He has also gained significant experience in the field of biological biomarkers. Dr. Sol holds an M.D. from the Paris-Sud University (Paris-Saclay) with a specialization in Medical Biology.

Alexandre Caratsch, General Counsel: Alexandre Caratsch is a Swiss-qualified attorney with 30 years' experience in private practice, multinational companies and in ventures. He initially worked as an in-house lawyer for E&Y and the SGS Group before specializing in healthcare, holding senior legal positions at Novartis and Medtronic. Before joining AC Immune, he led the Corporate Legal Affairs and Intellectual Property group for Medtronic's Europe, Middle East and Africa (EMEA) region. Mr. Caratsch has also co-founded two start-up companies in the field of information technology and medical technology, respectively, and has supported other start-up companies with strategic, transactional and general counsel. Mr. Caratsch holds a Master's degree in Law from the University of Neuchâtel, Switzerland and is admitted to the Bar of Geneva, Switzerland.

Bojana Portmann, Ph.D., VP IP and Business Development: Bojana Portmann joined AC Immune in 2011 as Intellectual Property Manager and has held multiple roles within the IP department with increasing responsibility over the past years, during which her work was mainly focused on creating and strengthening patent portfolios for biologicals, small molecules and liposomal technology. Dr. Portmann holds a Ph.D. degree from the EPFL University in Switzerland, and a LL.M. degree, Master of Intellectual Property Law and Management (MIPLM), from the CEIPI in France. She also received a M.Sc. (Dipl. Ing.) degree in Polymer and Chemical Engineering from the University of Belgrade in Serbia.

Julian Gray, M.D., Ph.D., Clinical Advisor: Julian Gray has served as Clinical Advisor to our programs in neurodegenerative diseases since January 2007 and works in this function exclusively for AC Immune. He has previously held the position of Head of CNS Therapeutics at Eisai Ltd in London leading the global development of early and late-stage CNS projects in Alzheimer's disease, Parkinson's disease and other CNS areas. Prior to this he served as Head of Alzheimer Clinical Research at Hoffmann-La Roche in Basel where he conducted large-scale clinical trials in the U.S. and Europe. After his studies he was Medical Expert at Sandoz Pharmaceuticals in Basel undertaking clinical studies of different compounds in dementia and Parkinson's disease. Dr. Gray holds the title of a Specialist in Pharmaceutical Medicine (Switzerland). He received his medical degree (MBBS) from the University of London, a B.A. and Ph.D. from the University of Oxford and an MBA from Oxford Brookes University.

Mark Danton, VP Information Systems, Security and Digital Technologies: Mark Danton is a globally recognized and experienced executive in Information Systems/Information Technology (IS/IT) with extensive experience in developing, launching and managing business-relevant IS, cybersecurity and digital technology solutions and services.

Prior to joining AC Immune, Mr. Danton served as IS/IT Global Manager at Nestlé and held a number of global roles at BT Global Services and in Dimension Data PLC. Mr. Danton holds an Executive MBA from the Business School Lausanne, graduating cum laude and as the Executive MBA Student of the Year.

Non-Executive Directors

Douglas Williams, Ph.D., Chair and Director: Douglas E. Williams is currently the President, CEO and member of the Board of Directors of Codiak BioSciences. He was previously Biogen's Executive Vice President, Research and Development, serving in this role from January 2011 to July 2015. He joined Biogen from ZymoGenetics, where he was most recently CEO and member of the Board of Directors. ZymoGenetics was purchased for $985 million by Bristol Myers Squibb during Dr. Williams' tenure. Previously, he held leadership positions within the biotechnology industry, including Chief Scientific Officer and Executive Vice President of Research and Development at Seattle Genetics, and

Senior Vice President and Washington Site Leader at Amgen. Dr. Williams served in a series of scientific and senior leadership positions over a decade at Immunex, including Executive Vice President and Chief Technology Officer and a member of the Board of Directors. During his 30+ year career in the biotechnology industry he has played a role in the development of several novel drugs including Enbrel, Tecfidera, and Spinraza. He has served on the board of numerous biotechnology companies and is currently Chair of the Board of AC Immune, and is a Director for Panacea II.

Thomas Graney, Director: Thomas Graney is currently the CEO, CFO, and member of the Board of Directors of Oxurion NV. Prior to Oxurion, he was CFO of Generation Bio, Senior Vice President and CFO at Vertex Pharmaceuticals Inc. and CFO and SVP of Finance & Corporate Strategy at Ironwood Pharmaceuticals. Prior to Ironwood Pharmaceuticals, Mr. Graney spent 20 years working with J&J and its affiliates, serving for 4 years as worldwide VP of Finance and CFO of Ethicon. Mr. Graney has extensive global experience that spans corporate development, commercial strategy, portfolio management and supply chain management, communication, and investor relations. Mr. Graney is currently on the Board of Directors of Mogrify LTD and Chair of the Audit Committee. A Chartered Financial Analyst charterholder, Mr. Graney holds a B.S. in accounting from the University of Delaware and an MBA in Marketing, Finance and International Business from the Leonard N. Stern School of Business at New York University.

Werner Lanthaler, Ph.D., Director: Werner Lanthaler is the CEO of Evotec AG, a drug discovery alliance and development partnership company focused on rapidly progressing innovative product approaches with leading pharmaceutical and biotechnology companies, academics, patient advocacy groups and venture capitalists. Since joining Evotec in 2009, Dr. Lanthaler has focused the company on collaborating with biotech and pharma companies and academia, supporting biotech innovation. He previously served as Chief Financial Officer at Intercell AG where he played a key role in many of that company's major milestones. During his tenure, Intercell undertook an IPO and developed from a venture-backed biotechnology company into a global vaccine player. Dr. Lanthaler has also served as Director of the Federation of Austrian Industry, and from 1995 to 1998 was a Senior Management Consultant at McKinsey & Company. Dr. Lanthaler is a Non-Executive Member of the Board of Directors of arGEN-X and is a member of the Supervisory Board of Topas Therapeutics GmbH. He holds a Doctorate in Economics from Vienna University, a Master's degree in Business Administration from Harvard University, and a degree in Psychology.

Roy Twyman, M.D., Director: Roy Twyman is a Neurologist and is founder and current CEO of Amron Neuroscience, LLC, a private consulting company focused on neuroscience drug development. Prior to this, Dr. Twyman spent almost 20 years at Janssen Research & Development, LLC (a Johnson & Johnson company) and was a member of the Neuroscience Therapeutic Area Leadership team responsible for clinical R&D and strategic planning of CNS neurology and psychiatry pipeline products. From 2012 to March 2018, Dr. Twyman was a Senior Vice President in the Neuroscience Therapeutic Area overseeing the Alzheimer's Disease Area. He currently participates as an independent Board Member or as a Scientific Advisory Board Member for a number of small biotech or pharmaceutical companies.

Carl June, M.D., Director: Carl June is Richard W. Vague Professor in Immunotherapy, Director of the Center for Cellular Immunotherapies and Director of the Parker Institute for Cancer Immunotherapy at the Perelman School of Medicine at the University of Pennsylvania. Due to his lifelong work on lymphocyte activation, Prof. June is considered a world authority on mechanisms related to immune tolerance and adoptive immunotherapy in the fields of chronic inflammation and cancer. He and his team pioneered the groundbreaking work in immunotherapy in which patients with refractory and relapsed chronic lymphocytic leukemia are treated with genetically engineered versions of their own T cells. This CAR-T therapy approach, which trains the immune system to attack and destroy cancer cells, has opened a new era of innovative treatments and personalized medicine for cancer patients.

Prof. June is a graduate of the Naval Academy in Annapolis, USA, and Baylor College of Medicine in Houston, USA, where he received his medical degree. Prof. June also completed graduate training in immunology and malaria with Dr. Paul-Henri Lambert at the World Health Organization, Geneva, Switzerland, and post-doctoral training in transplantation biology with E. Donnell Thomas and John Hansen at the Fred Hutchinson Cancer Research Center in Seattle, USA. He has published more than 500 manuscripts and is the recipient of numerous honors and prizes.

Alan Colowick, M.D., Director: Alan Colowick is currently a Managing Director at Matrix Capital Management and has served in executive and Board roles for numerous large and emerging biotech companies. From 2017 until January 2021, he was a Partner at Sofinnova, where he led investments for several clinical-stage companies. Previously, Dr. Colowick was Executive Vice President and served in various leadership roles at Celgene Corporation, including President for Celgene's EMEA regions and Senior Vice President of Global Medical Affairs. Before Celgene, he was the Chief Executive Officer at Gloucester Pharmaceuticals, Inc. which was acquired by Celgene in 2010. Dr. Colowick also served as the President of Oncology at Geron Corporation, as Chief Medical Officer of Threshold Pharmaceuticals, and in numerous positions of increasing responsibility at Amgen culminating with his role as VP, Medical Affairs Europe.

Dr. Colowick serves on the Board of Directors for several biopharma companies, and his prior roles as Chair include VelosBio (sold to Merck in 2020 for $2.75 billion) and Principia Biopharma (sold to Sanofi in 2020 for $3.7 billion). He received his medical degree from Stanford University, a Master's in Public Health from Harvard University, and a B.S. in Molecular Biology from the University of Colorado. He completed specialty training in Hematology-Oncology at Harvard Medical School, the Dana Farber Cancer Institute, and Brigham and Women's Hospital in Boston, USA.

Monika Bütler, Ph.D., Director: Monika Bütler is a leading Swiss economist and former Vice President of the independent Swiss Covid-19 Science Taskforce. She is a member of the Board of Directors and of the audit committees of both Schindler Holding AG and Swiss Life Holding AG, and a member of the Board of Directors and of the compensation and nomination committee of Huber & Suhner AG. Her international economic expertise is in public policy and managerial economics, including an advisory role to the World Bank and visiting appointments in the U.S., Australia and Europe. Dr. Bütler is a Vice President of the Foundation Board of the Gebert Rüf Foundation, a science and innovation foundation that supports entrepreneurial projects which are committed to achieving an impact.

Prof. Bütler holds a Ph.D. in Economics from the University of St. Gallen, a Doctorate Honoris Causa from the University of Lucerne, and a Diploma in Mathematics/Physics from the University of Zurich.

Monica Shaw, M.D., Director: Monica Shaw is a pharmaceutical industry expert who has held senior leadership positions and was involved in advancing more than 15 therapeutic products from first-in-man studies through regulatory approvals and commercialization across multiple geographies. She also played key business development roles in company acquisition and integration and co-development partnerships. Through her work, Dr. Shaw gained extensive specialty experience in the fields of dermatology, immuno-inflammation, HIV, neurology and oncology.

Currently, Dr. Shaw is the Chief Executive Officer for Oncopeptides AB. Dr. Shaw has previously held other broad leadership roles at other leading pharmaceutical companies, including as Executive Vice President Head Region Europe, Canada, Australia for Leo Pharma, Vice-President Commercial Head Asia Pacific region at GSK/ViiV Healthcare, and Medical Director and Chief Scientific Officer UK for Novartis, in addition to previous leadership positions at Norgine, Shire and Merck KGaA.

Monica Shaw holds an M.D. from the University of Oxford Medical School and is a Member of the Royal College of Physicians.

Family Relationships

None of our directors or executive officers has a family relationship as defined in Item 401 of Regulation S-K.

B. Compensation

Compensation of directors and executive officers

For the year ended December 31, 2022, the aggregate compensation accrued or paid to the members of our board of directors and our executive officers for services in all capacities was CHF 6.5 million.

During the year ended December 31, 2022, the total fair value of equity awards granted to directors and executive officers was CHF 2.0 million.

The amount set aside or accrued by us to provide pension, retirement or similar benefits to members of our board of directors and executive officers amounted to a total of CHF 0.3 million in the year ended December 31, 2022.

We incorporate by reference into this Annual Report the information in "Item 1. C—2021 Board Compensation" and "Item 2. C—2021 Executive Compensation" of Exhibit 99.4 to our report on Form 6-K filed with the SEC on March 22, 2022.

Equity incentive plans

In 2016, we ceased issuing new grants under our prior equity incentive plans, which we refer to as the Prior Plans, and adopted a new omnibus equity incentive plan under which we have the discretion to grant a broad range of equity-based awards to eligible participants.

Prior plan: C1

Since our inception in 2003, we have had four separate Prior Plans under which stock options were granted (Prior Plans A, B and C2 have terminated): Options granted under Plan C1 from 2013 through the adoption of the current 2016 Stock Option and Incentive Plan (SOIP) were taxed upon exercise instead of at grant due to a change in taxation rules.

Plan administration. Under Plan C1, an option, which can only be granted with the approval of our board of directors, is evidenced by an option agreement signed by the participant to indicate his or her acceptance of the option and is subject to the terms and conditions of the applicable Prior Plan.

Eligibility. Under Plan C1, options were granted to our directors, employees, advisors and agents.

Options exercise price. The exercise price of all options issued under the Prior Plan is CHF 0.15.

Vesting period. Under Plan C1, the options vesting period was 4 years with 25% of the options vesting each year.

Expiration period. The expiry dates for each plan are as follows:

Plan C1: 10 years

Amendment. Our board of directors has the authority to amend each of the Prior Plans.

2016 SOIP

At the November 15, 2016 AGM of the Company, our board of directors approved the 2016 SOIP (as amended and restated the "2016 SOIP"). The maximum number of shares available for issuance under the 2016 SOIP is 4,800,000 common shares. The shares available for issuance under the 2016 SOIP were initially registered with the SEC on a Form S-8 on March 8, 2017, and additional shares were registered on a Form S-8 on August 5, 2019. As of December 31, 2022, there were a total of 2,345,648 shares underlying options that were exercisable and 4,261,017 shares underlying outstanding options and 216,486 shares underlying outstanding restricted share units issued from both our Prior Plans and the 2016 SOIP.

Plan Administration. The 2016 SOIP is administered by either our board of directors or the compensation committee, or a similar committee performing the functions of the compensation committee. Approval of the plan administrator is required for all grants of awards under the 2016 SOIP, but the administrator may delegate to our CEO the authority to grant awards, subject to certain limitations set forth on the plan.

Awards. Awards may be granted in the form of incentive stock options, non-qualified stock options, stock appreciation rights, restricted share units, restricted share awards, unrestricted share awards, performance share awards and dividend equivalent rights.

Eligibility. Under the 2016 SOIP, full or part-time officers and other employees, non-employee directors and consultants of the Company and its subsidiaries who are selected by the administrator are eligible to participate in the plan.

Options exercise price. Under the 2016 SOIP, the option exercise price is determined by the plan administrator at the time of grant, but will not be less than fair market value (as defined in the 2016 SOIP) on the grant date, and for incentive stock options granted to any employee who is a 10 percent owner in the Company, will not be less than 110 percent of the fair market value on the grant date.

Vesting period. Vesting conditions are determined by the administrator at the time of grant and are specified in the applicable award certificate.

Accelerated vesting. The administrator may accelerate the exercisability or vesting of all or any portion of any award in circumstances involving the grantee's death, disability, retirement or termination of employment, or a change in control.

Amendment. Our board of directors has the authority to amend the 2016 SOIP.

Amendment and restatement to the 2016 SOIP

In June 2019, the Board authorized, and the shareholders approved, an increase in the maximum number of shares reserved for issuance under the 2016 SOIP. In October 2019, the Board authorized a second amendment and restatement to the 2016 SOIP. These amendments were made to align certain elements with Swiss statutory requirements and had no financial impact for the Company in 2022, 2021 or 2020.

Equity compensation

For the fiscal year ended December 31, 2022, the Company has granted our directors and executive officers, in the aggregate, options for the right to acquire 633,060 shares at an exercise price of USD 3.15 per share, which vest either over a 1 year or 3 year period with vesting to occur quarterly or annually depending on the nature of the award. The expiration date for these options granted in 2022 is 2032. The Company also granted to our directors and executive officers a total of 239,194 restricted share units in 2022. Restricted share units granted to directors vest over a 1 year period with vesting to occur annually. Restricted share units granted to executive officers vest over a 3 year period with vesting to occur quarterly or semi-annually. Please see "Note 18. Share-based compensation" for further detail.

C. Board practices

Composition of board of directors

Our board of directors is composed of nine directors. Each director is elected for a 1-year term, no later than the next Annual General Meeting (AGM). The current members of our board of directors were appointed at shareholders' meetings held on June 24, 2022 to serve until the 2023 AGM to be held in June 2023.

We are a foreign private issuer. As a result, in accordance with the Nasdaq stock exchange listing requirements, we rely on home country governance requirements and certain exemptions thereunder rather than relying on the stock exchange corporate governance requirements. For an overview of our corporate governance principles, see "Item 16G. Corporate governance."

Board meetings

Our Board of Directors met in accordance with their respective mandate both physically (as was practicable under current pandemic circumstances), by video-conference and telephonically throughout 2022. The Board members analyzed the scientific, business, financial, organizational and legal risks of the Company based on the external factors and internal changes that could potentially impact the risks for the Company in the future.

Director independence

As a foreign private issuer, under the listing requirements and rules of Nasdaq, we are not required to have independent directors on our board of directors, except to the extent that our audit and finance committee is required to comply with independence requirements, subject to certain phase-in schedules. However, our board of directors has determined that, under current listing requirements and rules of Nasdaq (which we are not subject to) and considering any applicable committee independence standards, Douglas Williams, Thomas Graney, Werner Lanthaler, Roy Twyman, Carl June, Alan Colowick, Monika Bütler and Monica Shaw are "independent directors." In making such determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances our board of directors deemed relevant in determining the director's independence, including the number of common shares beneficially owned by the director and his or her affiliated entities, if any.

Committees of the board of directors

Our board of directors established two separate permanent committees: an audit and finance committee and a compensation, nomination and corporate governance committee.

Audit and finance committee

The audit and finance committee, which consists of Monika Bütler (Chair), Thomas Graney (Member), and Werner Lanthaler (Member), assists our board of directors in overseeing our accounting and financial reporting processes and the audits of our consolidated financial statements. In addition, the audit and finance committee is directly responsible for the appointment, compensation, retention and oversight of the work of our independent registered public accounting firm. The audit and finance committee consists exclusively of members of our board who are financially literate, and Monika Bütler, Thomas Graney and Werner Lanthaler are considered to be "audit committee financial experts" as defined by the SEC. Our board of directors has determined that Monika Bütler, Thomas Graney and Werner Lanthaler satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act.

The audit and finance committee is governed by a charter that complies with Nasdaq rules. The audit and finance committee has the responsibility to, among other things:

- review and assess the qualifications, independence, performance and effectiveness of the independent auditor;
- review the scope of the prospective audit by the independent auditor, the estimated fees, and any other matters pertaining to the audit;
- approve any audit and non-audit services proposed to be provided by the independent auditor to ensure independent auditor independence;
- review and assess the independent auditor's report and management letters and take notice of all comments of the independent auditor on accounting procedures and systems of control, and review the independent auditor's reports with management;
- be responsible for the resolution of disagreements between the management and the independent auditor;
- review and evaluate the lead audit partner of the independent audit team and confirm and evaluate their rotation;
- review and discuss all (i) consolidated financial statements, (ii) reports intended for publication and (iii) any other financial statements intended for publication to consider significant financial reporting issues and judgments made in connection with the preparation of our consolidated financial statements, including any significant changes in our selection or application of accounting principles;

- approve the quarterly condensed consolidated financial statements;
- review with the management, personnel responsible for the design and implementation of the internal audit function, and the independent auditor in separate meetings any analysis or other written communication prepared by the management and/or the independent auditor setting forth significant financial reporting issues and judgments made in connection with the preparation of the consolidated financial statements, including critical accounting policies, the effect of regulatory and accounting initiatives, and off-balance sheet transactions and structures on our consolidated financial statements;
- review in cooperation with the independent auditor and the management whether the accounting principles applied are appropriate in view of our size and complexity;
- periodically review our policies and procedures for risk management and assess the effectiveness thereof, including discussing with management our major financial risk exposures and the steps that have been taken to monitor and control such exposure;
- discuss with management and external advisors any legal matters that may have a material impact on our consolidated financial statements and any material reports or inquiries from regulatory or governmental agencies that could materially impact our contingent liabilities and risks;
- review our disclosure controls and procedures and internal control over financial reporting, including significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting;
- establish procedures for the receipt, retention and treatment of complaints received regarding accounting, internal accounting controls or auditing matters, and the confidential, anonymous submission by employees of concerns regarding questionable accounting or auditing matters; and
- review and approve or ratify any related-person transaction in accordance with our related-person transaction policy.

The audit and finance committee will meet as often as it determines is appropriate to carry out its responsibilities, but in any event will meet at least four times per year.

Compensation, nomination and corporate governance committee

The compensation, nomination and corporate governance committee, consists of Douglas Williams (Chair), Roy Twyman (Member) and Thomas Graney (Member).

The compensation, nomination and corporate governance committee is governed by a charter that complies with SEC and home country governance rules. The compensation, nomination and corporate governance committee has the responsibility to, among other things:

- recommend to the board the guidelines for the overall compensation and equity awards for the board of directors and executive officers along with the rationale for such recommendations;
- recommend to the board the compensation of executive officers;
- propose the maximum total compensation of the board of directors and executive officers for approval at the Annual General Meeting;
- periodically review policies and principles for the Company’s corporate governance;

- establish the process for assessment of the performance of members of the board, its committees and individual members;
- prepare and reviews the Company's succession plan for members of the board and the executive committee;
- periodically review the Company's code of conduct and recommends changes as needed;
- recommend for presentation to our shareholders the compensation report for shareholder vote; and
- define guidelines for the selection of candidates for election or re-election as members of the board and our executive officers.

Swiss law requires that we adopt a compensation committee, so in accordance with Nasdaq Listing Rule 5615(a)(3), we will follow home country requirements with respect to the compensation, nomination and corporate governance committee. As a result, our practice will vary from the requirements of Nasdaq Listing Rule 5605(d), which sets forth certain requirements as to the responsibilities, composition and independence of compensation committees, and from the independent director oversight of director nomination requirements of Nasdaq Listing Rule 5605(e). We will be subject to the Swiss Ordinance Against Executive Compensation (Say on Pay) Rule. In addition, this committee will also be responsible for director and board committee nominations as well as reviewing and amending, if required, our corporate governance framework and guidelines.

D. Employees

As of December 31, 2022, we employed 156 employees, 30 of whom were part-time employees. 72 of our employees hold Ph.D. degrees and 50 hold M.Sc. degrees. Our 156 employees are from 30 countries. The average number of employees (calculated on full-time equivalents) in 2022 was 149. As of December 31, 2021 and 2020 we had 143 and 149 employees, respectively. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

E. Share ownership

See "Item 7. Major shareholders and related-party transactions—A. Major shareholders."

F. Disclosure of a Registrant's Action to Recover Erroneously Awarded Compensation

Not applicable.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED-PARTY TRANSACTIONS

A. Major shareholders

The following table presents information relating to the beneficial ownership of our common shares as of the date of this Annual Report by:

- each person, or group of affiliated persons, known by us to own beneficially 5% or more of our outstanding common shares;
- each of our executive officers and directors; and
- all executive officers and directors as a group.

The number of common shares beneficially owned by each entity, person, executive officer or director is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any common shares over which the individual has sole or

shared voting power or investment power as well as any common shares that the individual has the right to acquire within 60 days of March 1, 2023 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all common shares held by that person.

The percentage of outstanding common shares is computed on the basis of 83,620,364 common shares outstanding as of March 1, 2023. Common shares that a person has the right to acquire within 60 days of March 1, 2023 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all executive officers and directors as a group. Unless otherwise indicated below, the address for each beneficial owner is AC Immune, EPFL Innovation Park, Building B, 1015 Lausanne, Switzerland.

Shareholder	Number	Shares beneficially owned (%)
5% Shareholders		
dievini Hopp BioTech holding GmbH & Co KG[1]	16,316,742	19.5 %
Varuma AG[2]	11,999,999	14.4 %
Affiris AG[3]	10,133,474	12.1 %
Biotechnology Value Fund (BVF) Inc.[4]	7,428,379	8.9 %
Executive Officers and Directors		
Andrea Pfeifer[5]	3,007,933	3.6 %
Marie Kosco-Vilbois[6]	*	*
Johannes Rolf Streffer[7]	*	*
Piergiorgio Donati[8]	*	*
Christopher Roberts[9]	*	*
Howard Donovan[10]	*	*
Jean-Fabien Monin[11]	*	*
Douglas Williams[12]	*	*
Thomas Graney[13]	*	*
Werner Lanthaler[14]	*	*
Roy Twyman[15]	*	*
Carl June[16]	*	*
Alan Colowick[17]	*	*
Monika Bütler[18]	*	*
Monica Shaw[19]	*	*
All executive officers and directors as a group (15 persons)	4,379,159	5.2 %

* Indicates beneficial ownership of less than 1% of the total issued and outstanding common shares.

[1]Based on information set form in a Schedule 13G filed with the SEC by dievini Hopp BioTech holding GmbH & Co KG ("dievini") on February 10, 2023. These shares consist of 16,316,742 shares held by dievini.

DH-Capital GmbH & Co. KG ("DH-Capital") and OH Beteiligungen GmbH & Co. KG ("OH Beteiligungen") are collectively the holders of 100% of the limited partner interest in dievini and therefore, control the voting and dispositive decisions of dievini together and may be deemed to beneficially own the shares held by dievini. Dietmar Hopp, Oliver Hopp and Daniel Hopp are the ultimate controlling persons of dievini, DH-Capital and OH Beteiligungen, and control the voting and investment decisions of the ultimate parent company of dievini and therefore, may be deemed to beneficially own the shares held by dievini by virtue of their status as controlling persons of dievini.

The address of the principal business office of dievini and Dietmar Hopp is c/o dievini Hopp BioTech holding GmbH & Co. KG, Johann-Jakob-Astor Straße 57, 69190 Walldorf, Germany. The address of the principal business office of DH-

Capital GmbH & Co. KG and OH Beteiligungen GmbH & Co. KG is Opelstraße 28, 68789 St. Leon-Rot, Germany. The address of the principal business office of Oliver Hopp is Johann-Jakob-Astor-Straße 59, 69190 Walldorf, Germany.

[2]Represents 11,999,999 shares held by Varuma AG set forth in a Schedule 13G/A filed with the SEC on February 12, 2019. The address for Varuma AG is Aeschenvorstadt 55, CH-4051 Basel, Switzerland. Rudolf Maag controls the voting and investment decisions of Varuma AG.

[3]Based on information set forth in a Schedule 13G filed with the SEC by Affiris on February 14, 2023, (i) these shares consist of 6,724,840 shares held of record by Affiris AG, as well as 1,513,317 shares that were issuable upon the conversion of notes held by Santo Venture Capital GmbH and 1,895,317 shares that were issuable upon the conversion of notes held by FCPB Affi GmbH; and (iii) the address of Affiris AG is Karl-Farkas-Gasse 22, 1030 Vienna, Austria, the address of by Santo Venture Capital GmbH is Bergfeldstrasse 9, 83607 Holzkirchen, Germany and the address of FCPB Affi GmbH is Freihamer Strasse 2, 82166 Gräfelfing, Germany. The convertible notes held by Santo Venture Capital GmbH and FCPB Affi GmbH were fully settled in Q4 2021.

[4]Based on information set forth in a Schedule 13G filed with the SEC by BVF on February 14, 2023, these shares consist of 7,428,379 shares held of record by BVF Inc. The address of BVF Inc. is 44 Montgomery St., 40th Floor, San Francisco, California 94104.

[5]Consists of 2,364,918 of our common shares and options to purchase 643,015 of our common shares exercisable within 60 days of March 1, 2023.

[6]Consists of 68,995 of our common shares and options to purchase 143,438 of our common shares exercisable within 60 days of March 1, 2023.

[7]Consists of 198,200 of our common shares and options to purchase 78,777 of our common shares exercisable within 60 days of March 1, 2023.

[8]Consists of 9,547 of our common shares and options to purchase 93,220 of our common shares exercisable within 60 days of March 1, 2023.

[9]Consists of 2,500 of our common shares and options to purchase 10,800 of our common shares exercisable within 60 days of March 1, 2023.

[10]Consists of 5,096 of our common shares and options to purchase 11,180 of our common shares exercisable within 60 days of March 1, 2023.

[11]Consists of 298,156 of our common shares and options to purchase 82,813 of our common shares exercisable within 60 days of March 1, 2023.

[12]Consists of 12,818 of our common shares and options to purchase 58,803 of our common shares exercisable within 60 days of March 1, 2023.

[13]Consists of 15,851 of our common shares and options to purchase 47,329 of our common shares exercisable within 60 days of March 1, 2023.

[14]Consists of 11,906 of our common shares and options to purchase 47,329 of our common shares exercisable within 60 days of March 1, 2023.

[15]Consists of 0 of our common shares and options to purchase 65,511 of our common shares exercisable within 60 days of March 1, 2023.

[16]Consists of 0 of our common shares and options to purchase 37,826 of our common shares exercisable within 60 days of March 1, 2023.

[17]Consists of 0 of our common shares and options to purchase 20,511 of our common shares exercisable within 60 days of March 1, 2023.

[18]Consists of 0 of our common shares and options to purchase 25,310 of our common shares exercisable within 60 days of March 1, 2023.

[19]Consists of 0 of our common shares and options to purchase 25,310 of our common shares exercisable within 60 days of March 1, 2023.

Holders

As of March 1, 2023, we had approximately 250 shareholders of record of our common shares. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust or by other entities.

Significant changes in ownership by major shareholders

We have experienced significant changes in the percentage ownership held by major shareholders as a result of our IPO. Prior to our IPO in September 2016, our principal shareholders were dievini Hopp BioTech holding GmbH & Co KG and Varuma AG, which held shares representing 36.5% and 23.1% prior to our IPO, respectively. As of March 1, 2023, dievini Hopp BioTech holding GmbH & Co KG and Varuma AG held 19.5% and 14.4% of our outstanding common shares, respectively. BVF Inc. increased its holdings from 8.5% to 8.9% of our outstanding common shares. Affiris, Santo Venture Capital GmbH and FCPB GmbH became major shareholders in 2021 and continue to own 12.1% of our outstanding common shares as of December 31, 2022.

In September 2016, we completed our IPO and listed our common shares on the Nasdaq Global Market. In the IPO, we issued and sold 6,900,000 common shares, including 900,000 common shares sold to the underwriters pursuant to the underwriters' over-allotment option. While none of our existing shareholders sold common shares in the IPO, the percentage ownership held by certain shareholders decreased as a result of the issuance of the common shares sold by us in the IPO.

In July 2018, we completed three offerings of our common shares. In these offerings, we issued and sold 10,000,000 common shares, including 1,108,695 sold to the underwriters pursuant to the underwriters' over-allotment option. The percentage ownership held by certain shareholders decreased as a result of the issuance of the common shares sold by us in these offerings.

B. Related-party transactions

None.

Indemnification of directors and executive management

Our Articles of Association require us to indemnify our executive officers and directors to the fullest extent permitted by law. We entered into indemnification agreements with our executive officers and directors.

C. Interests of experts and counsel

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated statements and other financial information

Financial statements

See "Item 18. Financial statements," which contains our consolidated financial statements prepared in accordance with IFRS.

Legal proceedings

From time to time we may become involved in legal proceedings that arise in the ordinary course of business. As of the date of this Annual Report, we have not been a party to or paid any damages in connection with litigation that has had a material adverse effect on our financial position. No assurance can be given that future litigation will not have a material adverse effect on our financial position. When appropriate in the executive management's estimation, we may record reserves in our consolidated financial statements for pending litigation and other claims.

Dividends and dividend policy

We have never declared or distributed dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate distributing any dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Under Swiss law, any dividend must be approved by our shareholders. In addition, our auditors must confirm that the dividend proposal of our board of directors conforms to Swiss statutory law and our articles of incorporation. A Swiss corporation may pay dividends only if it has sufficient distributable profits brought forward from the previous business years (*report des bénéfices*) or if it has distributable reserves (*réserves à libre disposition*), each as evidenced by its audited standalone statutory balance sheet prepared pursuant to Swiss law and after allocations to reserves required by Swiss law and its articles of association have been deducted. Distributable reserves are generally booked either as "free reserves" (*réserves libres*) or as "reserve from capital contributions" (*apports de capital*). Distributions out of nominal share capital, which is the aggregate nominal value of a corporation's issued shares, may be made only by way of a share capital reduction.

B. Significant changes

A discussion of the significant changes in our business can be found under "Item 4. Information on the Company—A. History and development of the Company" and "Item 4. Information on the Company—B. Business overview."

ITEM 9. THE OFFER AND LISTING

A. Offering and listing details

See "Item 9–C. Markets" below.

B. Plan of distribution

Not applicable.

C. Markets

Our common shares trade on the Nasdaq Global Market under the symbol "ACIU."

D. Selling shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share capital

Not applicable.

B. Memorandum and articles of association

We incorporate by reference into this annual report on Form 20-F the description of our Articles of Association incorporated herein by reference to Exhibit 99.3 to the Company's Report on Form 6-K, filed with the SEC on June 24, 2022.

C. Material contracts

Except as otherwise disclosed in this Annual Report on Form 20-F (including the Exhibits), we are not currently, and have not been in the past 2 years, party to any material contract, other than contracts entered into in the ordinary course of business.

D. Exchange controls

There are no Swiss governmental laws, decrees or regulations that restrict, in a manner material to us, the export or import of capital, including any foreign exchange controls, or that generally affect the remittance of dividends or other payments to non-residents or non-citizens of Switzerland who hold our common shares.

E. Taxation

The following summary contains a description of the material Swiss and U.S. federal income tax consequences of the acquisition, ownership and disposition of common shares, but it does not purport to be a comprehensive description of all the tax considerations that may be relevant to a decision to purchase common shares. The summary is based upon the tax laws of Switzerland and regulations thereunder and on the tax laws of the United States and regulations thereunder as of the date hereof, which are subject to change.

Swiss tax considerations

This summary of material Swiss tax consequences is based on Swiss law and regulations and the practice of the Swiss tax administration as in effect on the date hereof, all of which are subject to change (or subject to changes in interpretation), possibly with retroactive effect. The summary does not purport to consider the specific circumstances of any particular shareholder or potential investor and does not relate to persons in the business of buying and selling common shares or other securities. The summary is not intended to be, and should not be interpreted as, legal or tax advice to any particular potential shareholder, and no representation with respect to the tax consequences to any particular shareholder is made.

Current and prospective shareholders are advised to consult their own tax advisors in light of their particular circumstances as to the Swiss tax laws, regulations and regulatory practices that could be relevant to them in connection with the acquiring, owning and selling or otherwise disposing of common shares and receiving dividends and similar cash or in-kind distributions on common shares (including dividends on liquidation proceeds and stock dividends) or distributions on common shares based upon a capital reduction (*remboursements de la valeur nominale*) or reserves paid out of capital contributions (*réserves sur les apports en capital*) and the consequences thereof under the tax laws, regulations and regulatory practices of Switzerland.

Taxation of AC Immune

AC Immune is subject to corporate Swiss federal, cantonal and communal taxation in Switzerland, Canton of Vaud, Commune of Ecublens, near Lausanne, respectively.

We are entitled under Swiss laws to carry forward any losses incurred for a period of 7 years and can offset our losses carried forward against future taxes. As of December 31, 2022, we had tax loss carry-forwards totaling CHF 264.1 million (provisional amount; tax loss is definitively recognized by Swiss tax authorities once set-off against taxable income). There is no certainty that we will make sufficient profits to be able to utilize these tax loss carry-forwards in full.

The effective corporate income tax rate (federal, cantonal and communal) where we are domiciled is currently 13.6%.

As of January 1, 2020, the Company may request a tax relief of 60%, which would be applied to income from patents and similar rights at communal and cantonal levels. Additionally, a so-called "super-deduction" may be granted for payroll and other expenses of research and development of Swiss origins.

However, the aforementioned tax relief based on the patent box and deductions for research and development may not exceed 50% of the overall taxable profit before these tax relief and deductions.

Notwithstanding the corporate income tax, the corporate capital is taxed at a rate of 0.1305% (cantonal and communal tax only, as there is no federal tax on capital). As of January 1, 2020 the capital attributable to patents and similar rights is considered with 50% relief in the capital tax calculation.

Federal, cantonal and communal individual income tax and corporate income tax

Non-resident shareholders

Except as described in "—*Swiss federal withholding tax"* below, shareholders who are not resident in Switzerland for tax purposes, and who, during the relevant taxation year, have not engaged in a trade or business carried on through a permanent establishment or fixed place of business situated in Switzerland for tax purposes (all such shareholders for purposes of this section termed, "Non-resident shareholders"), will not be subject to any Swiss federal, cantonal and communal income tax on dividends and similar cash or in-kind distributions on Shares (including liquidation proceeds and stock dividends) (for the purposes of this section, "dividends"), distributions based upon a capital reduction (*remboursements liés à la réduction de la valeur nominale des actions*) and distributions paid out of reserves from capital contributions (*apports de capital*) on shares, or capital gains realized on the sale or other disposition of shares.

Resident private shareholders

Swiss-resident individuals who hold their shares as private assets are required to include dividends, but not distributions based upon a capital reduction (*remboursements liés à la réduction de la valeur nominale des actions*) and distributions paid out of reserves from capital contributions confirmed by the Swiss Federal Tax Administration (*apports de capital*), in their personal income tax return and are subject to Swiss federal, cantonal and communal income tax on any net taxable income for the relevant taxation period, including the dividends, but not the distributions based upon a capital reduction (*remboursements liés à la réduction de la valeur nominale des actions*) and distributions paid out of

reserves from capital contributions confirmed by the Swiss Federal Tax Administration (*apports de capital)*. Shareholders holding shares representing at least 10% of the nominal share capital of the Company may be able to decrease the taxable dividend basis by 30% (70% taxable) at the federal level and up to 50% at the cantonal level, depending on their respective cantonal rates, as partial relief from economic double taxation. Capital gains resulting from the sale or other disposition of shares are, subject to a few exceptions such as in case of Taxable Repurchases as described in "*—Swiss federal withholding tax"* below, not subject to Swiss federal, cantonal and communal income tax, and conversely, capital losses are not tax-deductible for resident private shareholders (the shareholders referred to in this paragraph for the purposes of this section, "Resident private shareholders"). See "*Domestic commercial shareholders*" below for a summary of the taxation treatment applicable to Swiss-resident individuals, who, for income tax purposes, are classified as "professional securities dealers" or are otherwise deemed to hold Company shares in their commercial wealth.

Domestic commercial shareholders

Corporate and individual shareholders who hold their shares as part of a trade or business carried on in Switzerland, in the case of corporate and individual shareholders not resident in Switzerland, through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, are required to recognize dividends, distributions based upon a capital reduction (*remboursements liés à la réduction de la valeur nominale des actions*) and distributions paid out of reserves from capital contributions (*apports de capital*) received on shares and capital gains or losses realized on the sale or other disposition of shares in their income statement for the relevant taxation period and are subject to Swiss federal, cantonal and communal individual or corporate income tax, as the case may be, on any net taxable earnings for such taxation period. The same taxation treatment also applies to Swiss-resident private individuals who, for income tax purposes, are classified as "professional securities dealers" for reasons of, *inter alia*, frequent dealing, or leveraged investments, in shares and other securities (the shareholders referred to in this paragraph for purposes of this section, "Domestic commercial shareholders"). Domestic commercial shareholders who are natural persons holding shares representing at least 10% of the nominal share capital of the Company may be able to decrease the taxable basis by 30% (70% taxable) at the federal level and up to 50% at the cantonal level, depending on their respective cantonal rates, as partial relief from economic double taxation (in the case of capital gains provide the shares have been held for at least one year). Domestic commercial shareholders who are corporate taxpayers may be eligible for tax relief (*réduction pour participations*) in respect of dividends and distributions based upon a capital reduction (*remboursements liés à la réduction de la valeur nominale des actions*) and distributions paid out of reserves from capital contributions (*apports de capital*) if the shares held by them as part of a Swiss business have an aggregate market value of at least CHF 1 million or represent 10% or more of the outstanding share capital or the dividend rights, of the Company. Capital gains relief is generally available only if the sold shares represent 10% or more of the outstanding share capital or the dividend rights, of the Company and provided that the shares have been held for at least one year.

Swiss cantonal and communal private wealth tax and capital tax

Non-resident shareholders

Non-resident shareholders are not subject to Swiss cantonal and communal private wealth tax or capital tax.

Resident private shareholders and domestic commercial shareholders

Resident private shareholders and Domestic commercial shareholders who are individuals are required to report their shares as part of their private wealth or their Swiss business assets, as the case may be, and will be subject to Swiss cantonal and communal private wealth tax on any net taxable wealth (including shares), in the case of Domestic commercial shareholders to the extent the aggregate taxable wealth is allocable to Switzerland. Domestic commercial shareholders who are corporate taxpayers are subject to Swiss cantonal and communal capital tax on taxable capital to the extent the aggregate taxable capital is allocable to Switzerland.

Swiss federal withholding tax

Dividends (including scrip or stock dividends) that the Company pays on the shares are subject to Swiss Federal withholding tax *(impôt anticipé)* imposed on the gross amount of the taxable distribution at the then prevailing rate (currently, at a rate of 35% of the gross amount of the taxable distribution). The Company is required to withhold the Swiss federal withholding tax from the dividend and remit it to the Swiss Federal Tax Administration. Distributions based upon a capital reduction (*reboursements liés à la réduction de la valeur nominale des actions*) and distributions paid out of reserves from contributions confirmed by the Swiss Federal Tax Administration (*apports de capital*) are not subject to Swiss federal withholding tax. Capital gains realized on the sale of the shares are not subject to the Swiss federal withholding tax (other than in case of a sale to the Company (i) for cancellation, (ii) if the total of repurchased shares exceeds 10% of the Company's share capital or (iii) if the repurchased shares are not resold within the applicable time period after the repurchase, if and to the extent the redemption price less the nominal value of the redeemed shares is not booked against reserves from capital contributions confirmed by the Swiss Federal Tax Administration ("Taxable Repurchases")).

The Swiss federal withholding tax on a dividend will be refundable in full to a resident private shareholder and to a Domestic commercial shareholder, who, in each case, *inter alia,* as a condition to a refund, is the beneficial owner of the shares and the dividends or the distributions made or paid on the share and duly reports the dividend in his individual income tax return as income or recognizes the dividend in his income statement as earnings, as applicable.

A Non-resident shareholder may be entitled to a partial or full refund, as the case may be, of the Swiss federal withholding tax on a dividend if the country of his or her residence for tax purposes has entered into a bilateral treaty for the avoidance of double taxation with Switzerland and the conditions of such treaty are met. Such shareholders should be aware that the procedures for claiming treaty benefits (and the time required for obtaining a refund) might differ from country to country. A holder of the shares who is a resident of the U.S. for purposes of the Convention between the United States of America and the Swiss Confederation for the Avoidance of Double Taxation with Respect to Taxes on Income (Treaty), without taxable presence in Switzerland to which the shares are attributable or who is a qualified U.S. pension fund and who, in each case, is the beneficial owner of the shares and the dividend or distribution and who meets the other conditions of the Treaty may (i) in the case of qualified U.S. pension funds, apply for a full refund of the Swiss federal withholding tax, (ii) if the holder is a corporation owning at least 10% of the voting rights of the Company, apply for a refund of the Swiss federal withholding tax withheld in excess of the 5% reduced treaty rate, or (iii) apply for a refund of the Swiss federal withholding tax withheld in excess of the 15% treaty rate in all other cases. The applicable refund request form may be filed with the Swiss Federal Tax Administration following receipt of the dividend and the relevant deduction certificate, however no later than 31 December of the third year following the calendar year in which the dividend was payable.

Swiss federal stamp taxes

The Company will be subject to and pay to the Swiss Federal Tax Administration a 1% Swiss federal issuance stamp duty (droit de timbre *d'émissions*) on the consideration received for the issuance of the shares less certain costs incurred in connection with the issuance (in case of the implementation of the capital band, the issuance stamp duty is payable based on the net-principle at the end of the period of the validity of the capital band). The issuance and delivery of the shares to the initial shareholders at the settlement date is not subject to Swiss federal securities transfer stamp duty (*droit de timbre de négociation*).

Any subsequent dealings in the shares, for which a bank or another securities dealer in Switzerland or Liechtenstein, as defined in the Swiss Federal Stamp Tax Act, acts as an intermediary, or is a party, to the transaction, are, subject to certain exemptions provided for in the Swiss Federal Stamp Tax Act, subject to Swiss securities transfer stamp duty tax at an aggregate tax rate of up to 0.15% of the consideration paid for such shares.

Additional tax considerations associated with our ATM program

As of December 31, 2022, the Company held in total 6,214,021 fully paid-in treasury shares as part of its ATM offerings. These shares were established via two tranches (one in September 2020 and one in September 2021,

respectively). Under present Swiss tax laws, repurchases of shares for the purposes of cancellation are treated as a partial liquidation and are subject to 35% Swiss withholding tax on the difference between the repurchase price and the nominal value of the shares except, since January 1, 2011, to the extent these are booked against the reserves from capital contributions confirmed by the Swiss Federal Tax Administration (*apports de capital*) if any. No partial liquidation treatment applies and no withholding tax is triggered if the shares are not repurchased for cancellation but held by the Company as treasury shares, provided the limitations imposed by corporate law are respected (the nominal value of such shares does not exceed 10% of the outstanding share capital and the purchase price is covered by freely disposable equity). However, regarding the above-mentioned 6,214,021 treasury shares and given the specificities of the ATM offering, the Company sought and obtained a tax ruling from the Swiss Federal Tax Administration confirming that their acquisition by the Company did not constitute a direct partial liquidation and therefore does not trigger withholding tax. Further, the Company has obtained a tax ruling from the concerned Cantonal Tax Authority at its place of incorporation, to obtain confirmation that the placement of these treasury shares for a subscription price superior to their nominal value will not trigger any corporate income tax for the Company.

Of the remaining treasury shares, 2,600,000 shares have been reserved by the board of directors for use only under the Company's current Stock Option and Incentive Plan per a further tax ruling with the concerned Cantonal Tax Authority without corporate income tax consequences for the Company. 1,220,861 shares from the first tranche have not been sold and are still recorded as treasury shares as of December 31, 2022. In addition, 2,393,160 fully paid in treasury shares issued as part of second tranche for the ATM for future subscription (or, possibly, as part of a future share-dividend program, should the Company become profitable and have enough earnings carried forward to cover such distribution) have not been sold and are still recorded as treasury shares as of December 31, 2022. All these shares are covered by the same above-mentioned tax rulings (i.e. their acquisition does not trigger any withholding tax and their placement will not trigger any corporate income tax).

Material U.S. federal income tax considerations for U.S. Holders

The following is a description of material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our common shares. It does not describe all tax considerations that may be relevant to a particular person's decision to own common shares.

This discussion applies only to a U.S. Holder that holds common shares as capital assets for U.S. federal income tax purposes. In addition, it does not describe all of the U.S. federal income tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including alternative minimum tax consequences, the potential application of the provisions of the U.S. Internal Revenue Code of 1986, as amended (the "Code") known as the Medicare contribution tax and tax consequences applicable to U.S. Holders subject to special rules, such as:

- certain financial institutions;
- dealers or electing traders in securities that use a mark-to-market method of tax accounting;
- persons holding our common shares as part of a straddle, integrated transaction or similar transaction;
- U.S. Holders whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- entities classified as partnerships for U.S. federal income tax purposes;
- tax-exempt entities, "individual retirement accounts" or "Roth IRAs;"
- persons that received their common shares as compensation;
- persons that own or are deemed to own 10% or more of our shares, by vote or value; and

- persons holding our common shares in connection with a trade or business conducted outside of the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds common shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships and their partners should consult their tax advisers as to the particular U.S. federal income tax consequences of owning and disposing of the common shares.

This discussion is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury regulations, and the Treaty, all as of the date hereof, any of which is subject to change or differing interpretations, possibly with retroactive effect.

A "U.S. Holder" is a person that, for U.S. federal income tax purposes, is a beneficial owner of common shares and is any of the following:

- a citizen or individual resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia; and
- an estate or trust the income of which is subject to U.S. federal income taxation regardless of its source.

U.S. Holders should consult their tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of common shares in their particular circumstances.

Passive foreign investment company rules

As discussed in our Annual Report on Form 20-F for 2019 and 2020, we were likely a PFIC for these years. We were also likely a PFIC for 2022.

We will be a PFIC under the Code for any taxable year in which, after the application of certain look-through rules with respect to subsidiaries, either (i) 75% or more of our gross income consists of passive income (the "income test") or (ii) 50% or more of the average value of our assets (generally determined on a quarterly basis) consists of assets that produce, or are held for the production of, passive income (the "asset test"). Passive income generally includes dividends, interest, certain non-active rents and royalties, and gains from financial investments. Cash is generally a passive asset. Goodwill (the value of which may be determined by reference to the excess of the sum of a corporation's market capitalization and liabilities over the value of its assets) is generally an active asset to the extent attributable to business activities that produce active income. For purposes of the above calculations, we will be treated as if we hold our proportionate share of the assets of, and directly receive our proportionate share of the income of, any other corporation in which we directly or indirectly own at least 25% of the shares of such corporation by value.

We have not obtained valuations of our assets (including goodwill or going concern value) for 2022 and thus are not in a position to make a definitive determination regarding whether we were a PFIC for 2022. However, we believe that we were likely a PFIC for 2022 due to the decline and volatility of our market capitalization in 2022. If the value of our goodwill or going concern value is determined by reference to our market capitalization then we were a PFIC for 2022. For the same reason there is a significant risk that we will also be a PFIC for 2023, and possibly other taxable years. Because our PFIC status is a factual annual determination that can be determined only after the end of the relevant taxable year, we cannot express a view regarding our PFIC status for 2023 or any future taxable year.

In addition, the application of the income test to a company like us (whose overall losses from research and development activities significantly exceed its gross income) is not entirely clear. We will be a PFIC for any taxable year under the income test if 75% or more of our gross income (as determined for U.S. federal income tax purposes) for such year consists of interest and other passive income. Prior to the commercialization and sales of any of our product candidates, our gross income may consist primarily of upfront or milestone payments and grants (which we believe are

likely to be treated as active income) and interest (which is passive income). The receipt of upfront payments is non-recurring in nature, and the receipt of grants or milestone payments is subject to various conditions. Therefore, there can be no assurance as to the amount of grants, milestone payments or upfront payments (if any) that we will receive for any taxable year. Moreover, we may earn income from sublicensing, which may be passive unless certain conditions are satisfied. There is no assurance that the IRS will not challenge the classification of any of our income items for PFIC purposes for any taxable year. Accordingly, there is no assurance that we will not be a PFIC for any taxable year under the income test.

Under a rule commonly referred to as the "once a PFIC always a PFIC" rule, if we are a PFIC for any taxable year and a U.S. Holder owns our common shares during any portion of that year, we will continue to be treated as a PFIC with respect to the U.S. Holder even if we cease to be a PFIC for any subsequent taxable year. If we are a PFIC for any taxable year during which a U.S. Holder owns our common shares but cease to be a PFIC thereafter, a U.S. Holder may make a "deemed sale" election with respect to our common shares, in which case the U.S. Holder may be required to recognize income under the rules described in the subsequent paragraph without receiving any corresponding cash.

If a U.S. Holder owns our common shares in any year in which we are a PFIC, subject to the discussion above regarding the deemed sale election and the discussion below regarding the mark-to-market election, any gain recognized by the U.S. Holder on a sale or other disposition (including certain pledges) of the common shares will be allocated ratably over the U.S. Holder's holding period for the common shares. The amounts allocated to the taxable year of the sale or other disposition and to any year before we became a PFIC will be taxed as ordinary income. The amount allocated to any other taxable year will be subject to tax at the highest rate in effect for individuals or corporations, as appropriate, for that taxable year, and an interest charge will be imposed on the amount of tax allocated to that taxable year. Further, to the extent that distributions received by a U.S. Holder on its common shares during a taxable year exceed 125% of the average of the annual distributions on the common shares received during the preceding three taxable years or the U.S. Holder's holding period, whichever is shorter, the excess distribution will be subject to taxation in the same manner.

A U.S. Holder may be able to avoid the rules described above by making a mark-to-market election with respect to the common shares, provided that the common shares are regularly traded on Nasdaq or any other qualified exchange. If a U.S. Holder makes the mark-to-market election, it generally will recognize as ordinary income any excess of the fair market value of the common shares at the end of each taxable year in which we are a PFIC over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the common shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes this election, the U.S. Holder's tax basis in the common shares will be adjusted to reflect the income or loss amounts recognized. Any gain recognized on the sale or other disposition of common shares in a year in which we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election, with any excess treated as capital loss).

We do not intend to provide the information necessary for U.S. Holders to make a "qualified electing fund" election, which if available could materially affect the tax consequences to U.S. Holders of the ownership and disposition of our common shares if we are a PFIC for any taxable year. Therefore, U.S. Holders will not be able to make such elections.

In addition, if we are a PFIC (or are treated as a PFIC with respect to a particular U.S. Holder under the "once a PFIC always a PFIC" rule) for the taxable year in which we pay a dividend or for the prior taxable year, the preferential tax rate discussed below with respect to "qualified dividend income" received by certain non-corporate U.S. Holders will not be available.

If a U.S. Holder owns common shares during any taxable year in which we are a PFIC, the U.S. Holder generally must file annual reports on IRS Form 8621 with respect to us with the U.S. Holder's federal income tax return.

U.S. Holders should consult their tax advisers concerning our PFIC status for any taxable year and the consequences thereof.

Taxation of distributions

The following is subject to the discussion under "*—Passive foreign investment company rules*" above.

As discussed under "Item 8. Financial Information—Section A. Consolidated statements and other financial information—Dividends and dividend policy," we do not currently expect to make distributions on our common shares. In the event that we do make distributions of cash or other property on our common shares, other than certain *pro rata* distributions of our common shares, they will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not maintain calculations of our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Dividends paid to certain non-corporate U.S. Holders may be eligible for taxation as "qualified dividend income" and therefore, subject to applicable limitations, may be taxable at rates applicable to long-term capital gains, provided that we are not a PFIC (and are not treated as a PFIC with respect to a particular U.S. Holder under the "once a PFIC always a PFIC" rule) for our taxable year in which the dividend is paid or the preceding taxable year. Non-corporate U.S. Holders should consult their tax advisers regarding the availability of the reduced tax rate on dividends, if any, in their particular circumstances.

Dividends will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will be included in a U.S. Holder's income on the date of receipt. The amount of any dividend income paid in Swiss Francs will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars at that time. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt.

Dividends will be foreign-source income. The amount of dividend income will include any amounts withheld by us in respect of Swiss income taxes. Subject to applicable limitations, some of which vary depending upon the U.S. Holder's particular circumstances, Swiss income taxes withheld from dividends on our common shares (at a rate not exceeding the applicable Treaty rate in the case of U.S. Holders eligible for Treaty benefits) may be creditable against the U.S. Holder's U.S. federal income tax liability. The rules governing foreign tax credits are complex. For example, Treasury regulations provide that, in the absence of an election to apply the benefits of an applicable income tax treaty, in order for foreign income taxes to be creditable the relevant foreign income tax rules must be consistent with certain U.S. federal income tax principles, and we have not determined whether the Swiss income tax system meets this requirement. U.S. Holders should consult their tax advisers regarding the creditability of any Swiss taxes in their particular circumstances (including the U.S. Holder's eligibility for Treaty benefits). In lieu of claiming a credit, U.S. Holders may be able to elect to deduct any Swiss income taxes in computing their taxable income, subject to generally applicable limitations under U.S. law. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all creditable foreign taxes paid or accrued in the taxable year.

Sale or other disposition of common shares

The following is subject to the discussion under "*—Passive foreign investment company rules*" above.

Gain or loss realized on the sale or other disposition of common shares will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder owned the common shares for more than one year, or short-term capital gain or loss otherwise. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the common shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to various limitations.

Information reporting and backup withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless

(i) the U.S. Holder is a corporation or other exempt recipient (and establishes that fact if required to do so) or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle the U.S. Holder to a refund, provided that the required information is furnished in a timely manner to the IRS.

Certain U.S. Holders who are individuals (or certain specified entities) may be required to report information relating to our common shares or non-U.S. accounts through which they may be held. U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to the ownership and disposition of our common shares.

F. Dividends and paying agents

Not applicable.

G. Statement by experts

Not applicable.

H. Documents on display

We are subject to the informational requirements of the Exchange Act. Accordingly, we are required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. In addition, the SEC maintains an Internet website that contains reports and other information about issuers, such as us, that file electronically with the SEC. The address of that website is www.sec.gov.

Additionally, pursuant to Swiss law, any shareholder of record has the right to receive a free copy of this Annual Report and to inspect this Annual Report at any time at our registered office in Ecublens, near Lausanne, Canton of Vaud, Switzerland.

As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our executive officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

I. Subsidiary information

Not applicable.

J. Annual report to security holders

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The Company's activities expose it to the following financial risks: market risk (currency and interest rate risk), credit risk and liquidity risk. The Company's overall risk management program focuses on the unpredictability of financial markets and seeks to minimize potential adverse effects on the Company's financial performance.

Market risk arises from our exposure to fluctuation in currency exchange rates. We are exposed to market risks in the ordinary course of our business, which are principally limited to foreign currency exchange rate fluctuations and to a lesser degree, interest rate fluctuations.

Market risk

Foreign exchange risk

The Company is exposed to foreign exchange risk arising from currency exposures, primarily with respect to the EUR, USD and to a lesser extent to GBP, DKK and SEK. The currency exposure is not hedged. However, the Company has the policy of matching its cash holdings to the currency structure of its expenses. As of December 31, 2022, the Company holds approximately 77% of its overall cash and cash equivalents balance in CHF with the remainder predominantly in EUR and USD (see "Note 8. Cash and cash equivalents and short-term financial assets" of the consolidated financial statements). The Company holds almost 94% of its liquidity (cash and cash equivalents plus short-term financial assets) in CHF.

We have a number of collaboration agreements for which the upfront payments, milestone payments and future royalty payments are not denominated in Swiss Francs, our reporting currency. Furthermore, many of our research and development activities are subcontracted to parties outside of Switzerland and we purchase materials from suppliers outside of Switzerland. As a result, we are exposed to foreign exchange risk. Approximately 44% of our total costs are incurred in currencies other than the Swiss Franc. Due to the size of some of the income received from collaboration agreements and also the high percentage of our costs indirectly being in foreign currencies, a hypothetical 10% change in exchange rates relative to the Swiss Franc could have a material impact on our consolidated financial statements.

Interest rate risk

We maintain financial instruments in accordance with our treasury management policy. The primary objectives of our policy are to preserve principal, maintain proper liquidity and meet operating needs. Our financial assets are subject to interest rate risk and will decrease in value if market interest rates increase. Due to the current negative interest rates in Switzerland and our policy to maintain the majority of our cash and cash equivalents in our functional currency. However, due to the conservative nature of our investments and relatively short duration, interest rate risk is mitigated. We do not own derivative financial instruments. Accordingly, we do not believe that there is any material market risk exposure with respect to derivative or other financial instruments.

Credit risk

The Company maintains a formal treasury risk and investment management policy to limit counterparty credit risk. As of December 31, 2022, the Company's cash and cash equivalents and short-term financial assets are held with four financial institutions, each with a high credit rating assigned by international credit-rating agencies. The maximum amount of credit risk is the carrying amount of the financial assets. Receivables are fully performing, not past due and not impaired (see "Note 8. Cash and cash equivalents and short-term financial assets" and "Note 10. Other current receivables").

Liquidity risk

Inherent in the Company's business are various risks and uncertainties, including the high uncertainty that new therapeutic and diagnostic concepts will succeed. AC Immune's success may depend in part upon its ability to (i) establish and maintain a strong patent position and protection, (ii) enter into collaborations with partners in the pharmaceutical and biopharmaceutical industries, (iii) acquire and keep key personnel employed, and (iv) acquire additional capital to support its operations.

The Company's approach of managing liquidity is to ensure sufficient cash to meet its liabilities when due. Therefore, management closely monitors the cash position on rolling forecasts based on expected cash flow to enable the Company to finance its operations for at least 18 months.

Based on the Company's current liquidity position, comprised of cash and cash equivalents and short-term financial assets, the Company is financed into Q3 2024, excluding any potential milestones.

Safe Harbor

See “Forward-looking Statements.”

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt securities

Not applicable.

B. Warrants and rights

Not applicable.

C. Other securities

Not applicable.

D. American depositary shares

Not applicable.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

A. Defaults

No matters to report.

B. Arrears and delinquencies

No matters to report.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

A. Disclosure controls and procedures

As of December 31, 2022, under the supervision and with the participation of our management, including our Chief Executive Officer and VP Finance and Interim Chief Financial Officer, we performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act). There are inherent limitations to the effectiveness of any disclosure controls and procedures system, including the possibility of human error and circumventing or overriding them. Even if effective, disclosure controls and procedures can provide only reasonable assurance of achieving their control objectives.

Our Chief Executive Officer and VP Finance and Interim Chief Financial Officer concluded that our disclosure controls and procedures were effective in recording, processing, summarizing and reporting on a timely basis the information required to be included in periodic filings under the Exchange Act and that such information is accumulated and communicated to management, including our Chief Executive and Chief Financial Officers, as appropriate to allow timely decisions regarding required disclosure.

B. Management's Annual Report on internal control over financial reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) of the Exchange Act. Our internal control over financial reporting is supported by written policies and procedures. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our Chief Executive Officer and VP Finance and Interim Chief Financial Officer, management conducted an evaluation of the effectiveness of our internal control over financial reporting based upon criteria established in *Internal Control – Integrated Framework* (2013) by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our management, including our Chief Executive Officer and VP Finance and Interim Chief Financial Officer concluded that our internal control over financial reporting was effective as of December 31, 2022.

C. Attestation report of the registered public accounting firm

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by PricewaterhouseCoopers SA, an independent registered public accounting firm. Their report is included on page F-2. PricewaterhouseCoopers SA is a member of the Chamber of Public Accountants, Lausanne, Switzerland.

D. Changes in internal control over financial reporting

There have been no changes in the Company's internal control over financial reporting during the year ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. [RESERVED]

ITEM 16A. Audit committee financial experts

Our board of directors has determined that Monika Bütler, Thomas Graney and Werner Lanthaler are audit committee financial experts, as that term is defined by the SEC, and are independent for the purposes of SEC rules.

ITEM 16B. Code of Ethics

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics, which covers a broad range of matters including the handling of conflicts of interest, compliance issues and other corporate policies such as insider trading and equal opportunity and non-discrimination standards. Our Code of Business Conduct and Ethics applies to all of our directors, executive officers and employees. We have published our Code of Business Conduct and Ethics on our website, *www.acimmune.com*. The information contained on our website is not a part of this Annual Report.

ITEM 16C. Principal accountant fees and services

In CHF thousands	For the Year Ended December 31, 2022	2021
Audit fees	725	668
Audit-related fees	5	15
Total fees	730	683

For the year ended December 31, 2022, PwC was the Company's auditor for the IFRS and statutory accounts. At the ordinary Annual General Meeting on June 24, 2022, the shareholders appointed PwC as the Company's auditor for a term of office of 1 year.

Audit fees include fees for audit services primarily related to the integrated audit of (i) our annual consolidated financial statements and our internal control over financial reporting as required by Section 404(b) of the Sarbanes-Oxley Act of 2002, (ii) the review of our quarterly condensed consolidated financial statements, (iii) comfort letters, consents and assistance with and review of documents relating to our securities offerings, including our registration statement on Form F-3 related to our follow-on shelf registration in Q2 2021 and (iv) other accounting and financial reporting consultation billed as audit fees or necessary to comply with the standards of the Public Company Accounting Oversight Board (United States).

Audit-related fees consisted of fees billed for assurance and related services that were reasonably related to the performance of the audit or review of our financial statements or for services that were traditionally performed by the external auditor.

Pre-approval policies and procedures

In accordance with the requirements of the U.S. Sarbanes-Oxley Act of 2002 and rules issued by the SEC, we review and pre-approve any services performed by PwC. The procedure requires that all proposed future engagements of PwC for audit and permitted non-audit services are submitted to the Audit and Finance Committee for approval prior to the beginning of any such services. In accordance with this policy, all services performed by and fees paid to PwC in this Item 16C, were approved by the Audit and Finance Committee.

ITEM 16D. Exemptions from the listing standards for audit committees

Not applicable.

ITEM 16E. Purchases of equity securities by the issuer and affiliated purchasers

In 2022, no purchases of our equity securities were made by or on behalf of AC Immune SA or any affiliated purchaser.

ITEM 16F. Change in registrant's certifying accountant

Not applicable.

ITEM 16G. Corporate governance

Summary of Significant Corporate Governance Differences from Nasdaq Listing Standards

Our common shares are listed on the Nasdaq Global Market. We are therefore required to comply with certain of the Nasdaq's corporate governance listing standards (Nasdaq Standards). As a foreign private issuer, we may follow our home country's corporate governance practices in lieu of certain of the Nasdaq Standards. Our corporate governance practices differ in certain respects from those that U.S. companies must adopt in order to maintain a Nasdaq listing. A brief, general summary of those differences is provided as follows.

Independent directors

Swiss law does not require that a majority of our board of directors consist of independent directors. Our board of directors therefore may include fewer independent directors than would be required if we were subject to Nasdaq Listing Rule 5605(b)(1). In addition, we are not subject to Nasdaq Listing Rule 5605(b)(2), which requires that independent directors must regularly have scheduled meetings at which only independent directors are present.

Compensation, nomination and corporate governance committee

As Swiss law requires that we have a compensation, nomination and corporate governance committee, we will follow home country requirements with respect to such committee. As a result, our practice will vary from the requirements of Nasdaq Listing Rule 5605(d), which sets forth certain requirements as to the responsibilities, composition and independence of compensation, nomination and corporate governance committees.

Quorum requirements

In accordance with Swiss law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. Our practice thus varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock.

Solicitation of proxies

Our articles of association provide for an independent proxy holder elected by our shareholders, who may represent our shareholders at a general meeting of shareholders, and we must provide shareholders with an agenda and other relevant documents for the general meeting of shareholders. However, Swiss law does not have a regulatory regime for the solicitation of proxies, and company solicitation of proxies is prohibited for public companies in Switzerland. Thus, our practice will vary from the requirement of Nasdaq Listing Rule 5620(b), which sets forth certain requirements regarding the solicitation of proxies.

Shareholder approval

We have opted out of shareholder approval requirements for the issuance of securities in connection with certain events such as the acquisition of stock or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us and certain private placements. To this extent, our practice varies from the requirements of Nasdaq Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

ITEM 16H. Mine safety disclosure

Not applicable.

ITEM 16I. Disclosure regarding foreign jurisdictions that prevent inspections

Not applicable.

PART III

ITEM 17. Financial statements

We have responded to Item 18 in lieu of this item.

ITEM 18. Financial statements

Financial Statements are filed as part of this Annual Report, see page F-1.

ITEM 19. Exhibits

(a) The following documents are filed as part of Annual Report on Form 20-F:

3.1	Articles of Association of AC Immune SA (incorporated herein by reference to Exhibit 99.3 to the Company's Report on Form 6-K, filed with the SEC on June 24, 2022)
4.1	Research Collaboration and License Agreement between AC Immune SA Corporation and Genentech, Inc. dated November 6, 2006 (incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form F-1 (File No. 333-211714) filed with the SEC on May 31, 2016)
4.2	Amendment to the Research Collaboration and License Agreement between AC Immune SA Corporation and Genentech, Inc. dated May 7, 2015 (incorporated herein by reference to Exhibit 10.2 to the Company's Registration Statement on Form F-1 (File No. 333-211714) filed with the SEC on May 31, 2016)
4.3	Research Collaboration and License Agreement between AC Immune SA Corporation and Genentech, Inc. dated June 15, 2012 (incorporated herein by reference to Exhibit 10.3 to the Company's Registration Statement on Form F-1 (File No. 333-211714) filed with the SEC on May 31, 2016)
4.4	License and Collaboration Agreement between Piramal Imaging Ltd., Piramal Imaging SA and AC Immune SA, dated May 9, 2014 (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form F-1 (File No. 333-211714) filed with the SEC on May 31, 2016)
4.5	License, Development and Commercialization Agreement between Janssen Pharmaceuticals, Inc. and AC Immune SA, dated December 24, 2014 (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form F-1 (File No. 333-211714) filed with the SEC on May 31, 2016)
4.6*	Form of Indemnity Agreement
4.7	AC Immune SA 2013 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 to the Company's Registration Statement on Form F-1 (File No. 333-211714) filed with the SEC on May 31, 2016)
4.8	AC Immune SA 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 99.08 to the Company's Report on Form 6-K, filed with the SEC on October 13, 2016)
4.9	License Agreement between AC Immune SA and Eli Lilly and Company, dated December 11, 2018 (incorporated herein by reference to Exhibit 4.14 to the Amendment No. 1 to the Company's Annual Report on Form 20-F/A, filed with the SEC on April 19, 2019)
4.10	Convertible Note Agreement between AC Immune SA and Eli Lilly and Company, dated December 11, 2018 (incorporated herein by reference to Exhibit 4.15 to the Company's Annual Report on Form 20-F, filed with the SEC on March 21, 2019)
4.11	First Amendment to License Agreement between AC Immune SA and Eli Lilly and Company, dated September 19, 2019 (incorporated herein by reference to Exhibit 10.1 to the Company's Report on Form 6-K, filed with the SEC on September 20, 2019)
4.12	Second Amendment to License Agreement between AC Immune SA and Eli Lilly and Company, dated March 20, 2020 (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 6-K (File No. 001-37891) filed with the SEC on March 23, 2020)

4.13	Open Market Sale Agreement, dated as of May 5, 2021, between AC Immune SA and Jefferies LLC (incorporated herein by reference to Exhibit 1.1 to the Company's Current Report on Form 6-K (File No. 001-37891) filed with the SEC on May 5, 2021)
4.14	Asset Purchase and Contribution in Kind Agreement, dated as of July 26, 2021, between AC Immune SA and Affiris AG (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 6-K (File No. 001-37891) filed with the SEC on August 4, 2021)
4.15	Convertible Note Agreement, dated as of July 26, 2021, between AC Immune SA and Santo Venture GmbH (incorporated herein by reference to Exhibit 10.2 to the Company's Current Report on Form 6-K (File No. 001-37891) filed with the SEC on August 4, 2021)
4.16	Convertible Note Agreement, dated as of July 26, 2021, between AC Immune SA and FCPB Affi GmbH (incorporated herein by reference to Exhibit 10.3 to the Company's Current Report on Form 6-K (File No. 001-37891) filed with the SEC on August 4, 2021)
4.17*	Description of Securities
8.1*	List of subsidiaries
12.1*	Certification of Andrea Pfeifer pursuant to 17 CFR 240.13a-14(a)
12.2*	Certification of Christopher Roberts pursuant to 17 CFR 240.13a-14(a)
13.1*	Certification of Andrea Pfeifer pursuant to 17 CFR 240.13a-14(b) and 18 U.S.C.1350
13.2*	Certification of Christopher Roberts pursuant to 17 CFR 240.13a-14(b) and 18 U.S.C.1350
15.1*	Consent of PricewaterhouseCoopers SA
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document

* Filed herewith

(b) Financial Statement Schedules

None.

Signatures

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this Annual Report on its behalf.

AC IMMUNE SA

Date: March 16, 2023

By: /s/ Andrea Pfeifer
Name: Andrea Pfeifer
Title: Chief Executive Officer

By: /s/ Christopher Roberts
Name: Christopher Roberts
Title: Vice President Finance and Interim Chief Financial Officer

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Audited consolidated financial statements — AC IMMUNE SA

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of AC Immune SA

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of AC Immune SA and its subsidiary (the "Company") as of December 31, 2022 and December 31, 2021, and the related consolidated statements of income/(loss), comprehensive income/(loss), changes in equity and cash flows for each of the three years in the period ended December 31, 2022, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and December 31, 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022 in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Annual Report on Internal Control over Financial Reporting appearing under Item 15B. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Intangible asset – valuation

As described in Notes 6 and 7 to the consolidated financial statements, the Company has CHF 50,416 thousand of an in-process research and development (IPR&D) intangible asset as of December 31, 2022. The asset is defined as an intangible asset not yet ready for use. Therefore, in accordance with IAS 36 'Impairment of asset', the IPR&D asset is reviewed at least annually for impairment by assessing the fair value less costs to sell (recoverable amount) and comparing this to the carrying value of the asset. To determine the recoverable amount, management estimated the fair value less costs to sell of the intangible asset, using the same model used at the acquisition date. The significant assumptions used in the model include anticipated research and development costs, anticipated costs of goods and sales and marketing expenditures, probability of achieving clinical and regulatory development milestones in accordance with certain industry benchmarks, target indication prevalence and incidence rates, anticipated market share, general commercialization expectations such as anticipated pricing and uptake, expected patent life and market exclusivity periods, and the discount rate used to discount future cash flows.

The principal considerations for our determination that performing procedures relating to the intangible asset – valuation is a critical audit matter are the significant judgment by management when determining the value of the intangible asset. This in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating the audit evidence obtained related to the valuation of the intangible asset and management's assumptions related to anticipated research and development costs, anticipated costs of goods and sales and marketing expenditures, probability of achieving clinical and regulatory development milestones in accordance with certain industry benchmarks, target indication prevalence and incidence rates, anticipated market share, general commercialization expectations such as anticipated pricing and uptake, expected patent life and market exclusivity periods, and the discount rate used to discount future cash flows. In addition, the audit effort involved the use of professionals with specialized skill and knowledge.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to management's valuation of the intangible asset. These procedures also included, among others, (i) testing management's process for developing the fair value estimate; (ii) evaluating the appropriateness of the discounted cash flow model; (iii) testing the completeness and accuracy of underlying data used in the model; and (iv) evaluating the reasonableness of the significant assumptions used by management related to anticipated research and development costs, anticipated costs of goods and sales and marketing expenditures, probability of achieving clinical and regulatory development milestones in accordance with certain industry benchmarks, target indication prevalence and incidence rates, anticipated market share, general commercialization expectations such as anticipated pricing and uptake, expected patent life and market exclusivity periods, and the discount rate. Evaluating management's assumptions related to anticipated research and development costs, anticipated costs of goods and sales and marketing expenditures, probability of achieving clinical and regulatory development milestones in accordance with certain industry benchmarks, target indication prevalence and incidence rates, anticipated market share, general commercialization expectations such as anticipated pricing and uptake, expected patent life and market exclusivity periods, involved evaluating whether the assumptions used by management were reasonable considering (i) the consistency with market and industry data; and (ii) whether these assumptions were consistent with evidence obtained in other areas of the audit. Professionals with specialized skill and knowledge were used to assist in the evaluation of the Company's discounted cash flow model and the discount rate assumption.

/s/ PricewaterhouseCoopers SA

Lausanne, Switzerland
March 16, 2023

We have served as the Company's auditor since 2018.

Consolidated Financial Statements (IFRS)
AC Immune SA
Consolidated Balance Sheets
(In CHF thousands)

	Note	As of December 31, 2022	2021
Assets			
Non-current assets			
Property, plant and equipment	4	4,259	5,116
Right-of-use assets	5	2,808	2,914
Intangible asset	6/7	50,416	50,416
Long-term financial assets	5	361	363
Total non-current assets		57,844	58,809
Current assets			
Prepaid expenses	9	4,708	3,015
Accrued income	9/13	408	975
Other current receivables	10	392	428
Short-term financial assets	8	91,000	116,000
Cash and cash equivalents	8	31,586	82,216
Total current assets		128,094	202,634
Total assets		185,938	261,443
Shareholders' equity and liabilities			
Shareholders' equity			
Share capital	11	1,797	1,794
Share premium	11	431,323	431,251
Treasury shares	11	(124)	(124)
Currency translation differences		10	—
Accumulated losses		(264,015)	(200,942)
Total shareholders' equity		168,991	231,979
Non-current liabilities			
Long-term lease liabilities	5	2,253	2,340
Net employee defined benefit liabilities	17	3,213	7,098
Total non-current liabilities		5,466	9,438
Current liabilities			
Trade and other payables	12	929	2,003
Accrued expenses	12	9,417	16,736
Deferred income	13	587	717
Short-term lease liabilities	5	548	570
Total current liabilities		11,481	20,026
Total liabilities		16,947	29,464
Total shareholders' equity and liabilities		185,938	261,443

The accompanying notes are an integral part of these consolidated financial statements.

AC Immune SA
Consolidated Statements of Income/(Loss)
(In CHF thousands, except for per-share data)

		For the Year Ended December 31,		
	Note	2022	2021	2020
Revenue				
Contract revenue	13	3,935	—	15,431
Total revenue		3,935	—	15,431
Operating expenses				
Research & development expenses	14	(60,336)	(62,282)	(59,487)
General & administrative expenses	14	(15,789)	(17,910)	(18,557)
Other operating income/(expense), net	13.2	1,343	1,182	1,353
Total operating expenses		(74,782)	(79,010)	(76,691)
Operating loss		(70,847)	(79,010)	(61,260)
Financial income	14	69	6,485	78
Financial expense	14	(355)	(581)	(184)
Exchange differences	14	393	113	(555)
Finance result, net		107	6,017	(661)
Loss before tax		(70,740)	(72,993)	(61,921)
Income tax expense	16	(13)	(3)	—
Loss for the period		(70,753)	(72,996)	(61,921)
Loss per share:				
Basic and diluted loss for the period attributable to equity holders	20	(0.85)	(0.97)	(0.86)

Consolidated Statements of Comprehensive Income/(Loss)
(In CHF thousands)

		For the Year Ended December 31,		
	Note	2022	2021	2020
Loss for the period		(70,753)	(72,996)	(61,921)
Items that may be reclassified to income or loss in subsequent periods (net of tax):				
Currency translation differences		10	—	—
Items that will not to be reclassified to income or loss in subsequent periods (net of tax):				
Remeasurement gains on defined-benefit plans (net of tax)	17	4,426	956	726
Other comprehensive income		4,436	956	726
Total comprehensive loss, net of tax		(66,317)	(72,040)	(61,195)

The accompanying notes are an integral part of these consolidated financial statements.

AC Immune SA
Consolidated Statements of Changes in Equity
(In CHF thousands)

	Note	Share capital	Share premium	Treasury shares	Accumulated losses	Currency translation differences	Total
Balance as of January 1, 2020		1,437	346,526	—	(75,521)	—	272,442
Net loss for the period		—	—	—	(61,921)	—	(61,921)
Other comprehensive income	17	—	—	—	726	—	726
Total comprehensive loss		—	—	—	(61,195)	—	(61,195)
Share-based payments	18	—	—	—	4,088	—	4,088
Issuance of shares, net of transaction costs:							
Held as treasury shares	11	100	—	(100)	—	—	—
Restricted share awards	18	—	222	—	(222)	—	—
Exercise of options	18	1	142	—	—	—	143
Balance as of December 31, 2020		1,538	346,890	(100)	(132,850)	—	215,478

	Note	Share capital	Share premium	Treasury shares	Accumulated losses	Currency translation differences	Total
Balance as of January 1, 2021		1,538	346,890	(100)	(132,850)	—	215,478
Net loss for the period		—	—	—	(72,996)	—	(72,996)
Other comprehensive income	17	—	—	—	956	—	956
Total comprehensive loss		—	—	—	(72,040)	—	(72,040)
		—	—				
Share-based payments	18	—	—	—	4,126	—	4,126
Proceeds from sale of treasury shares in public offerings, net of underwriting fees and transaction costs	11	—	12,097	24	—	—	12,121
Issuance of shares, net of transaction costs:							—
IPR&D asset purchase	6/11	130	49,741	—	—	—	49,871
Asset acquisition - common shares	6/11	12	4,587	—	—	—	4,599
Conversion note agreements	11	61	16,683	—	—	—	16,744
Held as treasury shares	11	48	—	(48)	—	—	—
Restricted share awards	18	1	171	—	(178)	—	(6)
Exercise of options	18	4	1,082	—	—	—	1,086
Balance as of December 31, 2021		1,794	431,251	(124)	(200,942)	—	231,979

	Note	Share capital	Share premium	Treasury shares	Accumulated losses	Currency translation differences	Total
Balance as of January 1, 2022		1,794	431,251	(124)	(200,942)	—	231,979
Net loss for the period		—	—	—	(70,753)	—	(70,753)
Other comprehensive income	17	—	—	—	4,426	10	4,436
Total comprehensive loss		—	—	—	(66,327)	10	(66,317)
Share-based payments	18	—	—	—	3,330	—	3,330
Proceeds from sale of treasury shares in public offerings, net of underwriting fees and transaction costs	11	—	(8)	0	—	—	(8)
Issuance of shares, net of transaction costs:							
Restricted share awards	18	0	76	—	(76)	—	0
Exercise of options	18	3	4	—	—	—	7
Balance as of December 31, 2022		1,797	431,323	(124)	(264,015)	10	168,991

The accompanying notes are an integral part of these consolidated financial statements.

AC Immune SA
Consolidated Statements of Cash Flows
(In CHF thousands)

	Note	For the Year Ended December 31, 2022	2021	2020
Operating activities				
Loss for the period		(70,753)	(72,996)	(61,921)
Adjustments to reconcile net loss for the period to net cash flows:				
Depreciation of property, plant and equipment	4	1,793	1,897	1,535
Depreciation of right-of-use assets	5	566	509	432
Finance (income)/expense, net	14	(559)	(6,769)	376
Share-based compensation expense	18	3,330	4,126	4,088
Change in net employee defined benefit liability	17	541	590	705
Interest expense	5/14	355	573	175
(Gain)/loss on sale of fixed assets		—	13	(64)
Changes in working capital:				
(Increase)/decrease in prepaid expenses	9	(1,718)	791	(1,304)
Decrease/(increase) in accrued income	9	567	594	(507)
Decrease/(increase) in other current receivables	10	36	(99)	(25)
(Decrease)/increase in accrued expenses	12	(6,114)	5,214	(757)
(Decrease)/increase in deferred income	13	(130)	425	(4,157)
(Decrease)/increase in trade and other payables	12	(1,073)	(84)	2,177
Cash used in operating activities		(73,159)	(65,216)	(59,247)
Interest received	14	69	—	78
Interest paid	5/14	(470)	(465)	(339)
Finance expenses paid	14	(8)	(8)	(9)
Net cash flows used in operating activities		(73,568)	(65,689)	(59,517)
Investing activities				
Short-term financial assets, net	8	25,000	(51,000)	30,000
Purchases of property, plant and equipment	4	(1,239)	(2,635)	(1,706)
Proceeds from sale of property, plant and equipment	4	—	—	64
Rental deposits	5	2	(29)	(29)
Net cash flows provided by/(used in) investing activities		23,763	(53,664)	28,329
Financing activities				
Proceeds from issuance of convertible loan	11	—	23,463	—
Transaction costs on issuance of shares	11	—	(6)	—
Proceeds from sale of treasury shares in public offerings, net of underwriting fees and transaction costs	11	(8)	—	—
Proceeds from issuance of treasury shares, net of underwriting fees and transaction costs	11	—	12,121	100
Proceeds from issuance of common shares – asset acquisition, net of transaction costs	11	—	4,599	—
Proceeds from issuance of common shares – option plan, net of transaction costs	11	7	1,082	143
Principal payments of lease obligations	5	(569)	(513)	(432)
Transaction costs associated with issuance of shares in relation to asset acquisition previously recorded in Accrued expenses	12	(776)	—	—
Repayment of short-term financing obligation		—	—	(514)
Payment for the issuance of treasury shares	11	—	—	(100)
Net cash flows (used in)/provided by financing activities		(1,346)	40,746	(803)
Net decrease in cash and cash equivalents		(51,151)	(78,607)	(31,991)
Cash and cash equivalents at January 1		82,216	160,893	193,587
Exchange gain/(loss) on cash and cash equivalents		521	(70)	(703)
Cash and cash equivalents at December 31		31,586	82,216	160,893
Net decrease in cash and cash equivalents		(51,151)	(78,607)	(31,991)
Supplemental non-cash activity				
Capital expenditures in Trade and other payables or Accrued expenses	4	—	303	328
Issuance of shares for purchase of IPR&D asset in asset acquisition	6/7	—	50,416	—
Transaction costs associated with issuance of shares in relation to the asset acquisition recorded in Accrued expenses	6	—	776	—
Settlement of convertible notes recorded within Shareholders' equity	11	—	16,920	—

The accompanying notes are an integral part of these consolidated financial statements.

AC Immune SA
Notes to the Consolidated Financial Statements
(In CHF thousands except for share and per share data)

1. General information

AC Immune SA was founded in 2003. The Company controls a fully-owned subsidiary, AC Immune USA, Inc. ("AC Immune USA" or "Subsidiary" and, together with AC Immune SA, "AC Immune," "ACIU," "Company," "we," "our," "ours," "us"), which was registered and organized under the laws of Delaware, USA in June 2021. The Company and its Subsidiary form the Group.

AC Immune SA is a clinical-stage biopharmaceutical company leveraging our two proprietary technology platforms to discover, design and develop novel proprietary medicines and diagnostics for prevention and treatment of neurodegenerative diseases (NDD) associated with protein misfolding. Misfolded proteins are generally recognized as the leading cause of NDD, such as Alzheimer's disease (AD) and Parkinson's disease (PD), with common mechanisms and drug targets, such as amyloid beta (Abeta), Tau, alpha-synuclein (a-syn) and TDP-43. Our corporate strategy is founded upon a three-pillar approach that targets (i) AD, (ii) focused non-AD NDD including Parkinson's disease, ALS and NeuroOrphan indications and (iii) diagnostics. We use our two unique proprietary platform technologies, SupraAntigen (conformation-specific biologics) and Morphomer (conformation-specific small molecules), to discover, design and develop novel medicines and diagnostics to target misfolded proteins.

The Company was initially incorporated as a limited liability company on February 13, 2003 in Basel, and effective August 25, 2003 was transformed into a stock company. The Company's corporate headquarters are located at EPFL Innovation Park Building B, 1015 Lausanne, Switzerland.

2. Basis of preparation

Going concern

The Company believes that it will be able to meet all of its obligations as they fall due for at least 12 months from the filing date of this Form 20-F, after considering the Company's cash position of CHF 31.6 million and short-term financial assets of CHF 91.0 million as of December 31, 2022. Hence, these consolidated financial statements have been prepared on a going-concern basis.

To date, the Company has financed its cash requirements primarily from its public offerings, share issuances, contract revenues from license and collaboration agreements (LCAs) and grants. The Company is a clinical stage company and is exposed to all the risks inherent to establishing a business. Inherent to the Company's business are various risks and uncertainties, including the substantial uncertainty as to whether current projects will succeed and our ability to raise additional capital as needed. These risks may require us to take certain measures such as delaying, reducing or eliminating certain programs. The Company's success may depend in part upon its ability to (i) establish and maintain a strong patent position and protection, (ii) enter into collaborations with partners in the pharmaceutical and biopharmaceutical industries, (iii) successfully move its product candidates through clinical development, (iv) attract and retain key personnel and (v) acquire capital to support its operations.

Statement of compliance

The consolidated financial statements have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB). These consolidated financial statements were approved for issue by the Board of Directors on March 15, 2023.

Basis of measurement

The consolidated financial statements have been prepared under the historical cost convention except for items that are required to be accounted for at fair value.

3. Summary of significant accounting policies

The principal accounting policies adopted in the preparation of these consolidated financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

Functional and reporting currency

These consolidated financial statements and accompanying notes are presented in Swiss Francs (CHF), which is AC Immune SA's functional currency and the Group's reporting currency. The Company's subsidiary has a functional currency of the U.S. Dollar (USD). The respective functional currency represents the primary economic environment in which the entities operate.

The following exchange rates have been used for the translation of the financial statements of AC Immune USA:

	For the Year Ended December 31,		
	2022	2021	2020
CHF/USD			
Closing rate, USD 1	0.933	0.923	N/A
Weighted average exchange rate, USD 1	0.965	0.929	N/A

The results and financial position of AC Immune USA are translated into the presentation currency as follows:

i. assets and liabilities for each balance sheet presented are translated at the closing rate at the date of that balance sheet;

ii. income and expenses for each statement of income/(loss) are translated at average exchange rates; and

iii. all resulting exchange differences are recognized in other comprehensive income/(loss), within cumulative translation differences.

Basis of consolidation

The annual closing date of the individual financial statements is December 31. The Company fully-owns its Subsidiary and fully consolidates its financial statements into these consolidated financial statements. All intercompany transactions have been eliminated.

Foreign currency transactions

Foreign currency transactions are translated into the respective functional currency using prevailing exchange rates at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in the consolidated statements of income/(loss). Any gains or losses from these translations are included in the consolidated statements of income/(loss) in the period in which they arise.

Current vs. non-current classification

The Company presents assets and liabilities in the consolidated balance sheets based on current/non-current classification. The Company classifies all amounts to be realized or settled within 12 months after the reporting period to be current and all other amounts to be non-current.

Revenue recognition

The Company applies IFRS 15 *Revenue from Contracts with Customers*. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under IFRS 15, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of IFRS 15, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company applies the five-step model to contracts only when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of IFRS 15, the Company assesses the goods or services promised within each contract, and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company enters into LCAs which are within the scope of IFRS 15, under which it licenses certain rights to its product candidates and intellectual property to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, upfront license fees, development, regulatory and/or commercial milestone payments; payments for research and clinical services the Company provides through either its full-time employees or third-party vendors, and royalties on net sales of licensed products commercialized from the Company's intellectual property. Each of these payments results in license, collaboration and other revenues, which are classified as contract revenue on the consolidated statements of income/(loss).

Licenses of intellectual property

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are sold in conjunction with a related service, the Company uses judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the performance obligation is settled over time, the Company determines the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments

At the inception of each arrangement that includes development, regulatory and/or commercial milestone payments, the Company evaluates whether the milestones are considered highly probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is highly probable that a significant cumulative revenue reversal would not occur in future periods, the associated milestone value is included in the transaction price. These amounts for the performance obligations under the contract are recognized as they are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments recorded would affect contract revenues and earnings in the period of adjustment.

Research and development services

The Company has certain arrangements with our collaboration partners that include contracting our employees for research and development programs. The Company assesses if these services are considered distinct in the context of each contract and, if so, they are accounted for as separate performance obligations. These revenues are recorded in contract revenue as the services are performed.

Sublicense revenues

The Company has certain arrangements with our collaboration partners that include provisions for sublicensing. The Company recognizes any sublicense revenues at the point in time it is highly probable to obtain and not subject to reversal in the future.

Contract balances

The Company receives payments and determines credit terms from its customers for its various performance obligations based on billing schedules established in each contract. The timing of revenue recognition, billings and cash collections results in billed other current receivables, accrued income (contract assets), and deferred income (contract liabilities) on the consolidated balance sheets. Amounts are recorded as other current receivables when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be 1 year or less.

For a complete discussion of accounting for contract revenue, see "Note 13. Contract revenues."

Research and development expenses

Given the stage of development of the Company's products, all research and development expenditure is expensed as incurred as it does not meet the capitalization criteria outlined in IAS 38 *Intangible Assets*. The Company has not capitalized any R&D expenses to date. Research and development expenditures include:

- the cost of acquiring, developing and manufacturing active pharmaceutical ingredients for product candidates that have not received regulatory approval, clinical trial materials and other research and development materials;
- fees and expenses incurred under agreements with contract research organizations, investigative sites and other entities in connection with the conduct of clinical trials and preclinical studies and related services, such as administrative, data-management and laboratory services;
- fees and costs related to regulatory filings and activities;
- costs associated with preclinical and clinical activities;
- employee-related expenses, including salaries and bonuses, benefits, travel and share-based compensation expenses; and
- all other allocated expenses such as facilities and information technology (IT) costs.

For external research contracts, expenses include those associated with contract research organizations, or CROs, or contract manufacturing organizations, or CMOs. The invoicing from CROs or CMOs for services rendered do not always align with work performed. We accrue the cost of services rendered in connection with CRO or CMO activities based on our estimate of the "stage of completion" for such contracted services. We maintain regular communication with our CRO or CMO vendors to gauge the reasonableness of our estimates and accrue expenses as of the balance sheet date in the consolidated financial statements based on facts and circumstances known at the time.

Registration costs for patents are part of the expenditure for research and development projects. Therefore, registration costs for patents are expensed when incurred as long as the research and development project concerned does not meet the criteria for capitalization.

General and administrative expenses

General and administrative expenses are expensed as incurred and include personnel costs, expenses for outside professional services and all other allocated expenses. Personnel costs consist of salaries, cash bonuses, benefits and share-based compensation. Outside professional services consist of legal, accounting and audit services, IT and other consulting fees. Allocated expenses consist of certain IT, facilities and depreciation expenses.

Grant income

The Company has received grants, from time to time, from the Michael J. Fox Foundation (MJFF), the Target ALS Foundation (Target ALS) and other institutions to support certain research projects. Grants are recorded at their fair value in the consolidated statements of income/(loss) within other operating income/(expenses), net when there is reasonable assurance that the Company will satisfy the underlying grant conditions and the grants will be received. In certain circumstances, grant income may be recognized before formal grantor acknowledgement of milestone achievements. To the extent required, grant income is deferred and recognized on a systematic basis over the periods in which the Company expects to recognize the related expenses for which the grants are intended to compensate.

Leases

The Company applies IFRS 16 *Leases*, which provides the model for lessee accounting in which all leases, other than short-term and low-value leases, are accounted for by the recognition on the consolidated balance sheet of a right-of-use asset and a lease liability, and the subsequent amortization of the right-of-use asset over the earlier of the end of the useful life or the lease term. In accordance with IFRS 16, the Company (i) does not recognize right-of-use assets and lease liabilities for leases of low value (i.e. approximate fair value of USD 5,000). For a complete discussion of accounting, see "Note 5. Right-of-use assets, long-term financial assets and lease liabilities."

Right-of-use assets and lease liabilities

At inception of a leasing contract, the Company assesses whether a contract is, or contains, a lease based on whether the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration. The Company recognizes a right-of-use asset and a lease liability at the lease commencement date. The lease liability is initially measured at the present value of the lease payments that are not paid at the commencement date, discounted using the interest rate implicit in the lease or, if that rate cannot be readily determined, the Company's incremental borrowing rate. The lease liabilities are classified as current or non-current based on the due dates of the underlying principal payments.

Lease payments generally are fixed for the contract term. The lease liability is measured at amortized cost using the effective interest method. The lease liability is re-measured if there is a change in the estimated lease term, a change in future lease payments arising from a change in an index or rate, a change in the Company's estimate of the amount expected to be payable under a residual value guarantee or a change in assessment of whether it will exercise a purchase, extension or termination option.

At inception, the right-of-use asset comprises the initial lease liability and any initial direct costs. The right-of-use asset is depreciated over the shorter of the lease term or the useful life of the underlying asset. The right-of-use asset is periodically reduced by impairment losses, if any, and adjusted for certain re-measurements of the lease liability performed on as certain potential triggering events may arise (e.g. lease modifications). When the lease liability is re-measured, a corresponding adjustment is made to the carrying amount of the right-of-use asset or is recorded in profit or loss if the carrying amount of the right-of-use asset has been reduced to zero.

The estimated lease term by right-of-use asset categories are as follows:

Buildings	5 years
Office equipment	5 years
IT equipment	5 years

Both the right-of-use-assets and lease liabilities are recognized in the consolidated balance sheets.

Property, plant and equipment

Equipment is shown at historical acquisition cost, less accumulated depreciation and any accumulated impairment losses. Historical costs include expenditures that are directly attributable to the acquisition of the property, plant and equipment. Depreciation is calculated using a straight-line method to write off the cost of each asset to its residual value over its estimated useful life as follows:

IT equipment	3 years
Laboratory equipment	5 years
Leasehold improvements/furniture	5 years

The assets' residual values and useful lives are reviewed, and adjusted if appropriate, at each balance sheet date. Where an asset's carrying amount is greater than its estimated recoverable amount, it is written down to its recoverable amount.

Gains and losses on disposals are determined by comparing the disposal proceeds with the carrying amount and are included in the consolidated statements of income/(loss).

Intangible assets

AC Immune's acquired in process research and development (IPR&D) asset is stated at cost less any impairments. The Company does not deem this asset ready for use until the asset obtains market approval. Therefore, during the development period after the date of acquisition until market approval, the IPR&D asset is not amortized. Upon market approval, the Company will determine the useful life of the asset, reclassify it from IPR&D and commence amortization. If the associated R&D effort is abandoned, the related IPR&D will likely be written off and we will record the relevant impairment charge. Finally, the Company will not capitalize future development costs in respect to this IPR&D asset until they meet the criteria for capitalization of research and development costs in accordance with IAS 38 *Intangible Assets*.

Our IPR&D asset is subject to impairment testing at least annually or when there are indications that the carrying value may not be recoverable until the completion of the development process. The determination of the recoverable amounts include key estimates which are highly sensitive to, and dependent upon, key assumptions.

The Company uses a discounted cash flow method to determine the fair value less costs to sell (recoverable amount) of our IPR&D intangible asset. The Company starts with a forecast of all the expected net cash flows, which incorporates the consideration of a terminal value and then the Company applies a discount rate to arrive at a risk-adjusted net present value amount.

Any impairment losses are recognized immediately in the consolidated statements of income/(loss).

Fair value of financial assets and liabilities

The Company's financial assets and liabilities are composed of receivables, short-term financial assets, cash and cash equivalents, trade payables and lease liabilities. The fair value of these financial instruments approximates their

respective carrying values due to the short-term maturity of these instruments, and are held at their amortized cost in accordance with IFRS 9, unless otherwise explicitly noted.

Receivables

Receivables are recognized at their billing value. An allowance for doubtful accounts is recorded for potential estimated losses when there is evidence of the debtor's inability to make required payments and the Company assesses on a forward-looking basis the expected credit losses associated with these receivables held at amortized cost.

Short-term financial assets

Short-term financial assets are held with external financial institutions and comprise fixed-term deposits with maturities ranging from more than 3 through 12 months in duration.

The Company assesses whether there is objective evidence that financial assets are impaired annually or whenever potential impairment triggers may occur.

Cash and cash equivalents

Cash and cash equivalents include deposits held with external financial institutions and cash on hand. All cash and cash equivalents are either in cash or in deposits with original duration of less than 3 months.

Trade payables

Trade payables are amounts due to third parties in the ordinary course of business.

Share capital and public offerings

Common shares are classified as equity. Share issuance costs are capitalized as incurred and will be shown in equity as a deduction, net of tax, from the proceeds received from existing or future offerings. Should a planned equity offering not be assessed as probable, the issuance costs would be expensed immediately in the consolidated statements of income/(loss). See "Note 11. Share capital."

Treasury shares

Treasury shares are recognized at acquisition cost and deducted from shareholders' equity at the time of acquisition, until they are subsequently resold, distributed or cancelled. Where such shares are subsequently sold, any consideration received is included in shareholders' equity. See "Note 11. Share capital."

Employee benefits

Post-employment benefits

The Company operates the mandatory pension schemes for its employees in Switzerland. The schemes are generally funded through payments to insurance companies. The Company has a pension plan designed to pay pensions based on accumulated contributions on individual savings accounts. However, this plan is classified as a defined benefit plan under IAS 19.

The net defined benefit liability is the present value of the defined benefit obligation at the balance sheet date minus the fair value of plan assets. Significant estimates are used in determining the assumptions incorporated in the calculation of the pension obligations, which is supported by input from independent actuaries. The defined benefit obligation is calculated annually with the assistance of an independent actuary using the projected unit credit method, which reflects services rendered by employees to the date of valuation, incorporates assumptions concerning employees' projected salaries and pension increases as well as discount rates of highly liquid corporate bonds that have terms to maturity approximating the terms of the related liability.

To the extent that the fair value of the plan assets is greater than the present value of the defined benefit obligation as calculated by our independent actuary, the Company accounts for the effect of the asset ceiling test under IAS 19.

Re-measurements of the net defined benefit liability, which comprise actuarial gains and losses and the return on plan assets (excluding interest) are recognized immediately in the consolidated statements of other comprehensive income/(loss). Past service costs, including curtailment gains or losses, are recognized immediately as a split in research and development and general and administrative expenses within the operating results. Settlement gains or losses are recognized in either research and development and/or general and administrative expenses within the operating results. The Company determines the net interest expense/(income) on the net defined benefit liability for the period by applying the discount rate used to measure the defined benefit obligation at the beginning of the annual period or in case of any significant events between measurement dates to the then-net defined benefit liability, considering any changes in the net defined benefit liability during the period as a result of contributions and benefit payments. Net interest expense/(income) and other expenses related to defined benefit plans are recognized in the consolidated statements of income/(loss).

Share-based compensation

The Company operates an equity-settled, share-based compensation plan. The fair value of the employee services received in exchange for the grant of equity-based awards is recognized as an expense. The total amount to be expensed over the vesting period is determined by reference to the fair value of the instruments granted, excluding the impact of any non-market vesting conditions. Non-market vesting conditions are included in assumptions about the number of instruments that are expected to become exercisable. At each balance sheet date, the Company revises its estimates of the number of instruments that are expected to become exercisable. It recognizes the impact of the revision of original estimates, if any, prospectively in the consolidated statements of income/(loss), and a corresponding adjustment to equity over the remaining vesting period.

Stock options granted under the Company's stock option plans C1 and the 2016 Stock Option and Incentive Plan are valued using the Black-Scholes option-pricing model (see "Note 18. Share-based compensation"). This valuation model as well as parameters used such as expected volatility and expected term of the stock options are partially based on management's estimates.

The proceeds received net of any directly attributable transaction costs are credited to share capital (nominal value) and share premium when the options are exercised.

We estimate the fair value of restricted share units using a reasonable estimate of market value of the common shares on the date of the award. We classify our share-based payments as equity-classified awards as they are settled in common shares. We measure equity-classified awards at their grant date fair value and do not subsequently re-measure them. Compensation costs related to equity-classified awards are equal to the fair value of the award at grant date amortized over the vesting period of the award using the graded method. We reclassify that portion of vested awards to share capital and share premium as the awards vest.

Provisions

Provisions are recognized when the Company has a present legal or constructive obligation as a result of past events where it is more likely than not that an outflow of resources will be required to settle the obligation, and a reliable estimate of the amount can be made.

Taxation

Current income tax assets and liabilities for the period are measured at the amount expected to be recovered from or paid to the taxation authorities. The tax rates and tax laws used to compute the tax amounts are those that are enacted or substantively enacted, at the reporting date in accordance with the fiscal regulations of the respective country where the Company operates and generates taxable income. Deferred tax is provided using the liability method on temporary differences between the tax bases of assets and liabilities and their carrying amounts for financial reporting purposes at the reporting date.

Deferred tax assets and liabilities are measured at the tax rates that are expected to apply in the year when the asset is realized or the liability is settled, based on tax rates (and tax laws) that have been enacted or substantively enacted at the reporting date. If required, deferred taxation is provided in full using the liability method, on all temporary differences at the reporting dates. It is calculated at the tax rates that are expected to apply to the period when it is anticipated the liabilities will be settled, and it is based on tax rates (and laws) that have been enacted or substantively enacted at the reporting date.

Deferred income tax assets are recognized to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized. Deferred tax assets are reviewed at each reporting date and are reduced to the extent that it is no longer probable that the related tax benefit will be realized. Although the Company has substantial tax loss carry-forwards, historically, due to the fact that the Company had limited certainty on the achievement of key milestones, it has not recognized any deferred tax assets as the probability for use is low.

As disclosed in “Note 16. Income taxes,” the Company has tax losses that can generally be carried forward for a period of 7 years from the period the loss was incurred. These tax losses represent potential value to the Company to the extent that the Company is able to create taxable profits before the expiry period of these tax losses. The Company has not recorded any deferred tax assets in relation to these tax losses.

Earnings per share

The Company presents basic earnings per share for each period in the consolidated financial statements. The earnings per share are calculated by dividing the earnings of the period by the weighted-average number of shares outstanding during the period. Diluted earnings per share reflect the potential dilution that could occur if dilutive securities such as share options or non-vested restricted share units were vested or exercised into common shares or resulted in the issuance of common shares that would participate in net income. Anti-dilutive shares are excluded from the dilutive earnings per share calculation.

Critical judgments and accounting estimates

The preparation of financial statements in conformity with IFRS requires management to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, income and expenses.

The areas where AC Immune has had to make judgments, estimates and assumptions relate to (i) revenue recognition on LCAs, (ii) clinical development accruals, (iii) net employee defined benefit liability, (iv) income taxes, (v) share-based compensation, (vi) right-of-use assets and lease liabilities and (vii) our IPR&D asset. Actual results may differ from these estimates. Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimates are revised and in any future periods affected.

Segment reporting

The Company has one segment. The Company currently focuses most of its resources on discovering and developing therapeutic and diagnostic products targeting misfolded proteins.

The Company is managed and operated as one business. A single management team that reports to the chief operating decision maker comprehensively manages the entire business. Accordingly, the Company views its business and manages its operations as one operating segment. Non-current assets are located in, and revenue is allocated and recorded within, the Company's country of domicile, Switzerland.

Accounting policies, new standards, interpretations and amendments adopted by the Company

There are no new IFRS standards, amendments or interpretations that are mandatory as of January 1, 2022 that are relevant to the Company. Additionally, the Company has not adopted any standard, interpretation or amendment that has been issued but is not yet effective. Such standards are not currently expected to have a material impact on the entity in the current or future reporting periods and on foreseeable future transactions.

4. Property, plant and equipment

The following tables show the movements in the net book values of property, plant and equipment for the years ended December 31, 2022 and 2021, respectively:

	As of December 31, 2022					
In CHF thousands	Furniture	IT equipment	Laboratory equipment	Leasehold improvements	Assets under construction	Total
Acquisition cost:						
Balance at December 31, 2021	265	1,754	9,142	810	695	12,666
Additions	20	151	576	184	5	936
Transfers	—	4	47	646	(697)	—
Balance at December 31, 2022	285	1,909	9,765	1,640	3	13,602
Accumulated depreciation:						
Balance at December 31, 2021	(106)	(1,316)	(5,739)	(389)	—	(7,550)
Depreciation expenses	(53)	(283)	(1,278)	(179)	—	(1,793)
Balance at December 31, 2022	(159)	(1,599)	(7,017)	(568)	—	(9,343)
Carrying amount:						
December 31, 2021	159	438	3,403	421	695	5,116
December 31, 2022	126	310	2,748	1,072	3	4,259

	As of December 31, 2021					
In CHF thousands	Furniture	IT equipment	Laboratory equipment	Leasehold improvements	Assets under construction	Total
Acquisition cost:						
Balance at December 31, 2020	214	1,497	7,681	464	277	10,133
Additions	51	250	1,268	346	695	2,610
Transfers	—	7	270	—	(277)	—
Disposals	—	—	(77)	—	—	(77)
Balance at December 31, 2021	265	1,754	9,142	810	695	12,666
Accumulated depreciation:						
Balance at December 31, 2020	(61)	(970)	(4,405)	(281)	—	(5,717)
Depreciation expenses	(45)	(346)	(1,398)	(108)	—	(1,897)
Disposals	—	—	64	—	—	64
Balance at December 31, 2021	(106)	(1,316)	(5,739)	(389)	—	(7,550)
Carrying amount:						
December 31, 2020	153	527	3,276	183	277	4,416
December 31, 2021	159	438	3,403	421	695	5,116

AC Immune continues to enhance its laboratory equipment to support its R&D functions. This effort has continued for the year ended December 31, 2022, with CHF 0.8 million invested in lab equipment, including the expansion of our leased lab space, and IT equipment, representing an increase of 7%.

For the years ended December 31, 2022, 2021 and 2020, the Company incurred CHF 1.8 million, CHF 1.9 million and CHF 1.5 million in depreciation expenses, respectively.

5. Right-of-use assets, long-term financial assets and lease liabilities

The Company recognized additions and remeasurements of right-of-use of leased assets for buildings or for office equipment totaling CHF 0.5 million and CHF 1.2 million for the years ended December 31, 2022 and 2021, respectively. In 2022, these increases are predominantly associated with the remeasurement of our leased office space.

Regarding lease liabilities, the amortization depends on the rate implicit in the contract or the incremental borrowing rate for the respective lease component. The weighted averages of the incremental borrowing rates as of December 31, 2022 are 3.5% (2.5% for 2021) for buildings, 5.3% (5.3% for 2021) for office equipment and 2.6% (2.6% for 2021) for IT equipment.

The following tables show the movements in the net book values of right-of-use of leased assets for the years ended December 31, 2022 and 2021, respectively:

In CHF thousands	Buildings	Office equipment	IT equipment	Total
Balance as of December 31, 2021	2,776	98	40	2,914
Additions and remeasurements	460	—	—	460
Depreciation	(528)	(24)	(14)	(566)
Balance as of December 31, 2022	2,708	74	26	2,808

In CHF thousands	Buildings	Office equipment	IT equipment	Total
Balance as of December 31, 2020	2,106	63	54	2,223
Additions and remeasurements	1,144	71	—	1,215
Dispositions	—	(15)	—	(15)
Depreciation	(474)	(21)	(14)	(509)
Balance as of December 31, 2021	2,776	98	40	2,914

For the years ended December 31, 2022, and 2021, the impact on the Company's consolidated statements of income/(loss) and consolidated statements of cash flows is detailed in the table below.

	For the Year Ended December 31,	
In CHF thousands	2022	2021
Statements of income/(loss)		
Depreciation of right-of-use assets	566	509
Interest expense on lease liabilities	68	63
Expense for short-term leases and leases of low value	750	723
Total	1,384	1,295
Statements of cash flows		
Total cash outflow for leases	1,388	1,299

The following table presents the contractual undiscounted cash flows for lease liabilities as of December 31, 2022 and 2021:

In CHF thousands	As of December 31, 2022	2021
Less than one year	638	638
1-3 years	1,230	1,260
3-5 years	1,187	1,203
Total	3,055	3,101

The Company also has two deposits in escrow accounts totaling CHF 0.4 million for the lease of the Company's premises as of December 31, 2022 and 2021, respectively.

6. Asset acquisition

In 2021, the Company closed its acquisition with Affiris AG (Affiris) for the program portfolio of therapeutics targeting a-syn, notably ACI-7104.056 (previously PD01), a clinically-validated active vaccine candidate for the treatment of Parkinson's disease (the Transferred Assets). The Company acquired the Transferred Assets and USD 5.0 (CHF 4.6) million in cash in exchange for 7,106,840 shares of the Company at closing, for a total value of USD 58.7 (CHF 55.1) million.

With the closing of this transaction, the Company recorded an IPR&D intangible asset associated with ACI-7104.056 for USD 53.7 (CHF 50.4) million. The Company used a risk-adjusted discounted cash flow method to determine the fair value of the intangible asset using a discount rate of 15%. See "Note 7. Intangible assets" for further details on assumptions used.

As the Company transferred its own equity instruments in consideration for the asset transferred, the acquisition was assessed in accordance with IFRS 2 *Share-based Payment*.

The Company determined that the acquisition of the Transferred Assets did not qualify as a business combination in accordance with IFRS 3 *Business Combinations* and therefore was accounted for as an asset acquisition. Most of the fair value of the Transferred Assets is attributable to a single identifiable asset which is the in-process research and development asset. The purchase consideration for the Transferred Assets was allocated based on their relative fair values.

The following table summarizes the amounts of the Transferred Assets acquired:

In CHF thousands	
Cash	4,634
IPR&D asset	50,416
Total	55,050

7. Intangible assets

AC Immune's acquired IPR&D asset is a clinically-validated active vaccine candidate for the treatment of Parkinson's disease. The asset is not yet ready for use until the asset obtains market approval. The carrying amount and net book value are detailed below:

	As of December 31, 2022			As of December 31, 2021		
In CHF thousands	Gross carrying amount	Accumulated amortization	Net book value	Gross carrying amount	Accumulated amortization	Net book value
Acquired IPR&D asset	50,416	—	50,416	50,416	—	50,416
Total intangible assets	50,416	—	50,416	50,416	—	50,416

In accordance with IAS 36 *Impairment of Assets*, the IPR&D asset is reviewed at least annually for impairment by assessing the fair value less costs to sell (recoverable amount) and comparing this to the carrying value of the asset. The valuation is considered to be Level 3 in the fair value hierarchy in accordance with IFRS 13 *Fair Value Measurement* due to unobservable inputs used in the valuation. The Company has determined the IPR&D asset was not impaired as of December 31, 2022 and 2021, respectively.

The key assumptions used in the valuation model in accordance with an income approach to determine the recoverable amount include observable and unobservable key inputs as follows:

- Anticipated research and development costs;
- Anticipated costs of goods and sales and marketing expenditures;
- Probability of achieving clinical and regulatory development milestones in accordance with certain industry benchmarks;
- Target indication prevalence and incidence rates;
- Anticipated market share;
- General commercialization expectations such as anticipated pricing and uptake;
- Expected patent life and market exclusivity periods; and
- Other metrics such as the tax rate.

The Company's valuation model calculates the risk-adjusted, net cash flows through the projected period of market exclusivity across target sales regions. The Company uses a discount rate of 17% (15% for 2021), based on the assumed cost of capital for the Company over the forecast period.

See "Note 6. Asset acquisition" for further details.

8. Cash and cash equivalents and short-term financial assets

The Company's cash and cash equivalents are maintained in the following respective currencies as of December 31, 2022 and 2021:

In CHF thousands	As of December 31, 2022	2021
Cash and cash equivalents	31,586	82,216
Total	31,586	82,216
By currency		
CHF	24,418	64,941
EUR	1,313	2,253
USD	5,855	15,022
Total cash and cash equivalents	31,586	82,216

As of December 31, 2022 and 2021, the Company's funds were held in CHF, EUR and USD currencies. Funds held in EUR and USD were translated into CHF at a rate of 0.994 and 0.933 and 1.045 and 0.923, respectively, for each currency and year.

The following table summarizes the Company's short-term financial assets as of December 31, 2022 and 2021:

In CHF thousands	As of December 31, 2022	2021
Short-term financial assets due in one year or less	91,000	116,000
Total short-term financial assets	91,000	116,000

9. Prepaid expenses and accrued income

In CHF thousands	As of December 31, 2022	2021
Prepaid expenses	4,708	3,015
Accrued income	408	975
Total prepaid expenses and accrued income	5,116	3,990

The Company's prepaid expenses relate mainly to research contracts with down-payments at contract signature with the related activities to start or continue into 2023 as well as prepaid payroll-related expenses.

Accrued income consists of CHF 0.4 million as of December 31, 2022 associated with our MJFF grants and Target ALS (see "Note 13.2. Grant income"). This amount represents 100% of our total accrued income as of December 31, 2022. As of December 31, 2021, the Company recorded CHF 0.9 million of accrued income associated with our MJJF grants. This amount represented 87% of our total accrued income as of December 31, 2021.

10. Other current receivables

In CHF thousands	As of December 31, 2022	2021
Other current receivable	124	101
Swiss VAT	249	327
Withholding tax	19	—
Total other current receivables	392	428

The maturity of these assets is less than 3 months. The Company considers the counterparty risk as low and the carrying amount of these receivables is considered to approximate their fair value.

11. Share capital

As of December 31, 2022 and 2021, the issued share capital amounted to CHF 1,796,675 and CHF 1,794,013, respectively, and is composed of outstanding common shares of 83,620,364 and 83,479,013, respectively, and treasury shares of 6,214,021 and 6,221,617, respectively.

The table below summarizes the Company's capital structure:

			In CHF thousands		
	Common shares	Treasury shares	Share capital	Share premium	Treasury shares
December 31, 2020	76,936,738	(5,000,000)	1,538	346,890	(100)
Proceeds from sale of treasury shares in public offerings, net of underwriting fees and transaction costs	—	1,171,543	—	12,097	24
Asset purchase agreement, net of transaction costs	7,106,840	—	142	54,328	—
Conversion of note agreements, net of transaction costs	3,026,634	—	61	16,683	—
Issuance of shares – incentive plans, net of transaction costs	237,258	—	5	1,253	—
Issuance of shares to be held as treasury shares, net of transaction costs	2,393,160	(2,393,160)	48	—	(48)
December 31, 2021	89,700,630	(6,221,617)	1,794	431,251	(124)
Proceeds from sale of treasury shares in public offerings, net of underwriting fees and transaction costs	—	7,596	—	(8)	0
Issuance of shares – incentive plans, net of transaction costs	133,755	—	3	80	—
December 31, 2022	89,834,385	(6,214,021)	1,797	431,323	(124)

The common shares and treasury shares have nominal values of CHF 0.02 per share. All shares have been fully paid. These treasury shares held by the Company are not considered outstanding shares as of December 31, 2022 or 2021.

Authorized capital

The Company's Board of Directors is authorized to increase the share capital, in one or several steps, until June 24, 2024, by a maximum amount of CHF 400,000 by issuing a maximum of 20,000,000 registered shares with a par value of CHF 0.02 each, to be fully paid up. An increase of the share capital (i) by means of an offering underwritten by a financial institution, a syndicate or another third party or third parties, followed by an offer to the then-existing shareholders of the Company and (ii) in partial amounts, shall also be permissible.

Conditional share capital for bonds and similar debt instruments

The Company's share capital may be increased by a maximum aggregate amount of CHF 100,000 through the issuance of a maximum of 5,000,000 registered shares, payable in full, each with a nominal value of CHF 0.02 per share, through the exercise of conversion and/or option or warrant rights granted in connection with bonds or similar instruments, issued or to be issued by the Company or by subsidiaries of the Company, including convertible debt instruments.

Conditional share capital for employee benefit plans

The Company's share capital may be increased by a maximum aggregate amount of CHF 96,000 through the issuance of not more than 4,800,000 common shares, payable in full, each with a nominal value of CHF 0.02 per share, by the exercise of options rights that have been granted to employees, consultants, members of the board of directors, or other person providing services to the Company or a subsidiary.

Shelf registration statement

On April 28, 2021, the Company filed a Shelf Registration Statement on Form F-3 (Reg. No. 333-255576) (the "Shelf Registration Statement") with the SEC. The Shelf Registration Statement was declared effective by the SEC on May 5, 2021.

The Shelf Registration Statement allows the Company to offer and sell, from time to time, up to USD 350,000,000 of common shares, debt securities, warrants, purchase contracts, units, subscription rights or any combination of the foregoing in one or more future public offerings. The terms of any future offering would be determined at the time of the offering and would be subject to market conditions and approval by the Company's Board of Directors. Any offering of securities covered by the Shelf Registration Statement will be made only by means of a written prospectus and prospectus supplement authorized and filed by the Company.

At the market equity offering

In Q3 2020, AC Immune issued 5,000,000 common shares with a nominal value of CHF 0.02, which became treasury shares. The Company also established an "at the market offering program" ("ATM") for the sale of up to USD 80.0 (CHF 74.6) million worth of our common shares issued from time to time by entering into an Open Market Sale Agreement ("Sales Agreement") with Jefferies LLC ("Jefferies") as the sales agent under a prior registration statement on Form F-3 which expired in Q2 2021.

In Q2 2021, the Company filed a new registration statement on Form F-3 and an accompanying prospectus supplement in order to renew its ATM program. The Company also entered into a second Open Market Sale Agreement (the "new Sales Agreement") with Jefferies to continue the ATM program.

In Q3, 2021, the Company issued 2,393,160 common shares with a nominal value of CHF 0.02 to be held as treasury shares.

Through December 31, 2022, the Company has sold 1,179,139 common shares previously held as treasury shares pursuant to the new Sales Agreement, raising USD 13.3 (CHF 12.1) million, net of underwriting fees and transaction costs. We have paid commissions to Jefferies totaling USD 0.4 (CHF 0.4) million through December 31, 2022, for share issuances in accordance with our ATM programs.

For the years ended December 31, 2022, 2021 and 2020, the Company has expensed issuance costs of nil, nil and CHF 0.5 million, respectively, in the consolidated statements of income/(loss).

Convertible note agreement

Concurrently with the Asset Purchase Agreement, the Company entered into two separate Convertible Note Agreements with entities affiliated with each of Athos Service GmbH and First Capital Partner GmbH, both of which entities are shareholders of Affiris. Each Convertible Note Agreement provided for the sale of an unsecured subordinated Convertible Note of the Company with an aggregate principal amount of USD 12.5 (CHF 11.7) million for total net proceeds of USD 25 (CHF 23.5) million.

In 2021, the affiliated entities exercised their options to convert their respective USD 12.5 (CHF 11.7) million notes. As a result of these conversions, 1,513,317 common shares were issued to each Investor, totaling 3,026,634 common shares. The Company recorded an increase to its share capital for the nominal value of its shares and share premium for the difference associated with settlement of this liability. The Company also settled its derivative financial assets, which were embedded conversion features associated with the convertible debt, via an offset to its share premium. These convertible notes and derivative financial assets were fully settled in 2021 and there is no further equity or cash consideration due to the affiliated entities thereunder.

12. Trade and other payables and accrued expenses

	As of December 31,	
In CHF thousands	2022	2021
Trade and other payables	929	2,003
Total trade and other payables	929	2,003
Accrued research and development costs	5,360	10,361
Accrued payroll expenses	2,898	3,562
Other accrued expenses	1,159	2,813
Total accrued expenses	9,417	16,736

An accrual of CHF 2.1 million and CHF 2.3 million was recognized for performance-related remuneration within accrued payroll expenses for 2022 and 2021, respectively. In 2021, an accrual of CHF 3.7 million was recorded as part of our cost sharing arrangement with Janssen within accrued research and development costs and CHF 0.8 million was recorded as accrued stamp duty for the issuance of shares as part of the Company's asset acquisition within other accrued expenses.

13. Contract revenues

For the years ended December 31, 2022, 2021 and 2020, AC Immune generated contract revenues of CHF 3.9 million, nil and CHF 15.4 million, respectively.

The following tables provide contract revenue amounts from its LCAs for the years ended December 31, 2022, 2021 and 2020, respectively.

	For the Year Ended December 31,		
In CHF thousands	2022	2021	2020
Lilly	—	—	14,348
Janssen	—	—	1,083
Life Molecular Imaging	3,935	—	—
Total contract revenues	3,935	—	15,431

LMI accounted for 100% of our contract revenues in 2022 and Lilly accounted for 93% of our contract revenues in 2020.

During the years ended December 31, 2022, 2021 and 2020, the Company recognized the following contract revenues as a result of changes in the contract asset and the contract liability balances in the respective periods:

	For the Year Ended December 31,		
In CHF thousands	2022	2021	2020
Revenues recognized in the period from:			
Amounts included in the contract liability at the beginning of the period	—	—	4,477
Performance obligations satisfied in previous periods	3,935	—	10,000

13.1 Licensing and collaboration agreements

Morphomer Tau small molecule – 2018 license agreement with Eli Lilly and Company

In December 2018, we entered into an exclusive, worldwide licensing agreement with Eli Lilly and Company (Lilly) to research and develop Morphomer Tau small molecules for the treatment of AD and other neurodegenerative diseases. More specifically, this is an exclusive license with the right to Lilly to grant sublicenses under the ACIU Patents, the ACIU know-how, and ACIU's interests in the Joint Patents and the joint know-how to Exploit the Licensed Compounds and Licensed Products. The agreement became effective on January 23, 2019 (the "effective date") when the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, expired. In Q3 2019, the Company and Lilly entered into the first amendment to divide the first discretionary milestone payment under the agreement of CHF 60 million into two installments, with the first CHF 30 million paid in Q3 2019 and the second CHF 30 million to be paid on or before March 31, 2020 unless Lilly terminated the agreement earlier. In Q1 2020, the Company and Lilly entered into a second amendment to replace the second CHF 30 million to be paid on or before March 31, 2020 with two milestone payments, one of CHF 10 million to be paid on or before March 31, 2020 and the other of CHF 60 million following the first patient dosed in a Phase 2 clinical study of a licensed product in the U.S. or EU.

Per the terms of the agreement, the Company received an initial upfront payment of CHF 80 million in Q1 2019 for the rights granted by the Company to Lilly. To date, the Company has completed a Phase 1 clinical study with ACI-3024.

Additionally, the Company and Lilly have continued candidate characterization across the research program, identifying new and highly differentiated candidates with desired cerebrospinal fluid exposure and selectivity for pathological aggregated Tau. These will be broadly developed in Tau-dependent neurodegenerative diseases by Lilly. Lilly is responsible for leading and funding further clinical development and will retain global commercialization rights for all indications.

Per the terms of the agreement, the Company may become eligible to receive additional milestone payments totaling up to approximately CHF 880 million for clinical and regulatory milestones and CHF 900 million upon achievement of certain commercial milestones. In addition to milestones, we will be eligible to receive royalties on sales at a percentage rate ranging from the low double-digits to the mid-teens. The agreement will terminate by the date of expiration of the last royalty term for the last licensed product. However, under the terms of the agreement, Lilly may terminate the agreement at any time by providing 3 months' prior notice to us.

AC Immune assessed this arrangement in accordance with IFRS 15 and concluded that Lilly is a customer. The Company identified the following significant performance obligations under the contract: (i) a right-of-use license and (ii) research and development activities outlined in the development plan. Per the agreement, the Company was responsible for the preclinical and Phase 1 activities for the first clinical candidate, ACI-3024, which the Company determined was distinct and capable of being completed by Lilly or a third party. Preclinical activities for which AC Immune was responsible prior to their completion in Q2 2019 included final manufacturing of materials for use in the regulatory submission of the protocol and in the Phase 1 study. For the completed Phase 1, AC Immune was responsible for leading the study design, obtaining relevant regulatory agency approvals, arranging necessary third-party contracts, completing patient selection, ensuring patient treatment, following up with patients, drafting the clinical study report

development and other relevant clinical activities to ensure that the primary objective of the study was completed. The Company used CMOs for certain of its preclinical activities and CROs to complete certain Phase 1 activities and to issue the final clinical study report.

The Company's preclinical and Phase 1 activities did not represent integrated services with the licensed intellectual property for which Lilly contracted. Lilly purchased a license to the Company's Tau therapeutic small-molecule program, which was delivered at commencement of the agreement, and AC Immune's preclinical and Phase 1 activities did not affect the form or functionality of this license. The Company's objective for the Phase 1 activity was to assess safety and tolerability and did not modify or customize ACI-3024. The completion of these preclinical and Phase 1 activities does not affect the licensed intellectual property.

Finally, per the agreement, each party has three representatives on a joint steering committee (JSC). Depending upon the agenda, additional field experts can attend the JSC to provide the technical and scientific contribution required. The JSC meets on a regular basis depending on agreements between the representatives. The JSC is responsible for serving as the forum to (i) discuss, review and approve certain activities by reviewing and discussing the development progress with updates on back-up candidates, (ii) discuss, review and approve all amendments to the global development plan, (iii) periodically discuss and review commercialization of licensed products and (iv) review and approve reports related to development costs among other activities. The JSC is intended to ensure that communication between the parties remains consistent and that the development plan is progressing as intended.

The valuation of each performance obligation involves estimates and assumptions with revenue recognition timing to be determined by either delivery or the provision of services.

The Company used the residual approach to estimate the selling price for the right-of-use license and an expected cost plus margin approach for estimating the research and development activities. The right-of-use license was delivered on the effective date. The research and development activities were delivered over time as the services were performed. For these services, revenue was recognized over time using the input method, based on costs incurred to perform the services, as the level of costs incurred over time is thought to best reflect the transfer of services to Lilly. The Company determined the value of the research and development activities to be CHF 6.9 million and deferred this balance from the effective date. To date, the Company has cumulatively recognized CHF 6.9 million in contract revenue, resulting in no deferred income (contract liability) on the consolidated balance sheets. The remaining CHF 73.1 million from the upfront payment was allocated to the right-of-use license and recognized on the effective date.

At inception of the agreement, none of the clinical, regulatory or commercial milestones had been included in the transaction price, as all milestone amounts were fully constrained. To date, the Company has recognized CHF 40 million from milestone payments triggered in Q3 2019 and Q1 2020 related to the right-of-use license for intellectual property as there were no further constraints related to these milestones. In assessing that future clinical, regulatory or commercial milestones are fully constrained, the Company considered numerous factors to determine that these milestones are not highly probable to obtain, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Lilly and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For the years ended December 31, 2022, 2021 and 2020, we have recognized nil, nil and CHF 14.3 million, respectively, from this arrangement.

Anti-Abeta antibody in AD – 2006 agreement with Genentech, a member of the Roche Group

In November 2006, we signed an exclusive, worldwide licensing agreement for crenezumab, our humanized monoclonal therapeutic antibody targeting misfolded Abeta. The agreement was amended March 2009, January 2013, May 2014 and May 2015. The agreement also provides for the development of a second therapeutic product for a non-

AD indication based on the same intellectual property and anti-Abeta antibody compound. The value of this partnership is potentially greater than USD 340 (CHF 317) million.

The term of the agreement commenced on the effective date and, unless sooner terminated by mutual agreement or pursuant to any other provision of the agreement, terminates on the date on which all obligations between the parties with respect to the payment of milestones or royalties with respect to licensed products have passed or expired. Either party may terminate the agreement for any material breach by the other party, provided a cure period of 90 days from the date when that notice is given.

Genentech commenced a first Phase 3 clinical study in March 2016 for crenezumab (CREAD). In March 2017, Genentech started a second Phase 3 clinical trial (CREAD 2). Since 2013, crenezumab has also been studied in a Phase 2 preventive trial in individuals who carry the PSEN1 E280A autosomal-dominant mutation and do not meet the criteria for mild cognitive impairment due to AD or dementia due to AD and are, thus, in a preclinical phase of AD (autosomal dominant AD (ADAD)). In 2019, Genentech initiated a Tau Positron Emission Tomography (PET) substudy to the ongoing Phase 2 trial in ADAD to evaluate the effect of crenezumab on Tau burden, which may also increase the understanding of disease progression in the preclinical stage of ADAD.

If crenezumab receives regulatory approval, we will be entitled to receive royalties that are tied to annual sales volumes with different royalty rates applicable in the U.S. and Europe ranging from the mid-single digits to mid-teens. To date, we have received total milestone payments of USD 65 (CHF 70.1) million comprised of an upfront payment of USD 25 (CHF 31.6) million and of USD 40 (CHF 38.2) million for clinical development milestones achieved all-in prior to January 1, 2017. Genentech may terminate the agreement at any time by providing 3 months' notice to us. In such event all costs incurred are still refundable.

AC Immune assessed this arrangement in accordance with IFRS 15 and concluded that Genentech is a customer. The Company identified the following performance obligations under the contract: (i) a right-of-use license and (ii) conducting of research under a research plan. The Company considered the research and development capabilities of Genentech and Genentech's right to sublicense to conclude that the license has stand-alone functionality and is distinct. The Company's obligation to perform research does not significantly impact or modify the licenses' granted functionality.

At execution of the agreement, the transaction price included the upfront consideration received of USD 25 (CHF 31.6) million. At inception, none of the clinical or regulatory milestones had been included in the transaction price, as all milestone amounts were fully constrained. The Company has received three milestone payments since inception, totaling USD 40 (CHF 38.2) million. The Company could receive greater than USD 275 (CHF 256.4) million or more for further regulatory milestones for this exclusive, worldwide alliance. In assessing that future regulatory milestones are fully constrained, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to royalties will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Genentech and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

In January 2019, we announced that Roche, the parent of Genentech, is discontinuing the CREAD and CREAD 2 (BN29552 and BN29553) Phase 3 studies of crenezumab in people with prodromal-to-mild sporadic AD. The decision came after an interim analysis conducted by the Independent Data Monitoring Center (IDMC) indicated that crenezumab was unlikely to meet its primary endpoint of change from baseline in CDR-SB Score. This decision was not related to the safety of the investigational product. No safety signals for crenezumab were observed in this analysis and the overall safety profile was similar to that seen in previous trials.

For the years ended December 31, 2022, 2021 and 2020, we have recognized no revenues from this arrangement.

Anti-Tau antibody in AD – 2012 agreement with Genentech, a member of the Roche Group

In June 2012, we entered into a second agreement with Genentech to research, develop and commercialize our anti-Tau antibodies for use as immunotherapeutics and diagnostics. The agreement was amended in December 2015. The value of this exclusive, worldwide alliance is potentially greater than CHF 400 million and includes upfront and clinical, regulatory and commercial milestone payments. In addition to milestones, we will be eligible to receive royalties on sales at a percentage rate ranging from the mid-single digits to low-double digits. The agreement also provides for collaboration on at least one additional therapeutic indication outside of AD built on the same anti-Tau antibody program as well an anti-Tau diagnostic product.

The term of the agreement commenced on the effective date and, unless sooner terminated by mutual agreement or pursuant to any other provision of the agreement, terminates on the date on which all obligations between the parties with respect to the payment of milestones or royalties with respect to licensed products have passed or expired. Either party may terminate the agreement for any material breach by the other party, provided a cure period of 90 days from the date when that notice is given.

To date, we have received payments totaling CHF 59 million, including a milestone payment of CHF 14 million received and recognized in Q4 2017 associated with the first patient dosing in a Phase 2 clinical trial for AD with an anti-Tau monoclonal body known as semorinemab, a milestone payment of CHF 14 million recognized in Q2 2016 and received in July 2016, associated with the announcement of the commencement of the Phase 1 clinical study of semorinemab, and a milestone payment of CHF 14 million received in 2015 in connection with the ED-GO decision. As we met all performance obligations on reaching these milestones, we have recognized revenue in the respective periods. Genentech may terminate the agreement at any time by providing 3 months' notice to us.

AC Immune assessed this arrangement in accordance with IFRS 15 and concluded that Genentech is a customer. The Company identified the following performance obligations under the contract: (i) a right-of-use license and (ii) conduct of research under a research plan. The Company considered the research and development capabilities of Genentech and Genentech's right to sublicense to conclude that the license has stand-alone functionality and is distinct. The Company's obligation to perform research does not significantly impact or modify the licenses' granted functionality.

At execution of the agreement, the transaction price included an upfront consideration received of CHF 17 million. At inception, none of the clinical or regulatory milestones had been included in the transaction price, as all milestone amounts were fully constrained. The Company has received three milestones since inception totaling CHF 42 million. The Company could also receive up to an additional CHF 368.5 million in clinical, regulatory and commercial milestones. In assessing that future clinical, regulatory or commercial milestones are fully constrained, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Genentech and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

In September 2020, the Company reported that Genentech informed us of top line results from a Phase 2 trial of the anti-Tau antibody, semorinemab, in early (prodromal to mild) Alzheimer's disease (AD) which show that semorinemab did not meet its primary efficacy endpoint of reducing decline on CDR-SB compared to placebo. The primary safety endpoint was however met. Two secondary endpoints, Alzheimer's Disease Assessment Scale-Cognitive Subscale 13 (ADAS-Cog13) and Alzheimer's Disease Cooperative Study Group – Activities of Daily Living Inventory (ADCS-ADL), were not met.

In August 2021, the Company reported that Genentech had informed the Company that the Lauriet study had met one of its co-primary endpoints, ADAS-Cog 11. The second co-primary endpoint, ADCS-ADL, was not met. Safety data showed that semorinemab was well tolerated with an acceptable safety profile and no unanticipated safety signals. In November 2021, the Company reported that Genentech had presented the full top-line data from the Lauriet study during a late-breaking session at the 14th Clinical Trials on Alzheimer's Disease conference.

For the years ended December 31, 2022, 2021 and 2020, we have recognized no revenues from this arrangement.

Tau vaccine in AD – 2014 agreement with Janssen Pharmaceuticals, Inc.

In December 2014, we entered into an agreement with Janssen Pharmaceuticals, Inc. (Janssen), part of the Janssen Pharmaceutical Companies of Johnson & Johnson, to develop and commercialize therapeutic anti-Tau vaccines for the treatment of AD and potentially other Tauopathies. The value of this collaboration is potentially up to CHF 500 million and includes upfront and clinical, regulatory and commercial milestones. In addition to milestones, we will be eligible to receive royalties on sales at a percentage rate ranging from the high-single digits to the mid-teens for the phospho-Tau vaccine program. In April 2016, July 2017, January 2019, November 2019 and December 2022, the companies entered into the first, second, third, fourth and fifth amendments, respectively. These amendments allow for the alignment of certain payment and activity provisions with the Development Plan and Research Plan activities. We and Janssen have completed the co-development of the second-generation lead therapeutic vaccines, ACI-35.030 and JACI-35.054, through Phase 1b/2a. In November 2022, it was announced that ACI-35.030 was selected to advance into further development based on interim data from the ongoing Phase 1b/2a trial. AC Immune and Janssen will jointly share research and development costs until the completion of the first Phase 2b (AC Immune's contribution to the first Phase 2b trial is capped). From Phase 2b and onwards, Janssen will assume responsibility for the clinical development, manufacturing and commercialization of ACI-35.030.

Under the terms of the agreement, Janssen may terminate the agreement at any time after completion of the first Phase 1b clinical study in 2016 by providing 90 days' notice to us. If not otherwise terminated, the agreement shall continue until the expiration of all royalty obligations as outlined in the contract.

The agreement also allows for the expansion to a second indication based on the same anti-Tau vaccine program and based on intellectual property related to this program.

The Company received an upfront, non-refundable license fee of CHF 25.9 million, which we recognized as revenue in 2014. In May 2016, we received a payment of CHF 4.9 million for reaching a clinical milestone in the first Phase 1b study. As we met all performance obligations on reaching the milestone, we have recognized this income as revenue.

AC Immune assessed this arrangement in accordance with IFRS 15 and concluded that Janssen is a customer. The Company identified the following performance obligations under the contract: (i) a right-of-use license and (ii) research and development services including a development and chemistry, manufacturing and controls work plan. The Company considered the research and development capabilities of Janssen, Janssen's right to sublicense, and the fact that the research and development services are not proprietary and can be provided by other vendors, to conclude that the license has stand-alone functionality and is distinct. The Company's obligation to perform research and development services does not significantly impact or modify the licenses' granted functionality. Based on these assessments, the Company identified the license and the research and development services as the performance obligations at the inception of the arrangement, which were deemed to be distinct in the context of the contract.

At execution of the agreement, the transaction price included only the upfront consideration received of CHF 25.9 million. At inception, none of the clinical, regulatory or commercial milestones has been included in the transaction price, as all milestone amounts were fully constrained. The Company did receive a payment of CHF 4.9 million for reaching a clinical milestone in the first Phase 1b study in May 2016. The Company could also receive up to more than CHF 458 million in clinical, regulatory and commercial milestones as well as tiered, high-single digits to mid-teen royalties on aggregate net sales for the phospho-Tau vaccine program. In assessing that future clinical, regulatory or commercial milestones are fully constrained, the Company considered numerous factors to determine that these milestones are not highly probable to obtain, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Janssen and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For the years ended December 31, 2022, 2021 and 2020, we have recognized nil, nil and CHF 1.1 million, respectively, from this arrangement.

Tau-PET imaging agent –2014 agreement with Life Molecular Imaging (LMI) (formerly Piramal Imaging SA)

In May 2014 (as amended in June 2022), we entered into an agreement, our first diagnostic partnership, with LMI, the former Piramal Imaging SA. The partnership with LMI is an exclusive, worldwide licensing agreement for the research, development and commercialization of the Company's Tau protein PET tracers supporting the early diagnosis and clinical management of AD and other Tau-related disorders and includes upfront and sales milestone payments totaling up to EUR 160 (CHF 159) million, plus royalties on sales at a percentage rate ranging from mid-single digits to low-teens. LMI may terminate the LCA at any time by providing 3 months' notice to us.

In connection with this agreement, AC Immune received a payment of EUR 500 (CHF 664) thousand, which was fully recognized in 2015. In Q1 2017, we recorded a milestone payment of EUR 1 (CHF 1.1) million related to the initiation of "Part B" of the first-in-man Phase 1 study. In Q3 2019, the Company recognized EUR 2 (CHF 2.2) million in connection with the initiation of a Phase 2 trial of Tau-PET tracer in patients with mild cognitive impairment and mild–to-moderate AD in comparison with non-demented control participants. In Q3 2022, the Company recognized EUR 4 (CHF 3.9) million linked to the progression of the Tau-PET tracer into late-stage development in AD. The Company is eligible to receive additional variable consideration related to the achievement of certain clinical milestones totaling EUR 4 (CHF 4) million should the compound make it through Phase 3 clinical studies. We are also eligible to receive potential regulatory and sales-based milestones totaling EUR 148 (CHF 138) million. Finally, the Company is eligible for royalties from the mid-single digits to low-teens.

AC Immune assessed this arrangement in accordance with IFRS 15 and concluded that LMI is a customer. The Company has identified that the right-of-use license as the only performance obligation. The Company determined that transaction price based on the defined terms allocated to each performance obligation specified in the contract.

The upfront payment constitutes the amount of consideration to be included in the transaction price and has been allocated to the license. None of the clinical, regulatory or commercial milestones has been included in the transaction price as these variable consideration elements are considered fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts.

Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to LMI and therefore are recognized at the later of when the performance obligation is satisfied or the related sales occur. The Company considered LMI's right to sublicense and develop the Tau protein PET tracers, and the fact that LMI could perform the research and development work themselves within the license term without AC Immune, to conclude that the license has stand-alone functionality and is distinct. The Company believes that the contracted amount represents the fair value. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For the years ended December 31, 2022, 2021 and 2020, the Company has recognized CHF 3.9 million, nil and nil, respectively, from this arrangement.

13.2 Grant income

Grants from the Michael J. Fox Foundation

In May 2020, the Company, as part of a joint arrangement with Skåne University Hospital (Skåne) in Sweden, was awarded a USD 3.2 (CHF 3.0) million grant from the MJFF's Ken Griffin Alpha-synuclein Imaging Competition. As part of this grant, AC Immune is eligible to receive USD 2.5 (CHF 2.3) million directly from the MJFF. Skåne will receive USD 0.7 (CHF 0.7) million of the total grant directly from the MJFF over two years to conduct and support the clinical arm of the project. In August 2022, the Company received follow-on grant funding as part of its joint

arrangement with Skåne in Sweden totaling USD 0.5 (CHF 0.5) million for the continued development of its alpha-synuclein PET imaging diagnostic agent. As part of this grant, AC Immune received USD 0.4 (CHF 0.4) million directly from the MJFF. Skåne will receive USD 0.1 (CHF 0.1) million of the total grant directly from the MJFF over the duration of the grant period.

The MJFF expects that AC Immune and Skåne will complete tasks according to the agreed timelines. AC Immune's funding is variable depending on the satisfactory achievement of these specific tasks within a specific period of time.

In December 2021, the Company announced that it had been awarded two grants totaling USD 1.5 (CHF 1.4) million to advance small molecule PD programs. One award will support an existing early-stage program to develop small molecules that can prevent intracellular aggregation and spreading of a-syn. The other award will fund research on the therapeutic potential of chemically and mechanistically novel, brain penetrant small molecule inhibitors of NLRP3 inflammasome activation for the treatment of PD.

For the years ended December 31, 2022, 2021 and 2020, the Company has recognized CHF 1.2 million, CHF 1.1 million and CHF 1.3 million, respectively, from its MJFF grants. As of December 31, 2022, the Company recorded CHF 0.3 million in accrued income and CHF 0.5 million in deferred income, respectively.

14. Expenses by category

Research and development

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Operating expenses	41,166	44,289	43,787
Payroll expenses	17,548	16,465	14,424
Share-based compensation	1,622	1,528	1,276
Total research and development expenses	60,336	62,282	59,487

For the years ended December 31, 2022, 2021 and 2020, the Company incurred CHF 60.3 million, CHF 62.3 million and CHF 59.5 million in research and development expenses, respectively. The decrease in 2022 is mainly driven by decreases in direct R&D expenditures across various programs.

For the years ended December 31, 2022, 2021 and 2020, the Company had 122.4, 108.6 and 115.3 FTEs in our research and development functions.

General and administrative

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Operating expenses	6,207	7,031	7,471
Payroll expenses	7,874	8,281	8,274
Share-based compensation	1,708	2,598	2,812
Total general and administrative expenses	15,789	17,910	18,557

For the years ended December 31, 2022, 2021 and 2020, the Company incurred CHF 15.8 million, CHF 17.9 million and CHF 18.6 million in general and administrative expenses, respectively. The decrease in 2022 compared with the prior year predominantly relates to certain transaction costs associated with our prior year asset acquisition which did not repeat in 2022 as well as a reduction in headcount.

For the years ended December 31, 2022, 2021 and 2020, the Company had 22.5, 27.3 and 26.7 FTEs in our general and administrative functions.

Financial result, net

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Financial income	69	6,485	78
Financial expense	(355)	(581)	(184)
Exchange differences	393	113	(555)
Finance result, net	107	6,017	(661)

Our finance result primarily consists of interest expense associated with our short-term financial assets and lease liabilities as well as foreign currency exchange differences.

For the year ended December 31, 2022, the decrease in financial result, net related primarily to the prior year CHF 6.5 million gain on the conversion features related to the Company's convertible notes due to certain Affiris affiliated entities that did not recur.

15. Related-party transactions

Board of directors and executive management compensation

Key management includes the board of directors and executive management. For 2022, there were eight members (2021: eight and 2020: seven) of the Board (excluding the CEO) and seven members (2021: six and 2020: five) of executive management (including the CEO). Compensation was as follows:

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Short-term employee benefits	4,187	4,403	3,497
Post-employment benefits	295	266	214
Share-based compensation	2,503	2,997	2,578
Total compensation	6,985	7,666	6,289

16. Income taxes

The Group recognized less than CHF 0.1 million, less than CHF 0.1 million and nil in income taxes and no deferred tax asset or liability positions for the years ended December 31, 2022, 2021 and 2020, respectively. The Group's expected tax expense for each year is based on the applicable tax rates in each jurisdiction. In 2022, these rates ranged from 13.6% to 33.8% (13.6% - 32.9% for 2021 and 13.6% for 2020) in the Group's respective tax jurisdictions. The weighted average tax rate applicable to the Group was 13.6% (13.6% for 2021 and 2020, respectively).

The Group's income tax expense for each year can be reconciled to loss before tax as follows:

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Loss before income tax	(70,740)	(72,993)	(61,921)
Tax benefit calculated at the domestic rates applicable in the respective countries	(9,616)	(9,930)	(8,441)
(Income not subject to tax)/expenses not deductible for tax purposes	455	(375)	462
Effect of unused tax losses and tax offsets not recognized as deferred tax assets	9,174	10,308	7,979
Effective income tax rate (benefit)/expense	13	3	—

The Swiss tax rate used for the 2022 reconciliations is the corporate tax rate of 13.6% (13.6% in 2021 and 2020, respectively) payable by corporate entities in the Canton of Vaud, Switzerland on taxable profits under tax law in that jurisdiction.

The below table details the total unrecognized deductible temporary differences, unused tax losses and unused tax credits:

In CHF thousands	As of December 31, 2022	2021	2020
Unrecognized deductible temporary differences, unused tax losses and unused tax credits			
Deductible temporary differences, unused tax losses and unused tax credits for which no deferred tax assets have been recognized are attributable to the following:			
Tax losses	264,089	197,152	121,948
Deductible temporary differences related to:			
Right-of-use assets and lease liabilities, net	—	—	—
Retirement benefit plan	3,213	7,098	7,464
Total	267,302	204,250	129,412

The following table details the tax losses carry forwards of the Company and their respective expiry dates:

In CHF thousands	As of December 31, 2022	2021	2020
Tax losses split by expiry date:			
December 31, 2024	15,231	15,231	15,231
December 31, 2025	48,894	48,894	48,894
December 31, 2026	—	—	—
December 31, 2027	57,824	57,824	57,824
December 31, 2028	75,204	75,204	—
December 31, 2029	66,936	—	—
Total unrecorded tax loss carryforwards	264,089	197,153	121,949

The tax losses available for future offset against taxable profits have increased by CHF 66.9 million from 2021, representing the amount of tax losses that are additionally available as an offset, subject to expiration as disclosed in the table above, against future taxable income.

Consistent with prior years, the Company has not recorded any deferred tax assets in relation to the past tax losses available for offset against future profits as the recognition criteria were not met at the balance sheet date.

17. Retirement benefit plan

The Company participates in a collective foundation covering all of its employees including its executive officers. In addition to retirement benefits, the plan provides death or long-term disability benefits.

Contributions paid to the plan are computed as a percentage of salary, adjusted for the age of the employee and shared approximately 47% and 53% by employee and employer, respectively.

This plan is governed by the Swiss Law on Occupational Retirement, Survivors and Disability Pension Plans (BVG), which requires contributions to be made to a separately administered fund. The fund has the legal form of a foundation and it is governed by a board of trustees, which consists of an equal number of employer and employee representatives of its members. The board of trustees is responsible for the administration of the plan assets and for the definition of the investment strategy. The Company has no direct influence on the investment strategy of the foundation board.

The assets are invested by the pension plan, to which many companies contribute, in a diversified portfolio that respects the requirements of the Swiss BVG. Therefore, disaggregation of the pension assets and presentation of plan assets in classes that distinguish the nature and risks of those assets is not possible. Under the plan, both the Company and the employee share the costs. The structure of the plan and the legal provisions of the BVG mean that the employer is exposed to actuarial risks. The main risks are investment risk, interest risk, disability risk and the life expectancy of pensioners. Through our affiliation with the pension plan, the Company has minimized these risks, as they are shared between a much greater number of participants. On leaving the Company, a departing employee's retirement savings are transferred to the pension institution of the new employer or to a vested benefits institution. This transfer mechanism may result in pension payments varying considerably from year to year.

The pension plan is exposed to Swiss inflation, interest rate risks and changes in the life expectancy for pensioners. For accounting purposes under IFRS, the plan is treated as a defined benefit plan in accordance with IAS 19.

The following table sets forth the status of the defined benefit pension plan and the amount that is recognized in the consolidated balance sheets:

	As of December 31,		
In CHF thousands	2022	2021	2020
Defined benefit obligation	(32,410)	(33,889)	(30,213)
Fair value of plan assets	29,197	26,791	22,749
Total liability	(3,213)	(7,098)	(7,464)

The following amounts have been recorded as net pension cost in the consolidated statements of income/(loss):

	For the Year Ended December 31,		
In CHF thousands	2022	2021	2020
Service cost	1,712	1,648	1,626
Interest cost	126	79	71
Interest income	(87)	(48)	(42)
Net pension cost	1,751	1,679	1,655

The changes in defined benefit obligation, fair value of plan assets and unrecognized gains/(losses) are as follows.

A. Change in defined benefit obligation

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Defined benefit obligation as of January 1	(33,889)	(30,213)	(26,624)
Service cost	(1,712)	(1,648)	(1,626)
Interest cost	(126)	(79)	(71)
Change in demographic assumptions	29	—	1,428
Change in financial assumptions	8,397	156	(71)
Change in experience assumptions	(1,726)	(252)	(931)
Benefits deposited	(2,327)	(894)	(1,467)
Employees' contributions	(1,056)	(959)	(851)
Defined benefit obligation as of December 31	(32,410)	(33,889)	(30,213)

B. Change in fair value of plan assets

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Fair value of plan assets as of January 1	26,791	22,749	19,139
Interest income	87	48	42
Employees' contributions	1,056	959	851
Employer's contributions	1,210	1,089	950
Benefits deposited	2,327	894	1,467
Return on plan assets excluding interest income	(2,274)	1,052	300
Fair value of plan assets as of December 31	29,197	26,791	22,749

Expected contributions by the employer to be paid to the post-employment benefit plans during the annual period beginning after the end of the reporting period amount to approximately CHF 1.2 million.

C. Change in net defined benefit liability

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Net defined benefit liabilities as of January 1	7,098	7,464	7,485
Net pension cost through statement of income/(loss)	1,751	1,679	1,655
Remeasurement through other comprehensive income/(loss)	(4,426)	(956)	(726)
Employer's contribution	(1,210)	(1,089)	(950)
Net defined benefit liabilities as of December 31	3,213	7,098	7,464

D. Other comprehensive gains/(losses)

In CHF thousands	For the Year Ended December 31, 2022	2021	2020
Effect of changes in demographic assumptions	29	—	1,428
Effect of changes in financial assumptions	8,397	156	(71)
Effect of changes in experience assumptions	(1,726)	(252)	(931)
Return on plan assets excluding interest income	(2,274)	1,052	300
Total other comprehensive gain	4,426	956	726

The change in experience assumptions results from an increased sum of insured salaries.

The fair value of the plan assets is the cash surrender value of the insurance with the insurance company (AXA). The investment strategy defined by the board of trustees follows a conservative profile.

The plan assets are primarily held within instruments with quoted market prices in an active market, with the exception of real estate and mortgages.

The weighted-average duration of the defined benefit obligation is 14.9 years and 17.1 years as of December 31, 2022 and 2021, respectively.

The actuarial assumptions used for the calculation of the pension cost and the defined benefit obligation of the defined benefit pension plan for the years ended December 31, 2022, 2021 and 2020, respectively, are as follows:

	For the Year Ended December 31, 2022	2021	2020
Discount rate	2.25 %	0.30 %	0.20 %
Rate of future increase in compensations	1.75 %	1.75 %	1.75 %
Rate of future increase in current pensions	0.00 %	0.00 %	0.00 %
Interest rate on retirement savings capital	2.25 %	0.75 %	0.50 %
Mortality and disability rates	BVG 2020-CMI	BVG 2020-CMI	BVG 2020-CMI

In defining the benefits, the minimum requirements of the Swiss BVG and its implementing provisions must be observed. The BVG defines the minimum pensionable salary and the minimum retirement credits.

A quantitative sensitivity analysis for significant assumptions as of December 31, 2022 is shown below:

	Discount rate		Future salary increase		Future pension cost		Interest rate on savings capital	
Assumptions	0.5% increase	0.5% decrease	0.5% increase	0.5% decrease	0.5% increase	0.5% decrease	0.5% increase	0.5% decrease
	In CHF thousands							
Potential defined benefit obligation	30,201	34,916	32,940	31,841	33,601	31,322	33,322	31,545
Decrease/(increase) from actual defined benefit obligation	2,209	(2,506)	(530)	569	(1,191)	1,088	(912)	865

A quantitative sensitivity analysis for significant assumptions as of December 31, 2021 is shown below:

Assumptions	Discount rate		Future salary increase		Future pension cost		Interest rate on savings capital	
	0.5% increase	0.5% decrease	0.5% increase	0.5% decrease	0.5% increase	0.5% decrease	0.5% increase	0.5% decrease
	in CHF thousands							
Potential defined benefit obligation	31,190	37,006	34,578	33,176	35,497	32,435	34,822	33,007
Decrease/(increase) from actual defined benefit obligation	2,699	(3,117)	(689)	713	(1,608)	1,454	(933)	882

The sensitivity analyses above are subject to limitations and have been determined based on a method that extrapolates the impact on net defined benefit obligation as a result of reasonable changes in key assumptions occurring at the end of the reporting period.

18. Share-based compensation

Share-based option awards

As of December 31, 2022, there are equity-based instruments outstanding that the Company has granted under two different plans.

The Company's 2016 Share Option and Incentive Plan (SOIP) was approved by the shareholders at the ordinary shareholders' meeting in November 2016. The 2016 Plan authorizes the grant of incentive and non-qualified share options, share appreciation rights, restricted share awards, restricted share units, unrestricted share awards, performance share awards, performance-based awards to covered employees and dividend equivalent rights. The Company only grants equity-based instruments from the SOIP as of December 31, 2022.

The following table summarizes equity-settled share option grants for plans that existed during the period:

Plan	Number of options awarded (since inception)	Vesting conditions	Contractual life of options
Share option plan C1	6,775,250	4 years' service from grant date	10 years
2016 SOIP:			
Executives and directors	3,277,044	1 year, 3 year and 4 years' service from the date of grant, quarterly and annually	10 years
Employees	1,811,687	4 years' service from the date of grant, annually	10 years

The number and weighted-average exercise prices (in CHF) of options under the share option programs for Plans C1 and the 2016 SOIP are as follows:

	Number of options	Weighted-average exercise price (CHF)	Weighted-average remaining term (years)
Outstanding at January 1, 2020	1,981,629	5.93	8.3
Forfeited during the year	(53,591)	6.03	—
Expired during the year	(26,729)	4.38	—
Exercised during the year	(73,669)	2.00	—
Granted during the year	1,073,027	6.29	—
Outstanding at December 31, 2020	2,900,667	5.90	8.2
Exercisable at December 31, 2020	1,099,015	5.49	7.0
Outstanding at January 1, 2021	2,900,667	5.90	8.2
Forfeited during the year	(207,331)	6.13	—
Exercised during the year	(218,561)	4.97	—
Granted during the year	1,110,914	6.34	—
Outstanding at December 31, 2021	3,585,689	6.21	7.8
Exercisable at December 31, 2021	1,613,242	6.13	6.8
Outstanding at January 1, 2022	3,585,689	6.21	7.8
Forfeited during the year	(304,738)	6.32	—
Exercised during the year	(110,250)	0.15	—
Granted during the year	1,090,316	3.18	—
Outstanding at December 31, 2022	4,261,017	5.65	7.6
Exercisable at December 31, 2022	2,345,648	6.41	6.6

The outstanding stock options as of December 31, 2022 have the following range of exercise prices:

	Total options	Range of expiration dates
Range of exercise prices		
CHF 0.15	97,875	2022–2026
CHF 9.53	223,646	2027
USD 5.04 to USD 12.30	2,864,408	2028–2031
USD 2.76 to USD 4.57	1,075,088	2032
Total outstanding options	4,261,017	

The weighted-average exercise price for options granted in 2022, 2021 and 2020 is USD 3.44 (CHF 3.18), USD 6.95 (CHF 6.34) and USD 7.11 (CHF 6.29), respectively. The range of exercise prices for outstanding options was CHF 0.15 to CHF 9.53 for awards previously granted in CHF (prior to 2018) and USD 2.76 to USD 12.30 for awards granted in USD as of December 31, 2022.

For awards issued in 2022, the volatility is based on the Company's actual volatility for the period congruent with the expected term of the underlying option. The risk-free interest rate is based on yields of long-dated U.S. Treasury notes that align with the expected term of the award. The weighted-average share price of common share options exercised in 2022 is USD 3.55 (CHF 3.28).

The weighted-average grant date fair values of the options granted in 2022, 2021 and 2020 are USD 2.38 (CHF 2.20), USD 5.23 (CHF 4.78) and USD 5.25 (CHF 4.65), respectively. The following table illustrates the weighted-average assumptions for the Black-Scholes option-pricing model used in determining the fair value of these awards:

	For the Year Ended December 31,		
	2022	2021	2020
Exercise price (USD)	2.76-4.57	5.31-7.72	5.04-9.16
Share price (weighted average)	3.44	6.95	7.11
Risk-free interest rate	0-2.4 %	0 %	0 %
Expected volatility	67-80 %	80 %	80 %
Expected term (in years)	5.5 - 6.25	5.1 - 6	5.5 - 6
Dividend yield	—	—	—

Restricted share awards

A summary of non-vested share awards (restricted share and restricted share units) activity as of December 31, 2022 and changes during the year then ended is presented below:

Grantee type	Number of share awards granted	Vesting conditions	Contractual life of non-vested share awards
Restricted share units			
Directors	159,025	1 year service from date of grant, annually	10 years
Executives	274,872	3 year and 4 years' service from the date of grant, quarterly and semi-annually	10 years

	Number of non-vested shares	Weighted-average grant date fair value (CHF)
Non-vested at January 1, 2020	42,763	9.52
Forfeited during the year	(11,828)	9.47
Expired during the year	(7,804)	9.52
Exercised during the year	(84,638)	9.51
Granted during the year	—	—
Vested during the year	(23,269)	9.52
Non-vested at December 31, 2020	19,494	9.51
Vested and exercisable at December 31, 2020	49,289	9.47
Non-vested at December 31, 2020	19,494	9.51
Exercised during the year	(2,471)	9.46
Vested during the year	(18,697)	9.52
Non-vested at December 31, 2021	797	9.41
Vested and exercisable at December 31, 2021	65,515	9.48
Non-vested at December 31, 2021	797	9.41
Granted during the year	239,194	3.06
Vested during the year	(23,505)	3.28
Non-vested at December 31, 2022	216,486	3.06
Vested and exercisable at December 31, 2022	89,020	7.84

The weighted-average grant date fair values of the remaining non-vested share awards as of the respective year end for the restricted share units were CHF 3.06, CHF 9.41 and CHF 9.51 for the years ended December 31, 2022, 2021 and 2020, respectively. The fair values of these non-vested share awards granted were determined using a reasonable estimate of market value of the common shares on the date of the award.

The expense charged against the income statement was CHF 3.3 million, CHF 4.1 million and CHF 4.1 million for the years ended December 31, 2022, 2021 and 2020, respectively. The expense is revised by the Company based on the number of instruments that are expected to become exercisable.

19. Commitments and contingencies

The Company's commitments and contingencies relate to its ongoing operating activities, mainly research and development programs, as well as its leased corporate space.

In the normal course of business, we conduct product research and development programs through collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. We have contractual arrangements with these organizations. As of December 31, 2022, we have contractual obligations, other than for leases (see below), totaling CHF 23.0 million for 2023.

We lease our corporate, laboratory and other facilities under multiple leases at the EPFL Innovation Park in Ecublens, near Lausanne, Canton of Vaud, Switzerland. Our lease agreements have no termination clauses longer than a 12-month contractual notice period. The Company recognizes a right-of-use asset for its leases, except for short-term and low-value leases as indicated in Note 3. See "Note 5. Right-of-use assets, long-term financial assets and lease liabilities" for the contractual undiscounted cash flows for lease obligations.

	As of December 31,	
In CHF thousands	2022	2021
Within 1 year	23,336	19,785
Between 1 and 3 years	18,516	3,620
Between 3 and 5 years	9,229	243
More than 5 years	1,407	51
Total	52,488	23,699

20. Earnings per share

	For the Year Ended December 31,		
In CHF thousands except for share and per share data	2022	2021	2020
Loss per share (EPS)			
Numerator			
Net loss attributable to equity holders of the Company	(70,753)	(72,996)	(61,921)
Denominator			
Weighted-average number of shares outstanding used to compute EPS basic and diluted attributable to equity holders	83,554,412	74,951,833	71,900,212
Basic and diluted loss per share for the period attributable to equity holders	(0.85)	(0.97)	(0.86)

In periods for which we have a loss, basic net loss per share is the same as diluted net loss per share. We have excluded from our calculation of diluted loss per share all potentially dilutive in-the-money (i) share options, (ii) non-vested restricted share awards and (iii) shares that were issued upon conversion of two different convertible notes as their inclusion would have been anti-dilutive. The weighted-average number of potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	As of December 31,		
	2022	2021	2020
Share options issued and outstanding (in-the-money)	135,827	1,140,388	412,191
Restricted share awards subject to future vesting	117,292	6,264	28,418
Convertible shares	—	41,461	—
Total potentially dilutive securities	253,119	1,188,113	440,609

21. Financial instruments and risk management

The Company's activities expose it to the following financial risks: market risk (foreign exchange and interest rate risk), credit risk and liquidity risk. The Company's overall risk management program focuses on the unpredictability of financial markets and seeks to minimize potential adverse effects on the Company's financial performance.

The following table shows the carrying amounts of financial assets and financial liabilities:

In CHF thousands	As of December 31,	
	2022	2021
Financial assets		
Right-of-use assets	2,808	2,914
Long-term financial assets	361	363
Other current receivables	392	428
Short-term financial assets	91,000	116,000
Cash and cash equivalents	31,586	82,216
Total financial assets	126,147	201,921

In CHF thousands	As of December 31,	
	2022	2021
Financial liabilities		
Long-term lease liabilities	2,253	2,340
Trade and other payables	929	2,003
Accrued expenses	9,417	16,736
Short-term lease liabilities	548	570
Total financial liabilities	13,147	21,649

Foreign exchange risk

The Company is exposed to foreign exchange risk arising from currency exposures, primarily with respect to the EUR, USD and to a lesser extent to GBP, DKK and SEK. The currency exposure is not hedged. However, the Company has a policy of matching its cash holdings to the currency structure of its expenses, which means that the Company holds predominately CHF, with lesser balances of EUR and USD (see "Note 8. Cash and cash equivalents and short-term financial assets"). The Company recognized a gain of CHF 0.5 million and losses of CHF 0.1 million and CHF 0.7 million for the years ended December 31, 2022, 2021 and 2020, respectively, within "Finance result, net."

As of December 31, 2022, if the CHF had strengthened/weakened by 10% against the EUR and the USD with all other variables held constant, the net loss for the period would have been lower/higher by CHF 0.7 million (2021: CHF 1.7 million), mainly as a result of foreign exchange gains/losses on predominantly EUR/USD denominated cash and cash equivalents and short-term financial assets.

Interest rates

The Company's CHF cash holdings (inclusive of those held in short-term financial assets) were subject to negative interest rates at certain counterparty thresholds through the first three quarters of 2022. However, with the increase in interest rates, no current CHF cash holdings (inclusive of those held in short-term financial assets) are subject to negative interest rates with our counterparties. As of December 31, 2022 if the interest rates charged by the counterparties had increased/decreased by 10%, the net income for the period would have been higher/lower by less than CHF 0.2 million. Interest income and interest expense are recorded within finance results, net in our consolidated statements of income/(loss).

Credit risk

The Company maintains a formal treasury risk and investment management policy to limit counterparty credit risk. As of December 31, 2022, the Company's cash and cash equivalents and short-term financial assets are held with five financial institutions, each with a high credit rating ranging from A+ to BBB assigned by international credit-rating agencies. The maximum amount of credit risk is the carrying amount of the financial assets. Other receivables are fully performing, not past due and not impaired (see "Note 8. Cash and cash equivalents and short-term financial assets" and "Note 10. Other current receivables").

Liquidity risk

Inherent in the Company's business are various risks and uncertainties, including the high uncertainty that new therapeutic concepts will succeed. AC Immune's success may depend in part upon its ability to (i) establish and maintain a strong patent position and protection, (ii) enter into collaborations with partners in the pharmaceutical and biopharmaceutical industries, (iii) acquire and keep key personnel employed and (iv) acquire additional capital to support its operations.

The Company's approach of managing liquidity is to ensure sufficient cash to meet its liabilities when due. Therefore, management closely monitors the cash position on rolling forecasts based on expected cash flow to enable the Company to finance its operations for at least 18 months. The Company has CHF 0.9 million in trade and other payables, and CHF 9.4 million in accrued expenses which are due within 12 months from the reporting date. Finally, as it relates to the Company's lease liabilities please see "Note 5. Right-of-use assets, long-term financial assets and lease liabilities" for detail of when corresponding lease liabilities are due.

22. Capital risk management

The Company's objectives when managing capital are to safeguard the Company's ability to continue as a going concern and to preserve the capital on the required statutory level in order to succeed in developing a cure against (i) AD, (ii) focused non-Alzheimer's neurodegenerative diseases including NeuroOrphan indications and (iii) diagnostics.

23. Subsequent events

Management has evaluated subsequent events after the balance sheet date, through the issuance of these consolidated financial statements, for appropriate accounting and disclosures. The Company has determined that there were no other such events that warrant disclosure or recognition in these consolidated financial statements.

Exhibit 4.6

INDEMNITY AGREEMENT ("the Agreement")

BETWEEN

AC Immune SA, EPFL Innovation Park, bâtiment B, 1015 Lausanne, Switzerland (the **"Company")**

AND

[*Name of Indemnitee*] (the **"Indemnitee")**

the Company and the Indemnitee each a Party and together the "**Parties**"

Recitals

A) Both the Indemnitee and the Company recognize the increased risk of litigation and other claims being asserted against members of the board of directors and officers of public companies;

B) The shareholders of the Company have approved article 29 of the articles of association of the Company pursuant to which the Company may, to the extent permitted by law, indemnify members of board of directors and of the executive management for any disadvantages suffered in connection with proceedings, suits or settlements relating to their activity for the Company, advance the respective amounts and enter into respective D&O insurances;

C) The board of directors of the Company (the "**Board**") has determined that enhancing the ability of the Company to retain and attract as directors and officers the most capable persons is in the best interests of the Company and that the Company therefore should seek to assure such persons that full indemnification and D&O insurance coverage is available;

D) In recognition of these considerations and in order to provide such protection, the Company wishes to provide in this Agreement for the indemnification of, and the advancement of legal fees to, Indemnitee as set forth in this Agreement and to the extent insurance is maintained for the coverage of Indemnitee under the Company's D&O insurance policies.

1. Definitions

Agreement	means this Indemnity Agreement.
Board	has the meaning as defined in Recital C.
Claim	means any threatened, pending or completed action, claim, suit or proceeding, whether civil, criminal or administrative or governmental or regulatory investigation.
Company	has the meaning as defined on page one.
Expenses	means all reasonable costs, charges, fees (including court fees, retainers, attorneys' fees and experts' fees) and expenses (other than regular or overtime wages, salaries, lost revenues or fees of a member of the Board) incurred in defending or investigating any Claim.

Losses	are all costs, charges, losses, damages (including monetary judgments, fines, penalties, amounts paid in settlement) arising out of or relating to a Claim, including all Expenses.
Indemnitee	has the meaning as defined on page one.
Recital	means a recital of this Agreement.
Section	means a section of this Agreement.

2. Construction

Unless a contrary indication appears, any reference in this Agreement to:

(i) a "person" includes any individual, company, corporation, firm, partnership, joint venture, association, organization, trust or agency (in each case, whether or not having separate legal personality);

(ii) a provision of law is a reference to that provision as amended.

3. Indemnification

The Company shall indemnify and hold harmless the Indemnitee, to the fullest extent permitted by applicable law, out of the assets of the Company from and against all Losses, provided that:

(i) the Losses which the Indemnitee has incurred or sustained resulted from any act done or omitted in or about the execution of the Indemnitee's duty, or supposed duty as a member of the Board or as a member of the executive committee of the Company (or is serving at the request of the Company for any affiliates of the Company); and

(ii) with respect to any act or omission giving rise to such Losses, the Indemnitee had a reasonable belief that [he/she] was at all relevant times acting in good faith and in the best interests of the Company; and

(iii) in the case of a criminal or regulatory action, investigation or proceeding, the Indemnitee had no reasonable cause to believe that his conduct giving rise to such Losses was unlawful; and

(iv) the Indemnitee cooperates with the Company in relation to the Claim in respect of which indemnification is sought hereunder.

The conclusion of any Claim by judgment, order, settlement or conviction, or up-on a plea of *nolo contendere* or its equivalent, against an indemnified person shall not in itself create a presumption that the Indemnitee did not meet the criteria set forth in clauses (ii) and (iii) above. Without limitation, in determining whether an indemnified person meets the criteria set forth in clauses (ii) and (iii) above, it is relevant whether the Indemnitee's acts or omissions giving rise to such Losses were the result of knowingly fraudulent or deliberate dishonest behavior, willful or grossly negligent misconduct, or resulted in the Indemnitee's personal gain or a financial profit or other advantage to which the Indemnitee was not legally entitled.

Notwithstanding the foregoing, the Company will not indemnify the Indemnitee where to do so would or might, in the reasonable judgment of the Company, be contrary to applicable mandatory law. With respect to claims for breach of the fiduciary duty of care under Swiss law, this means inter alia that no indemnification will be made if the Indemnitee acted with willful intent or with gross negligence.

4. Indemnification Process

4.1 Notification

Upon becoming aware of any Claim, the Indemnitee must promptly notify the chair of the Board (or, if the Indemnitee is the chair of the Board, the vice-chair of the Board) in writing that [he/she] is seeking indemnification under this Agreement.

Any failure or delay to notify will not relieve the Company of the obligation to indemnify the Indemnitee under this Agreement provided however that the Company shall not be held liable for any damages, losses, damages or costs to the extent caused by the Indemnitee's failure to give due and timely notice.

The Company shall give prompt written notice to the applicable insurers in accordance with the procedures set forth in the applicable D&O policies. The Company shall provide to Indemnitee a copy of such notice delivered to the applicable insurers, and copies of all subsequent correspondence between the Company and such insurers regarding the Claim, in each case substantially concurrently with the delivery or receipt thereof by the Company.

4.2 Determination of Entitlement to Indemnification

In accordance with article 29 of the articles of association and article 9 of the Organizational Rules of the Company, indemnification under this Agreement (unless ordered differently by a court) is made by the Company as per this Agreement. Where the Company has to make assessments, decisions or a judgment on the behavior of the Indemnitee hereunder, the respective decisions are made as follows:

(i) by a majority vote of the members of the Board who are not parties to such Claim, even though less than a quorum;

(ii) by a committee of such members of the Board designated by a majority vote of the Board, even though less than a quorum; or

(iii) if there are no such members of the Board, or if such members of the Board so direct, by independent legal counsel in a written opinion.

Subject to the other provisions of this Agreement, where an Indemnitee is entitled to indemnification, the Company will pay any Expenses incurred by the Indemnitee in defending any Claim, and to the extent such Expenses are not directly paid by the Company, advance to the Indemnitee such Expenses within five (5) business days of a notification to the Company by the Indemnitee that such Expenses are payable, provided that such advances may not exceed the limit provided in article 39 of the articles of association.

The Company's obligation to pay or advance such Expenses is subject to receipt of an undertaking from the Indemnitee to repay any Expenses that the Company paid in accordance with Section 8 if it is subsequently determined that the Indemnitee is not or was not entitled to be indemnified by the Company. In addition, the Indemnitee is obliged to repay any Expenses paid or advanced by the Company if they are subsequently reimbursed to the Indemnitee by any other person or if advances are not used.

The Company will not indemnify the Indemnitee in respect of the Expenses of enforcing any indemnification right under this Agreement, unless the Indemnitee is successful in enforcing a right to indemnification.

5. Conduct of Claims

5.1 General

After notification of a Claim in accordance with Section 4.1, the Company may elect in writing to assume the defense of the Claim at its own expense and to engage legal counsel. Upon such election, the Company shall not be liable for any other attorney's fees subsequently incurred by the Indemnitee in connection with the Claim unless:

a) the Indemnitee's engagement of its own legal counsel has been authorized by the Company;

b) the Company has failed to timely engage reputable legal counsel;

c) in circumstances where the Company has assumed the defense of the Claim, the nature of such defense risks damaging the good name or reputation of the Indemnitee; or

d) the legal counsel whom the Company has engaged reasonably determined that his/her representation of the Indemnitee would present him/her with a conflict of interest and the Company has not provided an alternative.

5.2 Retention of Outside Counsel

If the Company does not elect to defend the Claim on behalf of the Indemnitee or in case of any circumstances of Section 5.1.a) to d) above, the Indemnitee may retain outside counsel.

5.3 Settlement of Claims without Consent

The Indemnitee must not settle the Claim without the prior written consent of the Company, such consent not to be unreasonably withheld. The Company shall not be liable to indemnify the Indemnitee under this Agreement for any amounts paid in settlement of any Claim without its written consent.

6. D&O Insurance

For the duration of Indemnitee's service as a member of the Board or of the executive committee of the Company, and for at least a period of six years thereafter (or for a longer period to the extent that such D&O insurance can be obtained thereafter for so long as Indemnitee shall be subject to any pending Claim) the Company will purchase D&O insurance against any liability asserted against Indemnitee in [his/her] capacity as such and continue to maintain in effect policy of Indemnitee's D&O insurance providing coverage that is at least substantially comparable in scope and amount to that provided by the Company's current policies of D&O insurance.

In all policies of D&O insurance maintained by the Company, the Indemnitee shall be considered as an insured in such a manner as to provide the Indemnitee the same rights and benefits as are provided to the most favorably insured of the Company's directors, if the Indemnitee is a director, or of the Company's member of the executive committee, if the Indemnitee is a member of the executive committee (and not a director) by such policy.

Upon request, the Company will provide to the Indemnitee copies of all D&O insurance applications, binders, policies, declarations, endorsements and other related materials.

Notwithstanding the foregoing, the Indemnitee acknowledges that:

- Upon change of control of the Company as a result of a merger or acquisition by a third party, the D&O Insurance may expire for Losses arising from causes occurring after such change of control event, and the Company will use commercially reasonable efforts to buy D&O insurance to cover events occurring after such change in control and, should the Company fail in its efforts, the Company will in any case use best efforts to purchase “Run-off Coverage” insurance for a period up to six years from the end of the D&O insurance; and

- prior to a renewal of a D&O insurance, the Company’s Audit & Finance Committee will make a determination on the economic reasonableness of the premium for a D&O insurance extension considering the overall coverage (including limits and deductible). Where the Audit & Finance Committee considers the extension of the coverage to be excessively onerous relative to the coverage, the Company shall have no obligation to extend any D&O insurance, provided that in such event, the Company will immediately inform the Indemnitee thereof, and provided further that the Company shall then be compelled to purchase “Extended Reporting Coverage” insurance for a period of three years from the end of the then current D&O insurance period as provided in the existing D&O insurance policy.

For the avoidance of doubt, the maintenance of a D&O insurance by the Company does not limit the Indemnitee's right to be fully indemnified and held harmless as set forth under Section 3 or as set forth in article 29 of the articles of association of the Company. Any Loss not covered by D&O insurance shall be borne by the Company.

7. Scope, Term and Termination

7.1 Scope and Term of Agreement

This Agreement (and in particular the rights of the Indemnitee under Section 3) is applicable to all Claims against the Indemnitee or Losses incurred by the Indemnitee resulting from acts done or omitted in or about the execution of the Indemnitee's duty or supposed duty as a member of the Board or of the executive committee of the Company during the entire period the Indemnitee is a member of the Board or of the executive committee of the Company (or is serving at the request of the Company for any affiliates of the Company), beginning with date of election as a member of the Board or of the executive committee and not with the date of this agreement and shall continue thereafter (i) for so long as the Indemnitee may be subject to any possible Claim (including any rights of appeal thereto) and (ii) throughout the pendency of any proceedings (including any rights of appeal thereto) commenced by the Indemnitee to enforce or interpret his or her rights under this Agreement, even if, in either case, the Indemnitee may have ceased to serve in such capacity at the time of any Claim. This Agreement shall be binding upon the Company and its successors and assigns and shall inure to the benefit of the Indemnitee. The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all the business or assets of the Company, to assume and agree to perform this Agreement in the same manner and to the same extent that the Company would be required to perform if no such succession had taken place.

7.2 Termination of Indemnification

Notwithstanding the forgoing, an Indemnitee is no longer entitled to indemnification in case the Indemnitee ceases to comply with the requirements set out in Section 3 (i) to (iv).

8. Repayment of Expenses

If the Company determines, applying the criteria in Section 3(i) –(iv), that the Indemnitee is no longer entitled to indemnification, the Company will immediately cease to pay the Expenses and the Company may require the Indemnitee to reimburse all advancements.

For the avoidance of doubt, the Indemnitee's obligation to reimburse the Company is unsecured and free of interest.

9. General Provisions

9.1 Duplication of Payments

Without limiting the rights of the Indemnitee to be indemnified under this Agreement at any time, this Agreement constitutes secondary coverage if the Indemnitee is entitled to recover under any other indemnification arrangement provided by a third party or under any D&O insurance policy purchased for the benefit of the Indemnitee. The Indemnitee is not entitled to multiple indemnifications.

9.2 Successors

This Agreement is binding upon the Company and its successors. References to the Company include all constituent corporations in a consolidation or merger in which the Company or a predecessor to the Company by consolidation or merger was involved. Any rights of indemnification passes to the benefit of the heirs, executors and administrators of the Indemnitee.

9.3 Subrogation

In the event of any indemnification under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, and Indemnitee shall execute all documents reasonably required and shall take such action that may be reasonably necessary to secure such rights.

9.4 Confidentiality

Parties shall keep confidential all matters relating to indemnification. This includes, but is not limited to, the Indemnitee's intention to apply for indemnification pursuant to this Agreement, any communications with the chair of the Board or other representatives of the Company regarding indemnification. The Indemnitee shall not discuss such information with or disclose documents relating to it to anyone apart from the relevant legal advisers of the Company, [his/her] legal counsel, financial advisers and accounting (if any), and [his/her] spouse/partner, if applicable, provided that such persons shall have agreed to maintain the confidential nature of all matters relating to the indemnification. Notwithstanding the foregoing, nothing will prevent the Indemnitee from disclosing such information:

a) where the Indemnitee is under a legal or regulatory obligation to disclosure such information (but only to the extent of such obligation); or

b) to the extent that it is already in the public domain (other than as a result of disclosure by the Indemnitee); or

c) with prior written consent of the Company (who shall not unreasonably withhold its consent).

Where the Indemnitee believes that a) or b) applies, the Indemnitee shall notify the Company in advance of any disclosures unless Indemnitee is legally prohibited from such notification.

9.5 Entire Agreement

This Agreement constitutes the entire Agreement between the Parties with respect to the subject matter of this Agreement and supersedes all other prior agreements or understandings of the Parties relating hereto.

9.6 Severability

The provisions of this Agreement shall be severable in the event that any of the provisions (including any provision within a particular paragraph or sentence) are held by a court of competent jurisdiction to be invalid, illegal, void or otherwise unenforceable, and the remaining provisions shall remain legally valid and enforceable to the fullest extent permitted by law.

9.7 Amendment

No amendment or termination of this Agreement shall impair the rights of the Indemnitee under this Agreement in respect of any Losses incurred after such amendment or termination to the extent that such Losses arise from events occurring:

a) before such amendment or termination; or

b) in the case of the Indemnitee holding an external function for the Company, after such amendment or termination but before the earliest time at which the Indemnitee could reasonably have resigned from that external function for the Company.

9.8 Notices

All notices, requests or other communications to be given to any Party under or in connection with this Agreement shall be made in English and in writing and shall be delivered by (i) registered mail (return receipt requested), (ii) an internationally recognized courier, such as Federal Express, DHL or UPS, or (iii) e-mail to the following addresses:

if to the Indemnitee:	**[***Name of Indemnitee***]** [Address and e-mail]
if to the Company:	**Chair of AC Immune SA,** EPFL Innovation Park, Building B 1215 Lausanne, Switzerland [e-mail]
with a copy to:	**Chief Administrative Officer at AC Immune SA** EPFL Innovation Park, Building B 1215 Lausanne, Switzerland Jean-fabien.monin@acimmune.com

Notices delivered by hand shall be deemed delivered when actually delivered. Notices given by courier shall be deemed delivered on the date delivery is promised by the courier. Notices given by facsimile or by electronic transmission shall be deemed given on the date of receipt (if a business day), otherwise the first business day following receipt; provided that a notice delivered by facsimile or electronic transmission shall only be effective if such notice is also delivered by hand, registered mail, or given by courier on or before 2 business days after its delivery by facsimile or electronic transmission.

9.9 Governing Law and Jurisdiction

This Agreement is governed by and construed in accordance with the laws of Switzerland.

The Parties hereto submit to the exclusive jurisdiction of the competent courts at the registered seat of the Company (currently Lausanne, Switzerland).

[Signatures on the next page]

Signatures

AC Immune SA

_____	_____
Name:	Name:
Title:	Title:

Date :_____ 2021

[*Name of Indemnitee*]

_____

Name:
Title:

Date :_____ 2021

DESCRIPTION OF THE REGISTRANT'S SECURITIES

REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES

EXCHANGE ACT OF 1934

The following is a summary of the material terms of our securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as of March 16, 2023. The following description of the terms of our common shares is not meant to be complete and is qualified by reference to our articles of association ("articles of association"), which is incorporated by reference as an exhibit to our Annual Report on Form 20-F, of which this exhibit is a part. We encourage you to read our articles of association and the applicable provisions of Swiss law for additional information.

The Company

We are a Swiss stock corporation (*société anonyme*) organized under the laws of Switzerland. We were formed as a Swiss limited liability company (*société à responsabilité limitée*) on February 13, 2003 with our registered office and domicile in Basel, Switzerland. We converted to a Swiss stock corporation (*société anonyme*) under the laws of Switzerland on August 4, 2003. Our domicile and registered office is in Ecublens, near Lausanne, Canton of Vaud, Switzerland. Our head office is currently located at EPFL Innovation Park, Building B, 1015 Lausanne, Switzerland.

Share Capital

As of March 16, 2023, our issued share capital is CHF 1,794,907.30, consisting of 89,745,365 common shares with a nominal value of CHF 0.02 each. We have no dividend rights certificates (*bons de jouissance*).

Articles of Association

On June 24, 2022, we adopted the articles of association and when we refer to our articles of association, we refer to the articles of association as filed as Exhibit 99.3 to our report on Form 6-K filed with the SEC on June 24, 2022.

Purpose

Under our articles of association, our purpose is the research, study, development, manufacture, promotion, sale and marketing of products and substances within the pharmaceutical and nutrition industry as well as the purchase, sale and exploitation of patents and licenses in this field. We may engage in any activities which are apt to favor our purpose directly or indirectly. We may also acquire and sell real estate. We may open branch offices in Switzerland and abroad and may also acquire participations in other companies. We may provide securities to our subsidiaries and supply guarantees.

Ordinary Capital Increase, Authorized and Conditional Share Capital

Under Swiss law, we may increase our share capital (*capital-actions*) with a resolution of the general meeting of shareholders (ordinary capital increase) that must be carried out by the board of directors within three months of the general meeting of shareholders in order to become effective. Under our articles of association, in the case of an increase of capital against payment of contributions in cash, a resolution passed by a simple majority of the votes cast at the general meeting of shareholders regardless of abstentions and empty or invalid votes is required. In the case of the limitation or withdrawal of subscription rights or in the case of an increase of capital out of equity, against contribution in kind, or for the purpose of acquisition of assets and the granting of special benefits, a resolution passed by at least two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented is required.

Furthermore, under the Swiss Code of Obligations, or the CO, effective at the time when our current Articles were adopted, our shareholders, by a resolution passed by at least two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented, may empower our board of directors to issue shares of a specific aggregate nominal amount up to a maximum of 50% of the share capital in the form of:

- conditional capital (*capital conditionnel*) for the purpose of issuing shares in connection with, among other things, (i) the exercise of conversion and/or option or warrant rights granted in connection with bonds or similar instruments, issued or to be issued by the Company or by one of our subsidiaries or (ii) the exercise of option rights granted to employees of the Company or a subsidiary, members of our board of directors or any consultant of the Company, or other persons providing services to the Company or a subsidiary; or

- authorized capital (*capital-actions autorisé*) to be utilized by the board of directors within a period determined by the shareholders but not exceeding two years from the date of the shareholder approval.

Pre-Emptive Rights

Pursuant to the CO, shareholders have in principle pre-emptive subscription rights (*droit préférentiel de souscription*). With respect to conditional capital in connection with the issuance of conversion rights, convertible bonds or similar debt instruments, shareholders have in principle advance subscription rights (*droit de souscrire préalablement*).

A resolution passed at a general meeting of shareholders by at least two-thirds of the shares represented and the absolute majority of the nominal value of the shares represented may authorize our board of directors to withdraw or limit pre-emptive subscription rights or advance subscription rights in certain circumstances.

If pre-emptive subscription rights are granted, but not exercised, the board of directors may allocate the non-exercised pre-emptive subscription rights as it elects but has to follow the principle of equal treatment of the shareholders.

Our Authorized Share Capital

Under Article 3a of our articles of association, board of directors is authorized to increase the share capital, in one or several steps until June 24, 2024, by a maximum amount of CHF 400,000 by issuing a maximum of 20,000,000 registered shares with a par value of CHF 0.02 each, to be fully paid up. An increase of the share capital (i) by means of an offering underwritten by a financial institution, a syndicate or another third party or third parties, followed by an offer to the then-existing shareholders of the Company and (ii) in partial amounts shall also be permissible.

For the currently effective Authorized Share Capital, the board of directors will determine the time of the issuance, the issue price, the manner in which the new registered shares have to be paid up, the date from which the registered shares carry the right to dividends, the conditions for the exercise of the preemptive rights and the allotment of preemptive rights that have not been exercised. The board of directors may allow the pre-emptive rights that have not been exercised to expire, or it may place with third parties such rights or registered shares, the pre-emptive rights of which have not been exercised, at market conditions or use them otherwise in the interest of the Company.

The board of directors is authorized to withdraw or limit the pre-emptive rights of the shareholders and to allot them to third parties:

- if the issue price of the new registered shares is determined by reference to the market price (with a customary discount);
- for the acquisition of an enterprise, part of an enterprise or participations, or for the financing or refinancing of any of such acquisition, or in the event of share placement for the financing or refinancing of such placement; or
- for raising of capital (including private placements) in a fast and flexible which probably could not be reached without the exclusion of the statutory pre-emptive right of the existing shareholders.

As of January 1, 2023, the new Swiss corporate law introducing the capital band mechanism has come into force. It will no longer be possible to renew the Company's current Authorized Share Capital beyond June 24, 2024. Instead, the Company can only introduce the capital band pursuant to Article 653s et seq. of the revised Swiss Code of Obligations which requires an amendment of the Articles by way of a resolution of a duly convened general meeting of shareholders of the Company. Under the capital band mechanism, the general meeting of shareholders can authorize the board of directors at any time within a maximum of five years to increase or decrease the share capital by a maximum amount of 50% of the current share capital.

Our Conditional Share Capital

Conditional Share Capital for Bonds and Similar Debt Instruments

Under Article 3b of our articles of association, our share capital may be increased by a maximum aggregate amount of CHF 100,000 through the issue of a maximum of 5,000,000 common shares, payable in full, each with a nominal value of CHF 0.02, through the exercise of conversion and/or option or warrant rights granted in connection with bonds or similar instruments, issued or to be issued by the Company or by one of our subsidiaries, including convertible debt instruments. Shareholders do not have pre-emptive subscription rights in such circumstances.

Shareholders' subscription rights are excluded. Shareholders' advance subscription rights with regards to new bonds or similar instruments may be restricted or excluded by decision of the board of directors in order to finance or re-finance the acquisition of companies or holdings, or new investments planned by the Company, or in order to issue convertible bonds and warrants on the international capital markets or through private placement. If advance subscription rights are excluded, then (i) the instruments are to be placed at market conditions; (ii) the exercise period is not to exceed ten years from the date of issue for warrants and twenty years for conversion rights; and (iii) the conversion or exercise price for the new shares is to be set at least in line with the market conditions prevailing at the date on which the instruments are issued. The respective holders of conversion and/or option or warrant rights are entitled to subscribe the new shares.

Conditional Share Capital for Employee Benefit Plans

Under Article 3c of our articles of association, our share capital may, to the exclusion of the pre-emptive subscription rights of shareholders, be increased by a maximum aggregate amount of CHF 96,000 through the issue of a maximum of 4,800,000 common shares, payable in full, each with a nominal value of CHF 0.02, in connection with the exercise of option rights granted to employees of the Company or one of our subsidiaries, members of the board of directors or any consultant, or other persons providing services to the Company or one of our subsidiaries.

Shareholders' subscription rights are excluded. These new registered shares may be issued at a price below the current market price. The board of directors specifies the precise conditions of issue including the issue price of the shares.

Uncertificated Securities

Our shares are uncertificated securities (*droits-valeurs*, within the meaning of Article 973c of the CO) and, when administered by a financial intermediary (*dépositaire*, within the meaning of the Federal Act on Intermediated Securities, "FISA"), qualify as intermediated securities (*titres intermédiés*, within the meaning of the FISA). In accordance with Article 973c of the CO, we maintain a non-public register of uncertificated securities (*registre des droits-valeurs*). We may at any time convert uncertificated securities into share certificates (including global certificates), one kind of certificate into another, or share certificates (including global certificates) into uncertificated securities. Following entry in our share register, a shareholder may at any time request from us a written confirmation in respect of the shares held by such shareholder, as reflected in the share register.

General Meeting of Shareholders

Ordinary/Extraordinary Meetings, Powers

The general meeting of shareholders is our supreme corporate body. Under Swiss law, ordinary and extraordinary general meetings of shareholders may be held. Under Swiss law, an ordinary general meeting of shareholders must be held annually within six months after the end of a Company's financial year. In our case, this generally means on or before June 30.

The following powers are vested exclusively in the general meeting of shareholders:

- adopting and amending the articles of association, including change of a company's purpose or domicile;
- electing and removal of the members of the board of directors, the chairman of the board of directors, the members of the compensation committee, the auditors and the independent proxy;
- approving the management report and the consolidated accounts;
- approving the annual accounts and resolutions on the allocation of the disposable profits, and in particular setting the dividend and the shares of profit to board members;
- approving the total compensation paid to members of the board of directors and executive management;
- resolving the interim dividend and approve the interim account required therefor;
- resolving on repaying the statutory capital reserve;
- discharging the members of the board of directors and executive management from liability with respect to their tenure in the previous financial year;
- dissolving a company with or without liquidation;
- resolving to delist the equity securities of the company; and
- passing resolutions concerning all matters which are reserved to the authority of the general meeting of shareholders by law or by the articles of association.

An extraordinary general meeting of shareholders may be called by a resolution of the general meeting, the board of directors or, under certain circumstances, by a company's auditor, liquidator or the representatives of convertible bond holders, if any. In addition, according to our current Articles, the board of directors is required to convene an extraordinary general meeting of shareholders if shareholders representing at least 10% of the share capital request such general meeting of shareholders in writing. Such request must set forth the items to be discussed and the proposals to be acted upon. The board of directors must convene an extraordinary general meeting of shareholders and propose financial restructuring measures if, based on a company's stand-alone annual statutory balance sheet, half of the share capital and reserves are not covered by its assets.

Voting and Quorum Requirements

Shareholder resolutions and elections (including elections of members of the board of directors) require the affirmative vote of the simple majority of the votes cast at the general meeting of shareholders regardless of abstentions or empty or invalid votes, unless statutory law or the articles of association state otherwise.

A resolution of the general meeting of the shareholders passed by at least two-thirds of the shares represented at the meeting, and the absolute majority of the nominal value of the shares represented is required for:

- amending a company's corporate purpose;
- the consolidation of shares, unless the consent of all the shareholders concerned is required;
- creating shares with privileged voting rights;
- restricting the transferability of common shares;
- creating conditional share capital or a capital band;
- increasing the share capital out of equity, against contributions in-kind or for the purpose of acquiring assets and granting of special benefits;
- limiting or withdrawing shareholder's pre-emptive subscription rights;
- changing a company's domicile;
- changing in the currency of the share capital;
- introducing a casting vote for the person chairing the general meeting;
- introducing a provision on holding the general meeting abroad;
- resolving the delisting of the equity securities of the company;
- introducing an arbitration clause in the articles of association;
- alleviating or withdrawing of restrictions upon the transfer of common shares and the removal of the voting cap of 33 1/3% as contained in article 4 of the articles of association;
- removing the indemnification provision for the board of directors and executive management as contained in article 29 of the articles of association;
- converting participation certificates into shares;
- dissolving or liquidating a company; and
- amending or eliminating article 17 (*resolutions and elections*) of the articles of association.

The same voting requirements apply, subject to mandatory law, to resolutions regarding transactions among corporations (including a merger, demerger or conversion of a corporation) based on Switzerland's Federal Act on Mergers, Demergers, Transformations and Transfer of Assets, or the Merger Act, see "—Compulsory Acquisitions; Appraisal Rights."

In accordance with Swiss law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. To this extent, our practice varies from the requirement of NASDAQ Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock.

Notice

General meetings of shareholders must be convened by the board of directors or, if necessary, by the auditors at least 20 days before the date of the meeting. The general meeting of shareholders is convened by way of a notice appearing in our official publication medium, currently the Swiss Official Gazette of Commerce. Registered shareholders may also be informed by ordinary mail or e-mail. The notice of a general meeting of shareholders must state the items on the agenda, the proposals to be acted upon and, in case of elections, the names of the nominated candidates. Except in the limited circumstances listed below, a resolution may not be

passed at a general meeting without proper notice. This limitation does not apply to proposals to convene an extraordinary general meeting of shareholders or to initiate a special investigation. No previous notification is required for proposals concerning items included in the agenda or for debates that do not result in a vote.

All of the owners or representatives of our shares may, if no objection is raised, hold a general meeting of shareholders without complying with the formal requirements for convening general meetings of shareholders (a universal meeting). This universal meeting of shareholders may discuss and pass binding resolutions on all matters within the purview of the ordinary general meeting of shareholders, provided that the owners or representatives of all the shares are present at the meeting.

Agenda Requests

Pursuant to our current Articles, one or more shareholders, whose combined shareholdings represent the lower of (i) at least one tenth of the share capital or (ii) an aggregate nominal value of at least CHF 1,000,000, may request that an item be included in the agenda for an ordinary general meeting of shareholders. A request for inclusion of an item on the agenda must in principle be requested in writing delivered to or mailed and received at the registered office of the Company at least 120 calendar days before the first anniversary of the date that the Company's proxy statement was released to shareholders in connection with the previous year's ordinary general meeting of shareholders. The request must contain, for each of the agenda items, the following information:

- a brief description of the business desired to be brought before the ordinary general meeting of shareholders and the reasons for conducting such business at the ordinary general meeting of shareholders;
- the name and address, as they appear in our share register, of the shareholder proposing such business;
- the number of shares of the Company which are beneficially owned by such shareholder;
- the dates upon which the shareholder acquired such shares;
- documentary support for any claim of beneficial ownership;
- any material interest of such shareholder in such business; and
- a statement in support of the matter and, for proposals sought to be included in the Company's proxy statement, any other information required by Securities and Exchange Commission Rule 14a-8.

In addition, if the shareholder intends to solicit proxies from the shareholders of the Company, such shareholder shall notify the Company of this intent in accordance with Securities and Exchange Commission Rule 14a-4 and/or Rule 14a-8.

Our annual business report, the compensation report and the auditor’s report must be made available for inspection by the shareholders at our registered office no later than 20 days prior to the general meeting of shareholders. Shareholders of record may be notified of this in writing.

Voting Rights

Each of our shares entitles its holder to one vote, regardless of its nominal value. The shares are not divisible. The right to vote and the other rights of share ownership may only be exercised by shareholders (including any nominees) or usufructuaries who are entered in our share register at cut-off date determined by the board of directors. Those entitled to vote in the general meeting of shareholders may be represented by the independent proxy holder (annually elected by the general meeting of shareholders), another registered shareholder or third person with written authorization to act as proxy or the shareholder’s legal representative. The chairman has the power to decide whether to recognize a power of attorney.

Our articles of association state that no individual or legal entity may, directly or indirectly, formally, constructively or beneficially own or otherwise control voting rights (“Controlled Shares”) with respect to 33 1⁄3% or more of the registered share capital recorded in the Commercial Register except if such individual or legal entity submits prior to the acquisition of such Controlled Shares an orderly tender offer to all shareholders with a minimum price of the higher of (i) the volume weighted average price of the last 60 trading days prior to the publication of the tender offer or (ii) the highest price paid by such individual or legal entity in the 12 months preceding to the publication of the tender offer. Those associated through capital, voting power, joint management or in any other way, or joining for the acquisition of shares, will be regarded as one person. The common shares exceeding the limit of 33 1/3% and not benefitting from the exemption regarding a tender offer will be entered in our share registered as shares without voting rights. The board of directors may in special cases approve exceptions to the above regulations. Additional voting caps apply to shareholders acquiring shares for other persons (nominees).

Dividends and Other Distributions

Our board of directors may propose to shareholders that a dividend or other distribution be paid but cannot itself authorize the distribution. Dividend payments require a resolution passed by a simple majority of the votes cast at a general meeting of shareholders regardless of abstentions or empty or invalid votes. In addition, our auditors must confirm that the dividend proposal of our board of directors conforms to Swiss statutory law and our articles of association.

Under Swiss law, we may pay dividends only from the disposable profit and from reserves formed for this purpose, each as evidenced by our audited stand-alone statutory balance sheet prepared pursuant to Swiss law, and after allocations to reserves required by Swiss law and the articles of association have been deducted.

Distributable reserves are generally booked either as "free reserves" (*réserves libres*) or as "reserve from capital contributions" (*apports de capital*). Under the CO, if our general reserves (*réserve générale*) amount to less than 20% of our share capital recorded in the Commercial Register (i.e., 20% of the aggregate nominal value of our issued capital), then at least 5% of our annual profit must be retained as general reserves. The CO permits us to accrue additional general reserves. Further, a purchase of our own shares (whether by us or a subsidiary) reduces the distributable reserves in an amount corresponding to the purchase price of such own shares. Finally, the CO under certain circumstances requires the creation of revaluation reserves which are not distributable.

Distributions out of issued share capital (i.e. the aggregate nominal value of our issued shares) are not allowed and may be made only by way of a share capital reduction. Such a capital reduction requires a resolution passed by a simple majority of the votes cast at a general meeting of shareholders regardless of abstentions or empty or invalid votes. The resolution of the shareholders must be recorded in a public deed and a special audit report must confirm that claims of our creditors remain fully covered despite the reduction in the share capital recorded in the Commercial Register. The share capital may be reduced below CHF 100,000 only if and to the extent that at the same time the statutory minimum share capital of CHF 100,000 is reestablished by sufficient new fully paid-up capital. Upon approval by the general meeting of shareholders of the capital reduction, the board of directors must give public notice of the capital reduction resolution in the Swiss Official Gazette of Commerce three times and notify creditors that they may request, within two months of the third publication, satisfaction of or security for their claims. The reduction of the share capital may be implemented only after expiration of this time limit.

Our board of directors determines the date on which the dividend entitlement starts. Dividends are usually due and payable shortly after the shareholders have passed the resolution approving the payment, but shareholders may also resolve at the ordinary general meeting of shareholders to pay dividends in quarterly or other installments.

Transfer of Shares

Shares in uncertificated form (*droits-valeurs*) may only be transferred by way of assignment. Shares that constitute intermediated securities (*titres intermédiés*) may only be transferred when a credit of the relevant intermediated securities to the acquirer's securities account is made in accordance with the relevant provisions of the FISA. Article 5 of our articles of association provides that the transfer of intermediated securities and the pledging of these intermediated securities are based on the provisions of the FISA and that transfer of propriety as collateral by means of written assignment are not permitted.

Voting rights may be exercised only after a shareholder (or usufructuaries) has been entered in our share register (*registre des actions*) with his or her name, first name and address (in the case of legal entities, the registered office) as a shareholder with voting rights. Our articles of association state that no individual or legal entity may, directly or indirectly, formally, constructively or beneficially own or otherwise control voting rights ("Controlled Shares") with respect to 33 1⁄3% or more of the registered share capital recorded in the Commercial Register except if such individual or legal entity submits prior to the acquisition of such Controlled Shares an orderly tender offer to all shareholders with a minimum price of the higher of (i) the volume weighted average price of the last 60 trading days prior to the publication of the tender offer or (ii) the highest price paid by such individual or legal entity in the 12 months preceding to the publication of the tender offer. Those associated through capital, voting power, joint management or in any other way, or joining for the acquisition of shares, will be regarded as one person. The common shares exceeding the limit of 33 1/3% and not benefitting from the exemption regarding a tender offer will be entered in our share registered as shares without voting rights.

Additional voting caps apply to shareholders acquiring shares for other persons (nominees).

Inspection of Books and Records

Under the CO, a shareholder has a right to inspect our share register with respect to his own shares and otherwise to the extent necessary to exercise his shareholder rights. No other person has a right to inspect our share register. Our books and correspondence may be inspected with the express authorization of the general meeting of shareholders or by resolution of the board of directors and subject to the safeguarding of our business secrets.

Special Investigation

If the shareholders' inspection rights as outlined above prove to be insufficient in the judgment of the shareholder, any shareholder may propose to the general meeting of shareholders that specific facts be examined by a special commissioner in a special investigation. If the general meeting of shareholders approves the proposal, we or any shareholder may, within 30 calendar days after the general meeting of shareholders, request the competent court sitting in Lausanne, Switzerland, our registered office, to appoint a special commissioner. If the general meeting of shareholders rejects the request, one or more shareholders representing at least 5 percent of the share capital may request that the court appoint a special commissioner. The court will issue such an order if the petitioners can make a *prima facie case* that the board of directors, any member of the board of directors or our executive management infringed the law or our articles of association and such infringement is likely to harm the Company or the shareholders. The costs of the investigation would generally be allocated to us and only in exceptional cases to the petitioners.

Compulsory Acquisitions; Appraisal Rights

Business combinations and other similar transactions (i.e. mergers, demergers, transformations and certain asset transfers) that are governed by the Swiss Merger Act are, if approved in accordance with the applicable provisions of the Swiss Merger Act, binding on all shareholders of the involved companies. A statutory merger or demerger requires approval by at least two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal value of the shares represented. If the merger agreement provides, however, only for a compensation payment, or in the event of an asymmetrical demerger, at least 90 percent of all shareholders of the transferring company who are entitled to vote must approve the merger agreement and the asymmetrical demerger, respectively.

Swiss corporations may be acquired by an acquirer through the direct acquisition of shares of the Swiss corporation. The Swiss Merger Act provides for the possibility of a so-called "cash-out" or "squeeze-out" merger if the acquirer controls 90% of the outstanding shares. If such a squeeze-out merger under the Swiss Merger Act occurs, a minority shareholder subject to the squeeze-out merger could seek to claim, within two months of the publication of the squeeze-out merger, that the consideration offered is "inadequate" and petition a Swiss competent court to determine what "adequate" consideration is.

In addition, under Swiss law, the sale of "all or substantially all of our assets" by us may require the approval of at least two-thirds of the number of shares represented at a general meeting shareholders and the absolute majority of the nominal value of the shares represented. Whether a shareholder resolution is required depends on the particular transaction, including whether the following test is satisfied:

- a core part of our business is sold without which it is economically impracticable or unreasonable to continue to operate the remaining business;
- our assets, after the divestment, are not invested in accordance with our statutory business purpose; and
- the proceeds of the divestment are not earmarked for reinvestment in accordance with our business purpose but, instead, are intended for distribution to our shareholders or for financial investments unrelated to our business.

If in a merger, demerger or transformation, equity or shareholder rights are not adequately preserved or the compensation paid is unreasonable, within two months after the publication of the merger, demerger or transformation resolution, each shareholder may demand that the competent court determines what is a reasonable amount of compensation. The decision of the court is legally binding on all shareholders of the company involved, provided that they are in the same legal position as the plaintiff. The costs of proceedings shall be borne by the acquiring company. If the particular circumstances justify it, the court may decide that the plaintiff shall bear all or part of the cost. An action to obtain a review of the protection of equity or shareholder rights does not affect the legal validity of the merger, demerger or transformation resolution.

Board of Directors

Our articles of association provide that the board of directors shall consist of at least three and not more than nine members.

The members of the board of directors and the chairman are elected annually by the general meeting of shareholders for a period until the completion of the subsequent ordinary general meeting of shareholders and are eligible for re-election. Each member of the board of directors must be elected individually.

Powers

The board of directors has the following non-delegable and inalienable powers and duties:

- the overall management of the Company and the issuing of all necessary directives;
- the determination of the Company's organization;

- the organization of the accounting, financial control and financial planning systems are required for management of the Company;
- the appointment and dismissal of persons entrusted with managing and representing the Company;
- the overall supervision of the persons entrusted with managing the Company, in particular with regard to compliance with the law, articles of association, operational regulations and directives;
- the compilation of the annual report, and the preparation for the general meeting of shareholders and implementing its resolutions;
- the preparation of the compensation report and to request approval by the general meeting of shareholders regarding the compensation of the board of directors and the executive committee; and
- the notification of the court in the event that the Company is over-indebted.

The board of directors may assign responsibility for preparing and implementing its resolutions or monitoring transactions to committees or individual members. It must ensure appropriate reporting to its members. Furthermore, the board of directors may, while retaining such non-delegable and inalienable powers and duties, delegate, in part or entirely, the management and the representation of the Company, within the limits of the law, to a one or more individual directors (Delegates) or to third parties pursuant to the organizational regulations issued by the board of directors.

Pursuant to Swiss law and Article 25 of our articles of association, details of the delegation and other procedural rules such as quorum requirements must be set in the organizational rules issued by the board of directors.

The board of directors assigns the persons with signatory power for the Company and the kind of signatory power.

Indemnification of Executive Management and Directors

Subject to Swiss law, Article 29 of our articles of association provides for indemnification of the current and former members of the board of directors, executive management and their heirs, executors and administrators, against liabilities arising in connection with the performance of their duties in such capacity, and permits us to advance the expenses of defending any act, suit or proceeding to our directors and members of the executive management.

In addition, under general principles of Swiss employment law, an employer may be required to indemnify an employee against losses and expenses incurred by such employee in the proper execution of their duties under the employment agreement with the employer.

Conflict of Interest, Management Transactions

Swiss law does not have a general provision regarding conflicts of interest. However, the CO contains a provision that requires our directors and the members of the executive management to safeguard the Company's interests and imposes a duty of loyalty and duty of care on our directors and the members of the executive management. This rule is generally understood to disqualify directors and members of the executive management from participating in decisions that directly affect them. Our directors and executive officers are personally liable to us for any breach of these provisions. In addition, Swiss law contains provisions under which directors and all persons engaged in the Company's management are liable to the Company, each shareholder and the Company's creditors for damages caused by an intentional or negligent violation of their duties. Furthermore, Swiss law contains a provision under which payments made to any of the Company's shareholders or directors or any person associated with any such shareholder or director, other than payments made at arm's length, must be repaid to the Company if such shareholder or director acted in bad faith.

Our board of directors has adopted a Code of Business Conduct and Ethics that covers a broad range of matters, including the handling of conflicts of interest.

Principles of the Compensation of the Board of Directors and the Executive Management

Pursuant to Swiss law, our shareholders must annually approve the compensation of the board of directors and the persons whom the board of directors has, fully or partially, entrusted with the management of the Company. The board of directors must issue, on an annual basis, a written compensation report that must be reviewed together with a report on our business by our auditor. The compensation report must disclose all compensation (as defined in section 14 of the Swiss Ordinance against Excessive Compensation in Listed Companies) granted by the Company, directly or indirectly, to current members of the board of directors and executive management as well as to former members of the board of directors and executive management but in the latter case only to the extent if such compensation is related to their former role within the Company or if such compensation is not on customary market terms.

The disclosure concerning compensation must in particular include the aggregate amount for the board of directors and the aggregate amount for the executive management, as well as the particular amount of compensation for each member of the board of directors and the highest paid member of the executive management, specifying the name and function of each person.

Certain forms of compensation are prohibited for members of our board of directors and executive management, such as:

- severance payments provided for either contractually or in the articles of association (compensation due until the termination of a contractual relationship does not qualify as severance payment);
- advance compensation;
- incentive fees for the acquisition or transfer of corporations, or parts thereof, by the Company or by companies being, directly or indirectly, controlled by the us;
- loans, other forms of indebtedness, pension benefits not based on occupational pension schemes and performance-based compensation not provided for in the articles of association; and
- equity securities and conversion and option rights awards not provided for in the articles of association.

Compensation to members of the board of directors and executive management for activities in entities that are, directly or indirectly, controlled by the Company is prohibited if the compensation (i) would have been prohibited if it was paid directly by the Company, (ii) is not provided for in the articles of association or (iii) has not been approved by the general meeting of shareholders.

The general meeting of shareholders annually votes on the proposals of the board of directors with respect to:

- the maximum aggregate amount of non-performance-related compensation of the board of directors for the next term of office;
- the maximum aggregate amount of a possible additional compensation of the board of directors for the preceding business year;
- the maximum aggregate amount of non-performance-related compensation of the executive management for the 12-month period starting on 1 July following the ordinary general meeting of shareholders;
- the maximum aggregate amount of variable compensation for the executive management for the current year; and
- the maximum aggregate amount of options or shares in the Company granted to the board of directors and the executive management.

The respective total compensation amounts include social security and occupational pension contributions for the benefit of the members of the board of directors, the executive management and the Company.

If the general meeting of shareholders refuses to approve a respective motion by the board of directors, the board of directors may either submit a new motion at the same meeting or determine a maximum total remuneration or several maximum partial remunerations, subject to the relevant principles of the compensation, or submit a new motion to the next general meeting of shareholders for approval.

In addition to fixed compensation, members of the executive management may be paid in cash a variable compensation, depending on the achievement of certain performance criteria. The performance criteria may include individual targets, targets of the Company or parts thereof and targets in relation to the market, other companies or comparable benchmarks, taking into account the position and level of responsibility of the recipient of the variable compensation. The board of directors or, where delegated to it, the compensation committee determines the relative weight of the performance criteria and the respective target values.

Compensation may be paid in cash or granted in form of options or shares in the Company. The board of directors or, to the extent delegated to it, the compensation committee determines grant, vesting, exercise and forfeiture conditions.

Borrowing Powers

Neither Swiss law nor our articles of association restrict in any way our power to borrow and raise funds. The decision to borrow funds is made by or under the direction of our board of directors, and no approval by the shareholders is required in relation to any such borrowing.

Repurchases of Shares and Purchases of Own Shares

The CO limits our right to purchase and hold our own shares. We and our subsidiaries may purchase shares only if and to the extent that (i) we have freely distributable reserves in the amount of the purchase price; and (ii) the aggregate nominal value of all shares held by us does not exceed 10 percent of our share capital. Pursuant to Swiss law, where shares are acquired in connection with a transfer restriction set out in the articles of association, the foregoing upper limit is 20 percent. If we own shares that exceed the threshold of 10 percent of our share capital, the excess must be sold or cancelled by means of a capital reduction within two years.

We currently hold 6,214,021 fully paid up common shares of par value CHF 0.02 each, as treasury shares.

Shares of the Company held by us or our subsidiaries are not entitled to vote at the general meeting of shareholders but are entitled to the economic benefits applicable to the shares generally, including dividends and pre-emptive subscription rights in the case of share capital increases.

In addition, selective share repurchases are only permitted under certain circumstances. Within these limitations, as is customary for Swiss corporations, we may purchase and sell our own shares from time to time in order to meet imbalances of supply and demand, to provide liquidity and to even out variances in the market price of shares.

Notification and Disclosure of Substantial Share Interests

The disclosure obligations generally applicable to shareholders of Swiss corporations under the Swiss Financial Market Infrastructure Act, FinMIA, do not apply to us since our shares are not listed on a Swiss stock exchange.

Stock Exchange Listing

Our common shares are listed on the NASDAQ Global Market under the symbol “ACIU.”

Transfer Agent and Registrar of Shares

Computershare Trust Company, N.A. acts as transfer agent and registrar for our common shares. The share register reflects only record owners of our shares. Swiss law does not recognize fractional share interests.

Exhibit 8.1

Subsidiaries of AC Immune SA

Name of Subsidiary	**Jurisdiction of Organization**
AC Immune USA, Inc.	United States

Exhibit 12.1

CERTIFICATION

I, Andrea Pfeifer, certify that:

1. I have reviewed this annual report on Form 20-F of AC Immune SA;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: March 16, 2023

/s/ Andrea Pfeifer
Andrea Pfeifer
Chief Executive Officer

Exhibit 12.2

CERTIFICATION

I, Christopher Roberts, certify that:

1. I have reviewed this annual report on Form 20-F of AC Immune SA;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: March 16, 2023

/s/ Christopher Roberts
Christopher Roberts
Vice President, Finance and Interim Chief Financial Officer

Exhibit 13.1

CERTIFICATION

The certification set forth below is being submitted in connection with AC Immune SA's annual report on Form 20-F for the year ended December 31, 2022 (the "Report") for the purpose of complying with Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934 (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code.

Andrea Pfeifer, the Chief Executive Officer of AC Immune SA, certifies that, to the best of her knowledge:

1. the Report fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of AC Immune SA.

Date: March 16, 2023

/s/ Andrea Pfeifer
Name: Andrea Pfeifer
Chief Executive Officer

Exhibit 13.2

CERTIFICATION

The certification set forth below is being submitted in connection with AC Immune SA's annual report on Form 20-F for the year ended December 31, 2022 (the "Report") for the purpose of complying with Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934 (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code.

Christopher Roberts, the Vice President, Finance and Interim Chief Financial Officer of AC Immune SA, certifies that, to the best of his knowledge:

1. the Report fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of AC Immune SA.

Date: March 16, 2023

/s/ Christopher Roberts
Name: Christopher Roberts
Vice President, Finance and Interim Chief Financial Officer

EXHIBIT 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form F-3 (No. 333-249655 and No. 333-255576) and on Form S-8 (No. 333-233019) of AC Immune SA of our report dated March 16, 2023 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 20-F.

/s/ PricewaterhouseCoopers SA

Lausanne, Switzerland
March 16, 2023