UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K

(Mark One)

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

For the fiscal year ended **December 31, 2021**

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

For the transition period from _____ to _____

Commission File Number: **001-36201**

Immunic, Inc.

(Exact name of registrant as specified in its charter)

Delaware		**56-2358443**
(State or other jurisdiction of incorporation or organization)		(I.R.S. Employer Identification No.)
1200 Avenue of the Americas,	**Suite 200**	
New York,	**NY**	**10036**
(Address of principal executive offices)		(Zip Code)

(332) 255-9818
(Registrant's telephone number, including area code)

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

Title of Each Class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value	IMUX	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No ☒
Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes No ☒

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 and post such files). Yes ☒ No ☐

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

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

If an emerging growth company, indicate by check mark 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. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the common equity held by non-affiliates of the Registrant, based on the closing price of the common stock on The Nasdaq Stock Market on June 30, 2021 was $225.0 million.

On February 18, 2022, 27,906,942 shares of common stock, $0.0001 par value, were outstanding.

Documents Incorporated by Reference: Certain portions of the registrant's definitive Proxy Statement for its 2022 Annual Meeting of Stockholders are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K.

Immunic, Inc.

ANNUAL REPORT ON FORM 10-K

For the Fiscal Year Ended December 31, 2021

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K ("Annual Report") contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These forward-looking statements are based on our management's current beliefs and assumptions and on information currently available to our management, and are contained principally in the sections entitled "Business," "Risk Factors," and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Forward-looking statements include all statements that are not historical facts and can be identified by terms such as "anticipates," "believes," "best in class," "could," "seeks," "estimates," "expects," "first-in-class," "focused," "goal," "intends," "may," "objective," "opportunity," "pipeline," "plans," "potential," "predicts," "projects," "pursuing," "should," "target," "treatment option," "will," "would," "might," "can," "continue" or similar expressions and the negatives of those terms.

These forward-looking statements include, among other things, statements about:

- the strategies, prospects, plans, expectations and objectives of management;
- our ability to maintain compliance with Nasdaq listing standards;
- strategies with respect to our development programs, including our ability to develop and commercialize our product candidates and the timing and expected data of clinical trials and preclinical studies;
- our estimates regarding revenues, expenses, capital requirements, projected cash requirements and needs for additional financing
- possible sources of funding for future operations;
- our ability to protect intellectual property rights and our intellectual property position;
- future economic conditions or performance;
- proposed products or product candidates;
- our ability to retain key personnel;
- our ability to maintain effective internal control over financial reporting; and
- beliefs and assumptions underlying any of the foregoing.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements including those described in "Risk Factors" and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this Annual Report, unless an earlier date is specified. You should read this Annual Report and the documents that we reference in this Annual Report and have filed with the Securities and Exchange Commission ("SEC") as exhibits hereto completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

PART I

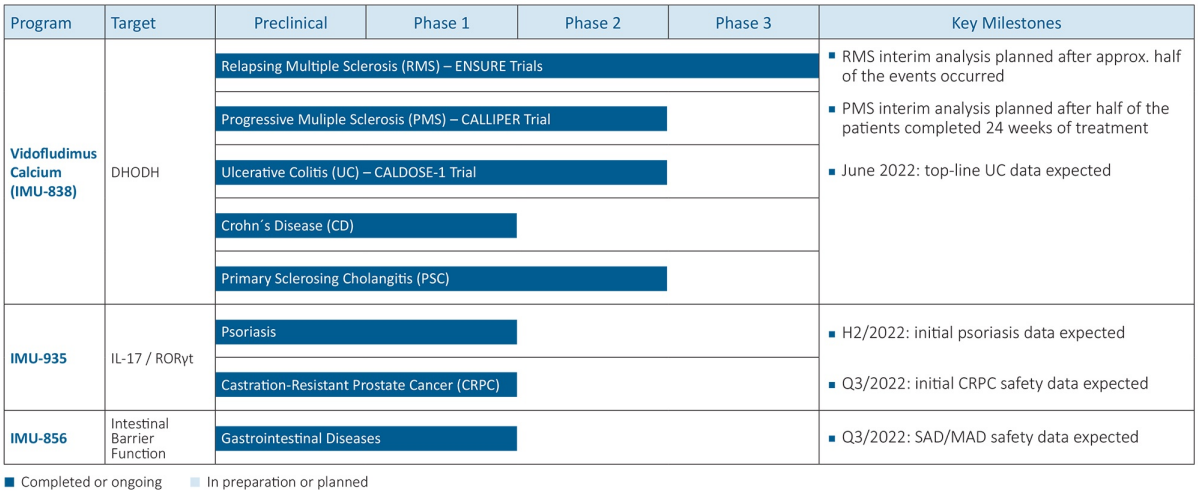
Item 1. Business.

Overview

Immunic, Inc. ("Immunic," “we,” “us,” “our” or the "Company") is a clinical-stage biopharmaceutical company with a pipeline of selective oral immunology therapies focused on treating chronic inflammatory and autoimmune diseases, including relapsing multiple sclerosis (“RMS”), ulcerative colitis (“UC”), Crohn’s disease (“CD”) and psoriasis. We are headquartered in New York City with our main operations in Gräfelfing near Munich, Germany. We currently have approximately 55 employees.

We are currently pursuing three development programs. These include the vidofludimus calcium (IMU-838) program, which is focused on the development of oral formulations of a small molecule inhibitor of the enzyme dihydroorotate dehydrogenase (“DHODH”); the IMU-935 program, which is focused on an inverse agonist of retinoic acid receptor-related orphan nuclear receptor gamma truncated (“RORγt”), an immune cell-specific isoform of RORγ; and the IMU-856 program, which involves the development of a drug targeting the restoration of intestinal barrier function and regeneration of bowel epithelium. These product candidates are being developed to address diseases such as RMS, UC, CD, and psoriasis. In addition to these large markets, these products are also being developed to address certain rare diseases with high unmet medical needs, such as primary sclerosing cholangitis (“PSC”), as well as metastatic castration-resistant prostate cancer (“mCRPC”).

The following table summarizes the potential indications, clinical targets and clinical development status of our three product candidates:



Our most advanced drug candidate, vidofludimus calcium (IMU-838), targets DHODH, a key enzyme in the intracellular metabolism of immune cells in the body. In the third quarter of 2020, we reported positive results from our Phase 2 EMPhASIS trial of vidofludimus calcium in relapsing-remitting multiple sclerosis (“RRMS”), achieving both primary and key secondary endpoints with high statistical significance. The first patient in our Phase 3 ENSURE program of vidofludimus calcium in RMS, comprising twin studies evaluating efficacy, safety, and tolerability of vidofludimus calcium versus placebo, was enrolled in November 2021. The first patient in our supportive Phase 2 CALLIPER trial of vidofludimus calcium in progressive multiple sclerosis (“PMS”) was enrolled in September 2021. In the first quarter of 2021, we announced that vidofludimus calcium showed evidence of clinical activity in our Phase 2 CALVID-1 trial in hospitalized patients with moderate coronavirus disease 2019 ("COVID-19"). Also, in the first quarter of 2021, we reported positive top-line data from an investigator-sponsored Phase 2 proof-of-concept clinical trial of vidofludimus calcium in primary sclerosing cholangitis which was conducted in collaboration with the Mayo Clinic. In addition, vidofludimus calcium is currently being tested in a Phase 2 trial in patients with ulcerative colitis (CALDOSE-1 trial), for which we expect top-line data to be available in June of 2022. Additional antiviral directed development activity remains ongoing through an investigator-sponsored Phase 2 clinical trial of vidofludimus calcium as well as preclinical development examining the potential to treat a broad set of viral indications with vidofludimus calcium and other DHODH inhibitors in combination with nucleoside analogues.

If approved, we believe that vidofludimus calcium has the potential to be a highly selective first-in-class DHODH inhibitor in inflammatory bowel disease ("IBD") and best-in-class DHODH inhibitor in RMS. Importantly, vidofludimus calcium has an attractive pharmacokinetic, safety and tolerability profile and has already been exposed to approximately 1,100 human subjects and patients in either of the drug's formulations.

Our second drug candidate, IMU-935, is a highly potent and selective inverse agonist of a transcription factor called RORγt. We believe that the nuclear receptor RORγt is the main driver for the differentiation of T-helper 17 ("Th17") cells and the release of cytokines involved in various inflammatory and autoimmune diseases. We believe this target is an attractive alternative to approved antibodies for targets, such as interleukin-23 ("IL-23"), the IL-17 receptor and IL-17 itself. We have observed strong cytokine inhibition targeting both Th1 and Th17 responses in preclinical testing, as well as indications of activity in animal models for psoriasis, graft versus host disease, MS and IBD. Preclinical experiments indicated that, while leading to a potent inhibition of Th17 differentiation and cytokine secretion, IMU-935 did not affect thymocyte maturation, one of the important physiological functions that should be maintained. Based on these preclinical data and the selectivity of the effect maintaining important physiological functions while providing the desired anti-Th17 effect, we believe that IMU-935 has potential to be a best-in-class therapy for various autoimmune diseases. A Phase 1 clinical trial exploring safety, pharmacodynamics and pharmacokinetics of IMU-935 in healthy human subjects and psoriasis patients is currently ongoing. Additionally, IMU-935 has been shown in preclinical models to target an established mechanism of treatment resistance to androgen receptor therapy, making it a potential treatment option for patients with resistant CRPC. A Phase 1 clinical trial exploring safety and tolerability of increasing doses of IMU-935 to establish the maximum tolerated dose and the recommended phase 2 dose is currently ongoing in patients with mCRPC.

Our third program, IMU-856, which we believe to be novel, is an orally available small molecule modulator that targets a protein which serves as a transcriptional regulator of intestinal barrier function and regeneration of bowel epithelium. We have not yet disclosed the molecular target for IMU-856. Based on preclinical data, we believe this compound may represent a new treatment approach, as the mechanism of action targets the restoration of the intestinal barrier function and regeneration of bowel epithelium in patients suffering from gastrointestinal diseases such as IBD, irritable bowel syndrome with diarrhea, celiac disease and other intestinal barrier function associated diseases. We believe that because IMU-856 has been shown in preclinical investigations to avoid suppression of immune cells, it may therefore have the potential to maintain immune surveillance for patients during therapy, an important advantage versus chronic treatment with potentially immunosuppressive medications. A Phase 1 clinical trial exploring safety, pharmacodynamics and pharmacokinetics of IMU-856 is currently ongoing.

We expect to continue to lead most of our research and development activities from our Gräfelfing, Germany location, where dedicated scientific, regulatory, clinical and medical teams conduct their activities. Due to these teams' key relationships with local and international service providers, we anticipate that this will result in timely, cost-effective execution of our development programs. In addition, we are using our subsidiary in Melbourne, Australia to expedite the early clinical trials for IMU-935 and IMU-856. We also conduct preclinical work in Halle/Saale, Germany through a collaboration with the Fraunhofer Institute.

Strategy

We are focused on the development of best-in-class molecules that maximize the therapeutic benefits for patients by uniquely addressing biologically relevant immunological targets. We take advantage of our established research and development infrastructure and operations in Germany and Australia to efficiently develop our product candidates in indications of high unmet need and where the product candidates have the potential to elevate the standard of care for the benefit of patients. Given the mechanisms of action and the data generated to date for our product candidates, we continue to execute on the clinical development of our programs for established indications as well as explore additional indications where patients could potentially benefit from the unique profiles of each product candidate.

We are currently focused on maximizing the potential of our development programs through the following strategic initiatives:

- Executing the ongoing ENSURE and CALLIPER clinical trial programs of vidofludimus calcium in MS.
- Delivering the results from the CALDOSE-1 trial of vidofludimus calcium in UC, with the path for future development to be assessed following analysis of the results.
- Executing the ongoing clinical studies of IMU-935 in patients with psoriasis and in patients with mCRPC, with the path for future development to be assessed following analysis of the results.
- Executing the ongoing Phase 1 clinical trials of IMU-856, with potential to expand into the treatment of patients with certain gastrointestinal diseases following sufficient safety and tolerability data.

- Continued preclinical research to complement the existing clinical activities, explore additional indications for future development, and where appropriate, generate additional molecules for future development.
- Facilitating readiness for potential commercial launch of our product candidates through targeted and stage-appropriate pre-commercial activities.
- Evaluating potential strategic collaborations for each product candidate in order to complement our existing research and development capabilities and to facilitate potential commercialization of these product candidates by taking advantage of the resources and capabilities of strategic collaborators in order to enhance the potential and value of each product candidate.

Liquidity and Financial Condition

Our business, operating results, financial condition and growth prospects are subject to significant risks and uncertainties, including the failure of our clinical trials to meet their endpoints, failure to obtain regulatory approval and needing additional funding to complete the development and commercialization of our three development programs.

We have no products approved for commercial sale and have not generated any revenue from product sales. We have never been profitable and has incurred operating losses in each year since inception (2016). We have an accumulated deficit of approximately $196.9 million as of December 31, 2021 and approximately $103.9 million as of December 31, 2020. Substantially all of our operating losses resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we continue the preclinical and clinical development of our product candidates and add personnel necessary to advance our pipeline of product candidates. We expect that our operating losses will fluctuate significantly from quarter-to-quarter and year-to-year due to timing of clinical development programs.

From inception through December 31, 2021, we have raised net cash of approximately $259.5 million from private and public offerings of preferred and common stock. As of December 31, 2021, we had cash and cash equivalents of approximately $86.9 million. We are dependent on financing activities to fund ongoing operations, and due to the inherent uncertainties in successfully completing financing transactions, and with our forecasted cash reach through the first quarter of 2023, these are indicators of an inability to continue as a going concern. However, we have the ability to manage the amount and timing of expenditures to reduce costs, have limited required fixed spend, and can manage working capital as needed and that coupled with the $16.2 million of cash raised so far in 2022 under our At The Market ("ATM") facility alleviates any uncertainty that we will have adequate liquidity to meet our obligations for at least the next 12 months from the financial statement release date.

Key Status Updates

Vidofludimus Calcium (IMU-838)

Phase 3 Program of Vidofludimus Calcium in RMS (ENSURE-1 and ENSURE-2 Trials)

On July 1, 2021, we announced U.S. Food and Drug Administration (“FDA”) clearance of our Investigational New Drug (“IND”) application for the Phase 3 ENSURE program of our lead product candidate, vidofludimus calcium in patients with RMS. The ENSURE program comprises two identical multicenter, randomized, double-blind Phase 3 trials designed to evaluate the efficacy, safety, and tolerability of vidofludimus calcium versus placebo in RMS patients. Based on vidofludimus calcium’s highly significant activity in preventing lesion formation in our Phase 2 EMPhASIS trial in RMS, the strong and consistent correlation observed between lesion formation and clinical relapse in third-party clinical trials, and the drug’s robust safety profile to date, we believe that this Phase 3 program should provide a relatively simple and straightforward path towards potential regulatory approval of vidofludimus calcium in RMS.

Each of the identical twin Phase 3 trials, titled ENSURE-1 and ENSURE-2, is expected to enroll approximately 1,050 adult patients with active RMS at more than 100 sites in more than 15 countries, including the United States, India and countries in Latin America, Central and Eastern Europe. Patients will be randomized in a double-blinded fashion to either 30 mg daily doses of vidofludimus calcium or placebo and the primary endpoint for both trials is time to first relapse up to 72 weeks. Key secondary endpoints include volume of new T2-lesions, time to confirmed disability progression, time to sustained clinically relevant changes in cognition, and percentage of whole brain volume change. With regard to the disability progression endpoint, the ENSURE program will apply a pooled analysis of disability worsening across both trials.

The ENSURE trials will be run concurrently. The first patient in ENSURE-1 was enrolled in November 2021. The first patient in ENSURE-2 was enrolled in January 2022. An interim analysis to assess event rates is planned to occur after a certain number of relapses have occurred in the double-blind treatment periods. This analysis is intended to inform potential sample size adjustment and help ensure that final study readout is not planned to occur before sufficient events have been achieved. This interim analysis will also allow for a non-binding futility analysis.

Phase 2 Program of Vidofludimus Calcium in PMS (CALLIPER Trial)

On July 1, 2021, we announced that the FDA also cleared our separate IND application for the supportive Phase 2 CALLIPER trial of vidofludimus calcium in patients with PMS. The first patient was enrolled in September 2021.

The multicenter, randomized, double-blind, placebo-controlled Phase 2 CALLIPER trial in PMS is intended to run concurrently with and to complement the Phase 3 program in RMS. In particular, CALLIPER is focused on progressive forms of multiple sclerosis ("MS") and is designed to corroborate vidofludimus calcium's neuroprotective potential, as exemplified by slowing of brain atrophy and delay in disability worsening. Neurodegeneration is a key concern in both PMS and RMS, since axonal and neural damage is responsible for the increasing and often severe disability experienced by patients. We believe that, if the CALLIPER trial is successful in showing a beneficial effect of vidofludimus calcium, this data, along with the ENSURE program and vidofludimus calcium's strong safety and tolerability profile, may allow for a meaningful clinical differentiation of vidofludimus calcium from other oral MS medications and a potentially attractive commercial positioning. Although a supportive trial, we do not believe that data from the CALLIPER trial are a pre-condition for filing a New Drug Application ("NDA") in RMS. Additional clinical studies and the potential regulatory path forward specific to the treatment of PMS will be informed by the results of the CALLIPER trial and will be further assessed accordingly.

The Phase 2 CALLIPER trial is expected to enroll approximately 450 patients with PMS at more than 70 sites in North America, Western, Central and Eastern Europe with patients randomized to either 45 mg daily doses of vidofludimus calcium or placebo in a double-blinded fashion. The trial's primary endpoint is the annualized rate of percent brain volume change up to 120 weeks. Key secondary endpoints include the annualized rate of change in whole brain atrophy and time to 24-week confirmed disability progression based on the expanded disability status scale which may further support disability data from the ENSURE trials.

An interim analysis comprising an unblinded analysis of serum neurofilament light chain ("NfL") is planned to occur once approximately half of the enrolled patients have completed 24 weeks of treatment. NfL has been shown in third-party research to consistently correlate with disease activity in neurodegenerative disorders and has become one of the most important serum biomarkers for axonal damage over the past few years. As previously reported, results of the Phase 2 EMPhASIS trial of vidofludimus calcium in RRMS showed a robust decrease in serum NfL at 24 weeks (-17.0% for 30 mg and -20.5% for 45 mg), as compared to baseline values, while the patients on placebo experienced a 6.5% increase in serum NfL over the same period.

Phase 2 Trial of Vidofludimus Calcium in UC (CALDOSE-1 Trial)

On October 28, 2021, we announced completion of enrollment of our Phase 2 CALDOSE-1 trial of vidofludimus calcium in UC. At completion of patient recruitment, the trial has randomized a total of 263 patients into four arms: three active dosing arms of 10 mg, 30 mg and 45 mg, as well as placebo. Top-line data for the induction phase are expected to be available in June of 2022.

On February 18, 2022, we announced the main blinded baseline characteristics of the CALDOSE-1 trial, including:

- 263 moderate-to-severe UC patients were enrolled in 78 study sites with the Ukraine and Poland representing the countries with highest number of patients and U.S. sites contributing 12.5% of the overall enrollment.
- Of the 263 patients, 148 (56.3%) were male and 115 (43.7%) were female patients. The mean age at baseline was 41.7 (18-77) years.
- All patients had to have failed at least one prior therapy option. Of the 263 patients, 83% were biologically naïve and 17% were biologically experienced (received at least 1 prior treatment with any biological agent approved in the UC indication).
- Enrolled patients had to show evidence of active moderate-to-severe UC disease. This is reflected in their baseline characteristics for patient-reported outcomes:
    - The baseline Mayo stool frequency scores were: (i) score of 3 for 59% of patients, (ii) score of 2 for 36% patients and (iii) score of 1 for 5% of patients.

- The Mayo rectal bleeding scores were: (i) score of 3 in 10% of patients, (ii) score of 2 for 54% of patients and (iii) score of 1 for 31% of patients.
- The average value for fecal calprotectin at baseline was approximately 1,320 µg/g for currently available, yet incomplete data.

- The trial employed a central independent reader to evaluate the endoscopic eligibility criteria and the following modified Mayo endoscopic scores were assessed at baseline:
  - 55% of patients with a score of 3; and
  - 45% of patients with a score of 2.
- At week 10 (the time point of the primary efficacy analysis), an adjudication procedure was used for endoscopy assessments. In the case of disagreement between two independent readers, a third independent reader was used for adjudication.

We believe that these blinded baseline characteristics of randomized patients and the methodology regarding endoscopic assessments contributes to ensuring an optimized study read-out.

Phase 2 Trial of Vidofludimus Calcium in PSC

On February 18, 2021, we announced positive top-line data from our investigator-sponsored proof-of-concept clinical trial of vidofludimus calcium in PSC, which was conducted at Mayo Clinic in Arizona and Minnesota, both of which are tertiary referral centers for PSC patients. As the next step in this indication, we are currently conducting a Phase 1 trial in hepatic impaired patients in order to explore dose optimization of vidofludimus calcium for potential future clinical activities in PSC. This Phase 1 trial started in September 2021 and is expected to run approximately six months.

IMU-935

Phase 1 Clinical Trial of IMU-935 in Healthy Human Subjects and Moderate to Severe Psoriasis Patients

On July 12, 2021, we provided an update on our IMU-935 program, including new preclinical and clinical data. The main result from preclinical investigations was that IMU-935 inhibits cytokine production (thought to be a pre-condition for its use in immunological and autoimmune diseases) while maintaining the known and required physiological functions of maturing T lymphocytes. In *ex vivo* mouse cell differentiation and maturation assays, IMU-935 was recently observed to selectively inhibit RORγt-dependent gene expression during Th17 differentiation without affecting either RORγt-dependent gene regulation relevant to thymocyte development, or the viability of these cells. In third-party research, impairment of thymocyte development has been shown to be associated with serious safety issues, including, among others, T cell malfunction and potential lymphoma formation. We believe that IMU-935's observed selectivity may enable it to inhibit both the generation of Th17 cells and the production of IL-17 cytokines that are responsible for the development of autoimmune diseases, without impairing thymocyte development, which is associated with the potential risk of lymphoma seen with other, third-party RORγt programs.

On December 14, 2021, we provided an update on the preclinical and clinical development of IMU-935, announcing that:

- Unblinded data from the single ascending dose part of the ongoing phase 1 clinical trial of a new powder-in-capsule formulation of IMU-935, in which healthy human subjects were treated with 100 mg, 200 mg, 300 mg and 400 mg of this new formulation or placebo, found these single ascending daily doses of IMU-935 to be safe and well-tolerated, and no maximum tolerated dose was reached. No serious adverse events occurred. A dose-proportional pharmacokinetic profile was observed across the investigated dose range.

- Unblinded data from the multiple ascending dose part of the ongoing phase 1 clinical trial, in which healthy human subjects were dosed for 14 days with 150 mg either once or twice daily doses of IMU-935 or placebo, found these multiple ascending doses of IMU-935 to be safe and well-tolerated, and no maximum tolerated dose was reached. Treatment emergent adverse events were generally mild in severity, with moderate treatment emergent adverse events reported in one of eleven IMU-935 treated subjects, compared with one of four subjects on placebo. No serious adverse events were reported. No dose-dependent changes in laboratory values (including no effects on liver enzymes or in hematological parameters), vital signs or in electrocardiographic evaluations were found. Pharmacokinetic analysis showed that stable steady-state plasma concentrations were achieved within the first week of dosing with an accumulation factor for IMU-935 allowing predictable trough levels during daily dosing.

- Based on the favorable safety and tolerability data observed in healthy human subjects, our phase 1 clinical trial of IMU-935 was expanded in October 2021 to include a third portion, part C, in which moderate to severe psoriasis patients are to be randomized to 28-day treatment of IMU-935 or placebo. Planned assessments include safety, tolerability, pharmacokinetic and pharmacodynamic markers, as well as skin evaluations. Recruitment of part C depends on several external factors which are not under our direct control, including, in particular, the relatively restrictive COVID-19-related rules in effect in Australia and New Zealand. This situation has and may further influence our ability to enroll study participants and/or perform on-site monitoring at clinical sites in those locations. In light of this, we have already initiated remedial measures, including the potential addition of sites outside of Australia and New Zealand, for the ongoing part C of IMU-935 in psoriasis patients. As a result, initial results from the third portion of the Phase 1 clinical trial in patients with moderate-to-severe psoriasis are now expected to be available in the second half of 2022, instead of at the end of the second quarter of 2022, as previously announced.

- In previous preclinical in vitro data, it was shown that IMU-935 selectively inhibits Th17 differentiation and IL-17 production, whereas RORγt was unaffected by IMU-935 during thymocyte maturation and, therefore, does not harm normal thymocyte maturation. Newly obtained data from acute and chronic treatment of mice corroborated in vivo that IMU-935 is the first molecule observed to impact neither thymus size, thymocyte numbers, nor the maturation status of thymocytes, in contrast to two other known inhibitors of RORγt.

Phase 1 Clinical Trial of IMU-935 in mCRPC

On July 12, 2021, we also presented new preclinical data highlighting IMU-935's therapeutic potential in CRPC. Recently published third-party studies have shown that RORγ plays an important pro-tumor role by driving expression of the androgen receptor (“AR”), leading to tumor growth. During tumor progression, AR tends to mutate into AR-V7, leading to resistance of AR-axis-targeted therapies. In preclinical studies, IMU-935 was observed to inhibit the expression of mutated AR-V7, and the tumor growth of prostate cancer cell lines *in vitro*. Finally, we believe IMU-935's potency in inhibiting tumorigenesis-promoting IL-17 and Th17 cells *in vitro* may result in further antitumoral activity in humans.

Based on these strong preclinical results, we have initiated an open-label Phase 1 dose-escalation trial designed to evaluate the safety and tolerability of increasing doses of IMU-935 to establish the maximum tolerated dose and the recommended phase 2 dose. The trial will also evaluate the anti-tumor activity of IMU-935 by means of prostate-specific antigen levels, circulating tumor cell numbers, and radiographic response assessments of tumor progression. The trial’s Principal Investigator is Johann Sebastian de Bono, MD, PhD, Regius Professor of Cancer Research and Professor in Experimental Cancer Medicine, The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, London, United Kingdom. The trial was approved by the Medicines and Healthcare products Regulatory Agency (MHRA), the Research Ethics Committee (REC) and the Health Research Authority (HRA) in the United Kingdom. The first patient was enrolled in December 2021. Initial clinical safety data are expected to be available in the third quarter of 2022.

IMU-856

Phase 1 Clinical Trial of IMU-856

A Phase 1 clinical trial of IMU-856 is ongoing and progressing in Australia. The trial includes single and multiple ascending dose parts in healthy human subjects designed to assess safety, pharmacodynamics and pharmacokinetics of IMU-856. All planned single ascending dose cohorts for the current tablet formulation of IMU-856 have been completed but have not yet been unblinded. Based on the favorable data available so far, the Ethics Committee in Australia has agreed to proceed to the multiple ascending dose part which is currently being dosed. Unblinded safety data from the single and multiple ascending dose parts in healthy human subjects are expected to be available in the third quarter of 2022.

We also plan to extend this trial to assess biomarkers, disease symptoms, safety and drug trough levels in patients with a model disease of altered intestinal barrier function to provide initial activity data. Initiation of this third portion of the Phase 1 clinical trial is expected in the first half of 2022.

Product Acquisition History

Our wholly-owned subsidiary Immunic AG acquired IMU-838 and IMU-935 in September 2016 through asset acquisitions from 4SC AG (hereinafter, “4SC”), a publicly traded company based in Planegg-Martinsried, Germany. On March

31, 2021, Immunic AG and 4SC entered into a Settlement Agreement, pursuant to which Immunic AG settled its remaining obligation of a 4.4% royalty on net sales for $17.25 million. The payment was made 50% in cash and 50% in shares of Immunic's common stock.

Our rights to IMU-856 are secured pursuant to an option and license agreement (the "Daiichi Sankyo Option") with Daiichi Sankyo Co., Ltd. (hereinafter, "Daiichi Sankyo") in Tokyo, Japan. On January 5, 2020, Immunic AG exercised its option under the Daiichi Sankyo Option to acquire the exclusive global rights to commercialize IMU-856. The license also grants Immunic AG the rights to Daiichi Sankyo's patent application related to IMU-856. Concurrent with the option exercise, Immunic AG paid to Daiichi Sankyo a one-time upfront licensing fee. Going forward, Daiichi Sankyo is eligible to receive future development, regulatory and sales milestone payments, as well as royalties related to IMU-856.

Leadership

We are led by a team of dedicated and committed experienced professionals with an entrepreneurial spirit and track record of successful licensing transactions in the healthcare industry worldwide (EU, the United States and Asia). The team brings together several decades of leadership experience in the pharmaceutical industry with a strong scientific background and sound knowledge in drug discovery, product development, chemistry, manufacturing and controls processes, intellectual property, clinical trial design, health economics and market access, merger and acquisitions, capital markets, corporate finance, business development, regulatory affairs and project valuation. Our team members are inventors on project-related patents and have successfully published project-related scientific publications.

Product Candidates

Vidofludimus Calcium (IMU-838)

Vidofludimus calcium is a small molecule investigational drug in development as an oral tablet formulation for the treatment of RMS, IBD and other chronic inflammatory and autoimmune diseases. By inhibiting DHODH, a key enzyme of pyrimidine *de novo* biosynthesis, highly metabolically activated T and B immune cells experience metabolic stress, which leads to a modulation of their activity and function. Thereby, pro-inflammatory cytokines, such as interferon gamma ("IFNγ"), tumor necrosis factor alpha ("TNFα"), IL-17A and IL-17F, produced by activated Th1 and Th17 cells, which represent subtypes of so-called T helper cells, are repressed and thereby reduce the inflammation associated with IBD, MS and other chronic inflammatory diseases.

In preclinical studies of vidofludimus, the active moiety and free acid form of vidofludimus calcium, apoptosis (or programmed cell death) was induced in activated T cells, which we believee may also play a crucial role in the activity of the drug in IBD by further dampening the inflammatory response. We believe that a key advantage of DHODH inhibition, in general, is that the sensitivity of specific immune cells to DHODH inhibition correlates with their intracellular metabolic activation state, and therefore may not negatively impact "normal" immune and bone marrow cells. In animal studies of vidofludimus calcium, animals treated with large doses of the active moiety of vidofludimus calcium were shown to lack detrimental effects on bone marrow, supporting the lack of an unspecific anti-proliferative effect regularly seen with many traditional immunomodulators.

Based on the selectivity toward metabolically activated cells (with a high need for ribonucleic acid and deoxyribonucleic acid production), DHODH inhibition also leads to a direct antiviral effect, which has been observed in various virus infected cells, such as Epstein-Barr virus ("EBV") infections, hepatitis C virus infections, severe acute respiratory syndrome coronavirus 2 ("SARS-CoV-2") infections, cytomegalovirus infections and even hemorrhagic fever-causing viruses, such as Arena virus infections. Treatment with vidofludimus calcium may avoid virus infections and reactivations, one of the major drawbacks of the long-term use of traditional immunomodulators in IBD and MS patients. Recently, we presented preclinical data demonstrating the activity of vidofludimus calcium to prevent the reactivation of latent EBV infection into lytic infection (Marschall et al. 2021). This mechanism may lead to reduce the regular cycle of reactivations and reinfections in the medium term, and thus the latent persistent EBV infection in patients in the long term.

Efficacy of vidofludimus has been observed in several animal disease models for IBD, MS, as well as systemic lupus erythematosus and transplant rejection. Previous filings by us with the SEC have summarized the development history of vidofludimus and the previous amorphous formulation of the free acid form of vidofludimus. After the consummation of the asset acquisition from 4SC, Immunic developed and filed a patent application for a new specific polymorph of the calcium salt formulation of vidofludimus, vidofludimus calcium, which we believe exhibits improved physicochemical and pharmacokinetic properties. In 2017, we completed two Phase 1 studies of single or repeated once-daily doses of vidofludimus calcium in

healthy volunteers, where we observed results supporting tolerability of repeated daily dosing of up to 50 mg of vidofludimus calcium.

Indication: Multiple Sclerosis

Diagnosis and Prevalence

MS is an autoimmune disease that affects the brain, spinal cord and optic nerve. In MS, myelin, the coating that protects the nerves, is attacked and damaged by the immune system. Thus, MS is considered an immune-mediated demyelinating disease of the central nervous system ("CNS"). MS is a progressive disease which, without effective treatment, leads to severe disability. We are developing vidofludimus calcium for the treatment of RRMS, the most common form of MS. Approximately 85% of patients with MS are expected to develop RRMS, with some of these patients later developing more progressive forms of the disease. RRMS is characterized by clearly defined attacks of new or increasing neurologic symptoms. These relapses are followed by periods of remissions, or partial or complete recovery. During remissions, all symptoms may disappear, or some symptoms may continue and become permanent.

MS is a disease with unpredictable symptoms that can vary widely. Common early signs of MS include vision problems, tingling and numbness or other unspecific neurological symptoms. Diagnosis of MS is confirmed via blood tests and a spinal tap, in which a small sample of fluid is removed from the spinal cord. However, most important for diagnosis are characteristic CNS lesions found using magnetic resonance imaging ("MRI").

According to DRG (Market Forecast Dashboard, Multiple Sclerosis (2020-2030), December 2021), MS affects more than 500,000 people in the United States, and more than 1.1 million people in the G7 countries (US, UK, Canada, Japan, Germany, France, Italy). The disease has a large economic impact as it affects mainly young adults in the prime working age, peaking around 30 years old, although MS can occur in children and in adults. MS is up to three times more common in women than in men. MS affects twice as many women and men in certain age cohorts and is more common in areas inhabited by people of northern European ancestry, such as Europe, the United States, Canada, New Zealand and parts of Australia.

A recent publication shed new light on the role of infection with the EBV previously postulated to trigger MS. Bjornevik et al. (2022) analyzed EBV antibodies in serum from 801 individuals who developed MS among a cohort of more than 10 million people active in the US military over a 20-year period (1993 to 2013). Risk of MS increased 32-fold after infection with EBV but was not increased after infection with other viruses, including the similarly transmitted cytomegalovirus. Serum levels of neurofilament light chain, a biomarker of axonal damage, increased only after EBV seroconversion. These findings cannot be explained by any known risk factor for MS and suggest EBV as the leading cause of MS. In addition, antibody producing cells directed against the latent EBV protein EBNA1 were found in the CSF of MS patients. Cross reactivity of anti-EBNA1 antibodies against GlialCAM, a protein that is predominantly expressed in glial cells in the CNS and potentially important in the myelination process of axons, further corroborates the connection between EBV infections and pathologic processes in MS (Lanz et al. 2022).

Current Treatment Options

There are currently two main treatment types available for RRMS. Some therapies, such as short-term corticosteroid medications, are used for treating relapses of MS symptoms. Other approaches are used as long-term treatments to reduce the number of relapses and prevent disability progression. The latter are referred to as disease-modifying therapies. We intend to develop vidofludimus calcium as a disease-modifying therapy for RRMS.

The initial treatment options for RRMS patients are often beta interferons (either as interferon beta-1a or interferon beta-1b) or glatiramer acetate, all of which are given by injection. For patients requiring more advanced treatment options, there are several oral medications, such as dimethyl fumarate, fingolimod, siponimod, teriflunomide, ozanimod or cladribine, and biologics, such as natalizumab, ocrelizumab, ofatumumab or alemtuzumab, approved for commercial use in MS in various countries. In addition, some of these drugs already have generic versions available in some countries and other drugs will become generic in the next years.

There is no specific guidance on which therapies or medications are used in which sequence of the MS disease course. Typically, treatments are escalated over time, considering:

- Persistent high MS disease activity under treatment with base medications (relapse(s), disability worsening, MRI lesions),
- Risks of long-term immunosuppression,
- Patient preferences or risks perceptions, and
- Safety/tolerability aspects.

Many drugs approved for patients with RRMS suppress the immune system, either broadly or by targeting classes of immune cells, altering how the immune system functions and fights certain infections. As a result, people who take these therapies are at higher risk for John Cunningham virus infection or re-activation, which is believed to be the cause of a rare and often lethal viral disease of the brain called progressive multifocal leukoencephalopathy ("PML"). To date, occurrences of PML have been reported in individuals with RRMS treated with natalizumab, dimethyl fumarate and fingolimod. No case of PML has yet been reported for the DHODH inhibitor teriflunomide, which has been one of the key differentiators of teriflunomide from other disease-modifying therapies in RRMS. The active moiety of vidofludimus calcium has also shown direct antiviral effects in several models of virus-infected cells, which we believe is caused by DHODH inhibition. Subject to further clinical trials, we believe that this could be a “class effect” of the DHODH inhibitors and if shown, could be an important potential differentiator against other drug classes in RRMS.

Depending on the results of future clinical trials, we believe that vidofludimus calcium has the potential to demonstrate medically important advantages compared with other treatments, particularly for the early treatment of RRMS patients, due to its anti-inflammatory and neuroprotective properties and safety and tolerability profile. Vidofludimus calcium could provide RRMS patients with a distinctive combination of the following properties:

- Targeted effect on hyperactive immune cells without suppression of normal immune function.
- Pronounced MRI lesion suppression of vidofludimus calcium compares favorably to other oral medications commercially available in RRMS.
- Improved rates of disability worsening, particularly in light of the apparent class effect of DHODH inhibition to disproportionally improve disability progression over the long-term.
- Robust decrease in serum neurofilament light chain, a biomarker for axonal damage, was observed for vidofludimus calcium and provides evidence of vidofludimus calcium’s potential neuroprotective activity.
- A very low discontinuation rate for vidofludimus calcium-treated RRMS patients, substantially below placebo, indicates an encouraging combination of tolerability and efficacy as well as maintenance of normal quality-of-life
- Absence of hepatotoxicity signals and other relevant adverse events leading to discontinuations distinguishes vidofludimus calcium well from other oral RRMS treatments.
- Broad spectrum antiviral effect of vidofludimus calcium may support in lowering the rate of viral infections and reactivations, including EBV reactivation, potentially resulting in slowing potential EBV-related neurodegenerative processes.

Current Development Plan and Ongoing Studies

Phase 2 Trial of Vidofludimus Calcium in RRMS (EMPhASIS Trial)

Our Phase 2 EMPhASIS trial of vidofludimus calcium in RRMS consisted of two cohorts: The full data set of Cohort 1, which evaluated efficacy and safety of 30 mg or 45 mg once daily vidofludimus calcium compared to placebo, was published by us in August and September 2020, respectively. Cohort 2, which evaluates efficacy and safety of 10 mg once daily vidofludimus calcium compared to placebo, was meanwhile also completed.

On August 2, 2020, we announced positive top-line data from our Phase 2 EMPhASIS trial of vidofludimus calcium in patients with RRMS. The study achieved statistical significance on all primary and key secondary endpoints, indicating activity in RRMS patients. In particular, the study met its primary endpoint, demonstrating a statistically significant reduction in the cumulative number of combined unique active (“CUA”) magnetic resonance imaging (“MRI”) lesions up to week 24 in patients receiving 45 mg of vidofludimus calcium once daily, by 62% ($p=0.0002$), as compared to placebo. The study also met its key secondary endpoint, showing a statistically significant reduction in the cumulative number of CUA MRI lesions for the 30 mg once daily dose by 70% ($p<0.0001$), as compared to placebo. On September 11, 2020, we published the full unblinded clinical data set from our Phase 2 EMPhASIS trial of vidofludimus calcium in patients with RRMS. The data confirmed and expanded on the previously announced top-line results.

On April 15, 2021, we announced interim data from Cohort 2 after 59 randomized patients completed week 12 MRI assessments. We concluded from this data, along with previously published data from Cohort 1, that 30 mg once daily vidofludimus calcium is the most appropriate anti-inflammatory dose for Phase 3 trials in patients with RMS.

Meanwhile, final data from Cohort 2 are also available showing that the anti-inflammatory effects of vidofludimus calcium at the 10 mg dose were observed to be lower (13% reduction of gadolinium-enhancing magnetic resonance imaging lesions up to 24 weeks, as compared to placebo) than those found with the 30 mg vidofludimus calcium dose in the pooled Cohort 1 and 2 data (78% reduction), providing further support for the selection of 30 mg dosing in the ongoing ENSURE trials in RMS. Final Cohort 2 data also provide evidence of dose-proportional neuroprotective activity. For instance, the highest decrease of the biomarker serum neurofilament light chain was observed with the 45 mg dose of vidofludimus calcium versus placebo (-26.0% median of differences between percentage change of serum neurofilament, Hodges-Lehmann estimation), a substantial decrease was seen with the 30 mg dose (-18.0%), while the smallest decrease was observed with the 10 mg dose of Cohort 2 (-9.0%). The 10 mg group in Cohort 2 also showed a signal with respect to improvement in Expanded Disability Status Scale ("EDSS"), consistent with those signals seen with the higher doses in Cohort 1, although all of these early signals need to be confirmed in a larger patient population with longer follow-up periods. Taken together, these last two observations suggest that higher doses, such as 45 mg vidofludimus calcium, may be preferred doses for clinical trials in which neuroprotective effects are the main mechanism for improvement, such as in PMS.

While Cohort 1 blinded treatment was completed right before the COVID-19 pandemic started, final Cohort 2 data provide additional evidence that ongoing vidofludimus calcium treatment may reduce the risk of COVID-19 infections, presumably related to its known antiviral activity. In the entire Cohort 2 population of 59 patients, who were enrolled during pandemic conditions, incidental COVID-19 infections in the active treatment group were less frequent (8.5%, n=4/47) than in the placebo group (25.0%, n=3/12). Additionally, we recently obtained new preclinical data underlining that vidofludimus calcium shows potent anti-EBV activity. We also confirmed that vidofludimus calcium can be detected to a noteworthy degree in the cerebrospinal fluid of animals, after oral dosing. We believe that this finding suggests that vidofludimus calcium may be able to act directly within the central nervous system.

We have designed the Phase 3 trials in RMS and the Phase 2 trial in PMS to provide additional insights how vidofludimus calcium may address all aspects of the MS disease, in particular, monitoring of potential neuroprotective effects. The EMPhASIS trial continues as an open-label extension ("OLE") treatment to obtain long-term safety data in RRMS patients. Currently, more than 200 patients are still on OLE treatment.

Further information regarding our EMPhASIS trial in RRMS can be found on ClinicalTrials.gov under the identifier NCT03846219.

Phase 3 Program of Vidofludimus Calcium in RMS (ENSURE-1 and ENSURE-2 Trials)

On July 1, 2021, we announced FDA clearance of our IND application for the Phase 3 ENSURE program of vidofludimus calcium in patients with RMS. The ENSURE program comprises two identical multicenter, randomized, double-blind Phase 3 trials designed to evaluate the efficacy, safety, and tolerability of vidofludimus calcium versus placebo in RMS patients. Based on vidofludimus calcium's highly significant activity in preventing lesion formation in our Phase 2 EMPhASIS trial in RMS, the strong and consistent correlation observed between lesion formation and clinical relapse in third-party clinical trials, and the drug's robust safety profile to date, we believe that this Phase 3 program should provide a relatively simple and straightforward path towards potential regulatory approval of vidofludimus calcium in RMS.

Each of the identical twin Phase 3 trials, titled ENSURE-1 and ENSURE-2, is expected to enroll approximately 1,050 adult patients with active RMS at more than 100 sites in more than 15 countries, including the United States, India and countries in Latin America, Central and Eastern Europe. Patients will be randomized in a double-blinded fashion to either 30 mg daily doses of vidofludimus calcium or placebo and the primary endpoint for both trials is time to first relapse up to 72 weeks. Key secondary endpoints include volume of new T2-lesions, time to confirmed disability progression, time to sustained clinically relevant changes in cognition, and percentage of whole brain volume change. With regard to the disability progression endpoint, the ENSURE program will apply a pooled analysis of disability worsening across both trials.

The ENSURE trials will be run concurrently. The first patient in ENSURE-1 was enrolled in November 2021. The first patient in ENSURE-2 was enrolled in January 2022. An interim analysis to assess event rates is planned to occur after a certain number of relapses have occurred in the double-blind treatment periods. This analysis is intended to inform potential sample

size adjustment and help ensure that final study readout is not planned to occur before sufficient events have been achieved. This interim analysis will also allow for a non-binding futility analysis.

Further information regarding our ENSURE program in RMS can be found on ClinicalTrials.gov under the identifiers NCT05134441 (ENSURE-1) and NCT05201638 (ENSURE-2), respectively.

The execution of clinical Phase 3 trials usually requires the use of a commercial formulation of the investigational drug manufactured at commercially usable quantities. Manufactures under contract with us have developed and produced a roller compactor formulation of vidofludimus calcium (IMU-838-RC) which would allow commercially usable production batches. An Phase 1 bioequivalence study between the previous wet granulation and the new IMU-838-RC formulation of vidofludimus calcium has completed the experimental phase and showed bioequivalence regarding drug exposure curve in blood plasma (area under the curve). A confirmatory relative bioavailability and food effect study demonstrated a high bioavailability of IMU-838-RC tablets as compared to a drinking solution and confirmed the *in vitro* finding of a complete and fast dissolution profile in human subjects. No food effect on the uptake or elimination of vidofludimus after administration of the IMU-838-RC tablet was observed.

Additional investigations regarding metabolite characterization, metabolic modeling and potential drug-drug interactions, as well as other activities relating to clinical pharmacology are also being finalized at this time in anticipation for presentation to regulatory authorities.

We are currently working with clinical and regulatory advisors to propose a pediatric development plan for vidofludimus calcium in RRMS in the near future.

Phase 2 Program of Vidofludimus Calcium in PMS (CALLIPER Trial)

On July 1, 2021, we announced that the FDA also cleared our separate IND application for the supportive Phase 2 CALLIPER trial of vidofludimus calcium in patients with PMS. The first patient was enrolled in September 2021.

The multicenter, randomized, double-blind, placebo-controlled Phase 2 CALLIPER trial is intended to run concurrently with and to complement the Phase 3 program in RMS. In particular, CALLIPER is focused on progressive forms of MS and designed to corroborate vidofludimus calcium's neuroprotective potential, as exemplified by slowing of brain atrophy and delay in disability worsening. Neurodegeneration is a key concern in both PMS and RMS, since axonal and neural damage is responsible for the increasing and often severe disability experienced by patients. We believe that, if the CALLIPER trial is successful in showing a beneficial effect of vidofludimus calcium, this data, along with the ENSURE program and vidofludimus calcium's strong safety and tolerability profile, may allow for a meaningful clinical differentiation of vidofludimus calcium from other MS medications and potentially attractive commercial positioning. Although a supportive trial, we do not believe that data from the CALLIPER trial are a pre-condition for filing an NDA in RMS. Additional clinical studies and the potential regulatory path forward specific to the treatment of PMS will be informed by the results of the CALLIPER trial and will be further assessed accordingly.

The Phase 2 CALLIPER trial is expected to enroll approximately 450 patients at more than 70 sites in North America, Western, Central and Eastern Europe with patients randomized to either 45 mg daily doses of vidofludimus calcium or placebo in a double-blinded fashion. The trial's primary endpoint is the annualized rate of percent brain volume change up to 120 weeks. Key secondary endpoints include the annualized rate of change in whole brain atrophy and time to 24-week confirmed disability progression based on the expanded disability status scale which may further support disability data from the ENSURE trials.

An interim analysis comprising an unblinded analysis of serum NfL is planned to occur once approximately half of the enrolled patients have completed 24 weeks of treatment. NfL has been shown in third-party research to consistently correlate with disease activity in neurodegenerative disorders and has become one of the most important serum biomarkers for axonal damage over the past few years. As previously reported, results of the Phase 2 EMPhASIS trial of vidofludimus calcium in RRMS showed a robust decrease in serum NfL at 24 weeks (-17.0% for 30 mg and -20.5% for 45 mg), as compared to baseline values, while the patients on placebo experienced a 6.5% increase in serum NfL over the same period.

Further information regarding our CALLIPER trial in PMS can be found on ClinicalTrials.gov under the identifier NCT05054140.

Indication: Ulcerative Colitis

Diagnosis and Prevalence

UC is a chronic inflammatory disease characterized by diffuse inflammation of the mucosa of the colon and rectum. The hallmark clinical symptoms of UC are diarrhea and bloody stool, and its clinical course is marked by exacerbations and remissions, which may occur spontaneously or in response to treatment changes or intercurrent illnesses.

UC is most commonly diagnosed in late adolescence or early adulthood, but it can occur at any age. The occurrence of UC worldwide has increased over the past few years, particularly in Latin America, Asia and Eastern Europe (Burisch et al. 2015). According to DRG (Market Forecast Dashboard, UC (2020-2030), November 2021), approximately one million patients are affected by UC in the United States, and more than 2.2 million in the G7 countries (US, UK, Canada, Japan, Germany, France, Italy). UC is almost equally distributed between genders (Kappelman et al. 2007).

Current Treatment Options

The severity and extent of UC are characterized based on clinical and endoscopic findings. The treatment approach often depends on disease severity and typically follows a stepwise treatment regimen. Patients with mild disease may initially receive aminosalicylates or non-systemic steroids, such as budesonide. Patients with moderate to severe disease activity may receive traditional immunomodulators (such as azathioprine or 6-mercaptopurine) or steroids (such as prednisone). If patients fail to respond to these therapies, treatment may be escalated to the use of biologics or selective immunomodulators (such as tofacitinib). The most common category of biologics used to treat UC includes TNFα antibody drugs, such as infliximab or adalimumab. New biologic options are alpha-4-beta-7 (α4ß7) integrin-specific antibodies, such as vedolizumab and anti-IL-12/IL-23 antibodies, such as ustekinumab. All biologics currently used to treat UC are injectables. Biologics are usually the most expensive treatment option and reserved for patients who have failed other therapies.

Currently, there are several new oral treatment options for UC patients in advanced clinical development or in regulatory review. Most of them fall into one of the following two categories: sphingosine-1-phosphate (“S1P”) agonists, or Janus kinase (“JAK”) inhibitors. Some of these drug candidates have been or may be approved by regulatory authorities for commercial use before vidofludimus calcium may receive approval. However, depending on the results of future clinical trials, we believes that vidofludimus calcium has the potential to demonstrate medically important advantages compared with other treatments, particularly for long-term therapy in UC patients, due to the selectivity of DHODH targeting of metabolically activated lymphocytes, the absence of general detrimental effects on bone marrow and the immune system, its safety and tolerability profile and the direct antiviral activity.

Treatment of UC is differentiated between induction treatment (during periods of disease symptoms or following relapse) and maintenance treatment (often a long-term treatment to keep a patient relapse-free). Since UC patients ultimately fail to respond to treatments, cease to respond to their treatments or develop unacceptable side effects, there is a need for safe and effective treatments for UC with novel mechanisms. Additionally, patients often prefer the convenience of oral treatments over injections. For some of the currently available oral immunomodulators or those in clinical testing, a higher rate of infections (particularly virus re-activations) have been reported versus placebo control, which can be a medically significant event for patients.

Vidofludimus calcium is being developed to be a new treatment option for patients with moderate to severe UC who are candidates for therapy escalation. As a potentially highly selective, first-in-class oral therapy, vidofludimus calcium has the potential to become a new standard of care in the treatment armamentarium for patients with moderate to severe UC. This potential is supported by the following properties of vidofludimus calcium:

- Targeted effect on hyperactive immune cells without suppression of normal immune function.
- First-in-class mode of action targeting relevant immune cell populations not currently addressed by existing therapeutic options, particularly in patients who are not sufficiently responsive to available therapies.
- Potential best-in-class safety and tolerability profile, as has been observed to date across the full scope of clinical trials for vidofludimus calcium.
- Potential for combination treatment with established biologics through synergistic effects.
- Increased flexibility for dosing and administration outside of infusion centers.
- Long-term treatment potential with small molecule approach, avoiding the decreasing responsiveness shown with existing antibody treatments as a result of anti-drug antibody development.

- Antiviral effects that potentially avoid virus reactivations which is known to be connected to several currently approved medications in UC.

Clinical Development Plan and Ongoing/Planned Clinical Studies

Before commencing clinical development in IBD, including UC, we had developed a clinical development plan in collaboration with a group of well-known and experienced physicians from North America and Europe, and had received formal regulatory advice for our Phase 2 development program from the FDA.

Phase 2 Trial of Vidofludimus Calcium in UC (CALDOSE-1 Trial)

The CALDOSE-1 trial of vidofludimus calcium in moderate to severe UC is a Phase 2b, dose-finding, multicenter, double-blind, placebo-controlled study including a blinded induction and maintenance phase, with double randomization (initial randomization for induction and second randomization for maintenance). The trial also includes an option for an open-label treatment extension for patients discontinuing from or completing blinded treatment. The primary endpoint comprises a composite of patient-reported outcome and endoscopy-assessed outcome, both evaluated following ten weeks of induction treatment with vidofludimus calcium or placebo. We have an active IND application for vidofludimus calcium in UC with the FDA.

CALDOSE-1 is being conducted at more than 100 sites in 19 countries, including the United States and Western, Central and Eastern Europe. Enrollment in the study includes a central, blinded and independent assessment of endoscopy at screening to confirm patient eligibility. We believe that it has taken prudent steps to ensure that the study is conducted in a manner that is consistent with the study protocol in all countries in which the study is being conducted, even though such countries have varying healthcare systems and practices. This includes an endoscopy-based patient eligibility assessment by a central independent reader and a multiple read and potential adjudication process for week 10 endoscopy when the primary study endpoint is assessed.

On October 28, 2021, we announced that the final patient has been enrolled and randomized in the CALDOSE-1 trial. At the completion of patient recruitment, the trial has randomized a total of 263 patients into four arms: three active dosing arms of 10 mg, 30 mg and 45 mg, as well as placebo. Top-line data for the induction phase are expected to be available in June of 2022.

Under an agreement between us and the FDA, reached during our pre-IND meeting in 2017, the UC Phase 2b trial was designed to begin enrollment with three active dosing arms of 10 mg, 30 mg and 45 mg, respectively, in addition to a placebo arm. At the end of August 2019, an interim dosing analysis was performed by an unblinded and independent data review committee, which has concluded that the lowest dose of 10 mg appeared not to be likely ineffective, the highest dose of 45 mg was not intolerable, and no safety signal was identified for any of the trial's three doses of vidofludimus calcium. The data review committee has not shared with us any of the unblinded data underlying these conclusions, and the study remains blinded to us, the investigators and the enrolled patients. The interim dosing analysis was not designed to be a futility analysis nor was the primary endpoint or any other endpoint of the study tested statistically. As a result of these findings, the trial's steering committee has recommended continuation of all three dosing arms, which recommendation was implemented by us. Expansion of vidofludimus calcium's potentially effective dose range required continuation of all three dose groups and increased the overall number of patients expected to be included in the ongoing trial from a previously anticipated 195 patients, to a total of 240 patients.

Further information regarding our CALDOSE-1 trial in UC can be found on ClinicalTrials.gov under the identifier NCT03341962.

Indication: Crohn's Disease

Diagnosis and Prevalence

CD is an idiopathic chronic inflammatory disease of unknown etiology with genetic, immunologic and environmental influences. Like UC, it is one of the major diseases that are generally characterized as IBD. Both UC and CD are caused by chronic inflammation in the gastrointestinal ("GI") tract, but CD can involve the entire GI tract, from the mouth to the anus (but it most commonly involves both the large and small intestines), whereas UC is restricted to the colon and rectum. Distinguishing CD from UC can be challenging when inflammation is confined to the colon. CD typically involves all layers of

the bowel wall, thereby causing complications, such as abscesses, strictures and fistulas, that regularly require surgical intervention.

Hallmark clinical symptoms of CD are chronic diarrhea and abdominal pain. However, the diagnosing physician needs to evaluate laboratory tests, endoscopy results, pathology findings and radiographic tests to arrive at a clinical diagnosis of CD. In general, it is the presence of chronic intestinal inflammation that leads to a diagnosis of CD.

CD is most commonly diagnosed in late adolescence or early adulthood, but it can manifest at any age. According to DRG (Market Forecast Dashboard, Crohn's Disease (2020-2030), December 2021), more than 900,000 patients are affected by CD in the United States, and more than 1.7 million in the G7 countries (US, UK, Canada, Japan, Germany, France, Italy). CD is slightly more prevalent in women than in men.

Current Treatment Options

Treatment of CD is similar to treatment of UC. However, some of the therapies available for UC (such as tofacitinib) have shown varying levels of activity in CD. Conversely, and based on the treatment needs of patients with CD, some drugs have been primarily developed for CD. One such example is the biologic ustekinumab, an antibody directed against IL-12 and IL-23. There are now some approved treatments, such as alofisel, that target the specific structural complications of CD, including fistulas.

Leflunomide is used off-label in patients with CD and has shown an initial suggestion of the possible value of DHODH inhibition in this patient population (Holtmann et al. 2008, Prajapati et al. 2003). In two small investigator trials of leflunomide in CD patients, investigators observed DHODH inhibitor activity in the treatment of moderate to severe CD in patients who have failed or are intolerant to traditional immunomodulator therapy. However, the side effect profile of leflunomide included diarrhea. The prescribing information for teriflunomide, leflunomide's active metabolite, lists a 15-18% rate of diarrhea, which makes it one of the most prevalent side effects of this DHODH inhibitor. We believe that despite the findings of efficacy for leflunomide in the investigator trials in CD patients, the side effect profile makes it unlikely that this type of DHODH inhibitor can be developed in the indication of IBD, and particularly in CD.

Current Development Plan and Ongoing Studies

We are considering our development strategy for vidofludimus calcium for the treatment of CD. During the previously noted discussions with the FDA regarding our UC trial, we and the FDA reached agreement that a clinical trial of vidofludimus calcium in CD could commence when the interim dosing analysis for the Phase 2b CALDOSE-1 trial in UC has been completed. This would allow us to execute its development of vidofludimus calcium in CD with the remaining active dose groups from CALDOSE-1 and placebo, thereby potentially allowing more efficient recruitment into this trial. We had also received additional written advice from the FDA regarding patient-reported outcomes to be used in this trial, called CALDOSE-2. Given the outcome of the interim dosing analysis of the CALDOSE-1 trial, we are currently re-evaluating the trial design in CD and also prefers to evaluate the upcoming CALDOSE-1 results prior to the start of a potential CALDOSE-2 clinical trial. In addition, we are evaluating the optimal time for efficiently executing such study following the COVID-19 pandemic.

Indication: Primary Sclerosing Cholangitis

We are also exploring the use of vidofludimus calcium in orphan diseases that may allow for an accelerated path to commercialization. We are exploring such orphan diseases in conjunction with interested investigators.

Diagnosis and Prevalence

PSC is a rare liver disease in which the bile ducts in the liver become inflamed, narrow and prevent bile from flowing properly. According to Toy et al. (2011), PSC has a prevalence of approximately 4.15 per 100,000 in the United States. The exact cause and disease mechanism of PSC are still unknown, but an autoimmune mechanism may play a role. According to Singh et al. (2013), there is an association with IBD, most often with UC and less commonly with CD. Progressive biliary and hepatic damage results in portal hypertension and hepatic failure in a significant majority of patients over a 10-15 year period from initial diagnosis.

Current Treatment Options

Treatment of PSC is supportive, with a focus on monitoring the disease progression and treating symptoms and complications as they arise. The only substantial treatment is liver transplantation, which may be an option when the disease progresses to cirrhosis and liver function is significantly affected. When some of the larger bile ducts become blocked in patients with PSC, one potential is to open them with endoscopy-based methods, balloon dilatation or stent placement. No medication is currently approved to treat PSC, but medications may be used to control symptoms. Although many trials have failed to meet their endpoints in PSC, there are now a few studies for medications (such as obeticholic acid) that have shown limited activity in PSC.

Current Development Plan and Ongoing Studies

We have entered into a collaboration with investigators at the Mayo Clinic to explore the use of vidofludimus calcium in PSC. An investigator-sponsored proof-of-concept clinical trial of vidofludimus calcium in PSC, for which we provided the study medication, was conducted at the Mayo Clinic in Arizona and Minnesota, both of which are tertiary referral centers for PSC patients. The study was led by Elizabeth Carey, M.D., Professor of Medicine, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Mayo Clinic, who had received Investigator IND approval from the FDA and had been granted Institutional Review Board ("IRB") approval to conduct the study. The study was supported by a grant from the National Institutes of Health (“NIH”).

The study planned to enroll 30 patients with PSC, aged 18 to 75 years, who received 30 mg of vidofludimus calcium once daily for a period of 24 weeks. Enrollment for the study took place between July 2019 and September 2020, but almost all enrollment occurred in 2019 and early 2020. During the COVID-19 pandemic, recruitment for this study was hampered, as patients with PSC are at a high risk of COVID-19 infections and were advised to avoid travel and unnecessary social contacts such as those required to participate in a clinical trial. Together with the investigators, we determined to readout data of the 18 patients who were enrolled prior to the COVID-19 pandemic. The ongoing pandemic situation also triggered the principal investigator’s decision to terminate the study in late 2020, before the intended recruitment goal of 30 patients was reached.

On February 18, 2021, we announced positive top-line data from the study which was designed to investigate vidofludimus calcium's potential to improve various biochemical parameters in PSC patients and help determine whether any such activity warrants further investigation randomized PSC trials. 18 of the targeted 30 patients were enrolled in the study (intent-to-treat population, “ITT”), of whom only 11 patients completed the full vidofludimus calcium treatment course and were evaluable over the 24-week treatment period (per-protocol population, “PP”).

The primary objective of this study was to determine whether vidofludimus calcium reduces serum alkaline phosphatase (“ALP”) in adult patients diagnosed with PSC. The main analysis for the primary objective was whether patients could achieve a reduction of ALP at week 24 which is greater or equal to 25%, as compared to baseline, with an AST increase at week 24 of no more than 33%, as compared to baseline. This positive primary outcome was achieved by 3 of 11 patients in the PP population (27.3%, 95% CI: 6-61%). By virtue of inclusion criteria, patients at baseline had to have an elevated ALP value of at least 1.5 times the upper limit of normal. In addition, time from baseline was calculated as a continuous variable and treated as the primary predictor using a random intercept model which was adjusted for age at baseline and gender. For this longitudinal analysis of ALP from baseline to week 24 in the PP population, the ALP value statistically significantly (p=0.041) decreased by an average of 5.76 IU/L every 30 days (95% CI: -11.29, -0.23; statistical model). The time trend was not statistically significant in the ITT analysis (p=0.578) due to missing data following the high rate of treatment discontinuations during the COVID-19 pandemic. A consistent individual pattern of a stable decrease in ALP values was observed in the PP population between baseline and week 24, without any single patient showing an increase of more than 20% of ALP.

Secondary objectives were to investigate the liver biochemistry parameters, AST, ALT, and total/direct/indirect bilirubin, as well as the concentrations of proinflammatory cytokines, as compared to baseline. The longitudinal analysis of both AST and ALT as well as total, direct and indirect bilirubin values showed a stable pattern in the PP population with no statistically significant change over time and the confidence interval to include the no-change scenario (AST: average 30 day change 1.22 IU/L, 95% CI: -0.53, 2.97, p=0.170; ALT: average 30 day change 0.85 IU/L, 95% CI -1.46, 3.15, p=0.467, total bilirubin: average 30 day change 0.00 mg/dL, 95% CI -0.01, 0.02, p=0.561, direct bilirubin: average 30 day change 0.00 mg/dL, 95% CI -0.01, 0.01, p=0.861, indirect bilirubin: average 30 day change 0.00 mg/dL, 95% CI -0.01, 0.01, p=0.556). Similar results were found in the ITT population. In addition, a decrease in the Ulcerative Colitis Clinical Score was observed in evaluated patients, although the number of assessed patients was limited. The study also found that vidofludimus calcium is a safe and well-tolerated oral drug for PSC patients and treatment-emergent adverse events were rare and generally mild.

Further information regarding the PSC study can be found on ClinicalTrials.gov under the identifier NCT03722576.

As the next step in this indication, we are currently conducting a Phase 1 trial in hepatic impaired patients in order to explore dose optimization of vidofludimus calcium for potential future clinical activities in PSC. This Phase 1 trial has started in September 2021 and is expected to run approximately six months.

Indication: COVID-19

Diagnosis and Prevalence

The World Health Organization ("WHO") declared SARS-CoV-2 infections causing COVID-19 a pandemic on March 11, 2020. Main clinical symptoms include fever, cough, myalgia or fatigue, expectoration, and dyspnea, but a range of other symptoms have been connected to COVID-19 as well. The symptoms of COVID-19 typically appear within 3 to 14 days after initial exposure to SARS-CoV-2. If any patient develops characteristic symptoms of COVID-19 or was exposed to a person with COVID-19, infection with SARS-CoV-2 leading to COVID-19 has to be considered.

As there are no specific clinical features that can reliably distinguish COVID-19 from other viral respiratory infections, the patient will then need to undergo specific testing for SARS-CoV-2. Although several testing methods have been developed, polymerase chain reaction testing remains the primary and most reliable COVID-19 diagnostic testing method in the United States and in most developed countries. Generally, a sample from the nose (nasopharyngeal swab) or throat (throat swab) is taken and then sent to a laboratory for testing.

Current Treatment Options

As of January 2022, at least three vaccines have been authorized and recommended by the FDA for preventing COVID-19:

- Pfizer-BioNTech's COVID-19 vaccine (Comirnaty®, BNT162b2)
- Moderna's COVID-19 vaccine (Spikevax®, mRNA-1273)
- Janssen's COVID-19 vaccine (JNJ-78436735)

Current approaches to COVID-19 therapies generally fall into two categories: antivirals, which prevent the virus from multiplying, and immune modulators, which help the immune system to fight the virus or stop it from overreacting dangerously. Some potential therapies act in a different way or via multiple mechanisms.

In May 2020, the FDA issued an Emergency Use Authorization ("EUA") for emergency use of remdesivir (Veklury®) for the treatment of hospitalized patients with severe COVID-19. Remdesivir is a direct acting antiviral drug that inhibits viral RNA synthesis. On November 20, 2020, the WHO issued a conditional recommendation against the use of remdesivir in hospitalized COVID-19 patients, regardless of disease severity, as there is currently no evidence that remdesivir improves survival and other outcomes in these patients.

In December 2021, the FDA issued an EUA for Pfizer's Paxlovid® (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use) for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kilograms or about 88 pounds) with positive results of direct SARS-CoV-2 testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

In addition, the FDA has issued initial EUAs for several monoclonal antibodies for the treatment and, partially, prevention of COVID-19 in adult and pediatric patients. Monoclonal antibodies are laboratory-made molecules acting as substitute antibodies. The immune system can recognize and respond more effectively to the COVID-19 infection, making it more difficult for the virus to reproduce and cause harm. Some EUAs were revised or revoked later based on updated data when those became available.

Current Development Plan and Ongoing Studies

A publication from scientists in Wuhan, China (Xiong et al. 2020) had shown promising activity of DHODH inhibitors against SARS-CoV-2 in *in vitro* cellular studies. On April 21, 2020, we announced that vidofludimus calcium had successfully demonstrated preclinical activity against SARS-CoV-2. Specifically, vidofludimus calcium was observed to inhibit

replication of clinical isolates of SARS-CoV-2 associated with COVID-19. In cellular assays, vidofludimus calcium demonstrated this antiviral activity at concentrations which are well below the blood concentrations associated with vidofludimus calcium dosing regimens studied in ongoing and previous clinical trials.

Phase 2 Trial of Vidofludimus Calcium in Moderate COVID-19 (CALVID-1 Trial)

The CALVID-1 trial was a prospective, multicenter, randomized, placebo-controlled, double-blind clinical trial in hospitalized patients with moderate COVID-19, designed to evaluate efficacy, safety and tolerability of vidofludimus calcium. The aim of the CALVID-1 trial was to investigate vidofludimus calcium as an oral treatment option for COVID-19 and to support potential use of vidofludimus calcium as a treatment for current and potential future viral pandemic threats. Patients were enrolled at 20 sites in eleven countries, including the United States, Germany, and a range of other European countries. Patients were randomized to receive either 22.5 mg of vidofludimus calcium twice daily (45 mg/day), or placebo twice daily, for 14 consecutive days. Patients in both arms were also eligible to receive investigator's choice of standard-of-care therapy throughout the duration of the study. Inclusion criteria called for hospitalized adult patients with a confirmed SARS-CoV-2 infection fulfilling clinical status category 3 or 4, as assessed with the nine-category ordinal scale proposed by the World Health Organization (WHO) COVID-19 Therapeutic Trial Synopsis, as well as certain additional clinical and laboratory criteria.

On February 17, 2021, we announced that vidofludimus calcium has shown evidence of clinical activity in hospitalized patients with moderate COVID-19. This planned main analysis of the CALVID-1 trial was based on data from 204 randomized patients and included top-line clinical efficacy, safety, disease marker, and virology data. Although the trial found very low rates of serious complications (e.g., mortality, rate of intensive care unit submissions and rate of invasive ventilations) in the population of hospitalized patients with moderate COVID-19, the data did show clinical activity of vidofludimus calcium based on multiple secondary endpoints, including clinically meaningful improvements in time to clinical recovery, time to clinical improvement, and disease markers. In addition, high-risk patients and patients over 65 years of age experienced a more substantial treatment effect of vidofludimus calcium. Vidofludimus calcium also prevented many COVID-19-related adverse events of higher severity. Finally, vidofludimus calcium was found to be safe and well-tolerated in this patient population.

The full analysis of all 223 randomized patients supports the conclusions made for the main analysis. However, the full analysis also provided data on a few additional endpoints that were not assessed in the main analysis. The rate and timing of anti-SARS-CoV-2 antibodies patients are developing in response to the infection was found to be identical between the vidofludimus calcium and placebo treatment arms. We believe that this is an important confirmation of the mechanism of action of vidofludimus calcium that selectively targets highly metabolically activated cells involved in the disease process, but leaves antibody production relatively unaffected. Although no specific data are available at this point, we also believe that these data may support that vaccinations, including those for SARS-CoV-2, may be effectively given during vidofludimus calcium therapy. Many immunomodulatory therapies are known to interfere with vaccinations, however several studies with another DHODH inhibitor (teriflunomide) had shown that this is not the case for these class of drugs. The CALVID-1 SARS-CoV-2 antibody data are supportive of this finding as well. The full analysis was also able to detect a relationship between drug trough levels in blood plasma and the clinical recovery endpoint. Higher drug levels correlate with shorter clinical recovery periods. We believe that this is another important finding to provide evidence of clinical activity in moderate COVID-19 patients.

Further information regarding our CALVID-1 trial in COVID-19 can be found on ClinicalTrials.gov under the identifier NCT04379271.

The CALVID-1 trial was able to highlight important differentiators of vidofludimus calcium as compared to existing medications in MS and UC. Many other immunomodulatory drugs commercially used provide a beneficial effect on the disease but are also known to have a higher rate of virus reactivations as adverse drug reactions. For example, some drugs used in ulcerative colitis are known for elevated rates of zoster virus reactivation (shingles). Drugs approved for multiple sclerosis have shown the rare but clinically very important side effect of PML which is highly lethal and caused by a virus reactivation and infection of the brain tissue. vidofludimus calcium has not shown an increased rate of infections and infestations, as compared to placebo, in the CALVID-1 trial. The same finding was already observed in other controlled clinical trials of vidofludimus calcium, including the Phase 2 EMPhASIS trial in RRMS. We believe that both the underlying selectivity of DHODH inhibition on the immune system and the broad antiviral properties of vidofludimus calcium contribute to these findings.

The results of the CALVID-1 trial also corroborate the broad antiviral activity of vidofludimus calcium, already known from previous *in vitro* testing in a range of different virus families. We believe that these results support the ability of a host-cell directed antiviral mechanism of vidofludimus calcium to provide antiviral activities largely independent of mutational variants. We will continue to explore the broad antiviral properties of vidofludimus calcium, including testing its combination

potential with other drugs in further *in vitro* and *in vivo* preclinical studies. In other clinically important virus diseases, such as hepatitis or AIDS, combination treatments are already the mainstay of therapy, whereas monotherapy was found to be inferior to such combinations. This additional research will enable us to explore the potential of vidofludimus calcium to target preparedness for potential future pandemics and for clinically important and underserved viral diseases.

Investigator-Sponsored Phase 2 Trial of Vidofludimus Calcium in Combination with Oseltamivir in Moderate to Severe COVID-19 (IONIC Trial)

On July 27, 2020, we announced enrollment of the first patients in an investigator-sponsored Phase 2 trial of vidofludimus calcium for the treatment of patients with moderate to severe COVID-19. This trial is run by sponsor and lead site, University Hospitals Coventry and Warwickshire NHS Trust, London, United Kingdom, and is a prospective, randomized, parallel-group, open-label Phase 2b trial, designed to evaluate efficacy and safety of vidofludimus calcium in combination with the neuraminidase inhibitor, Oseltamivir (Tamiflu®), in approximately 120 adult patients with moderate to severe COVID-19. An interim analysis of approx. 30 patients provided evidence for potential activity of the combination treatment of oseltamivir and vidofludimus calcium and the trial is currently being expanded to include additional sites.

Further information regarding the IONIC trial in COVID-19 can be found on ClinicalTrials.gov under the identifier NCT04516915.

Vidofludimus Calcium Registration Plan

All of our drug development candidates require approval from the FDA and corresponding agencies in other countries before they can be marketed for sale. The activities required before drugs or biologics may be marketed in the United States include:

- preclinical laboratory tests, *in vitro* and *in vivo* preclinical studies and formulation and stability studies;
- the submission to the FDA of an application for human clinical testing, which is known as an IND;
- adequate and well-controlled human clinical trials to demonstrate the safety and effectiveness of the drug;
- the submission of an NDA for a drug; and
- the approval by the FDA of an NDA.

The FDA reviews all available data relating to safety, efficacy and quality and assesses the risk/benefit profile of a product candidate before granting approval. The data assessed by the FDA in reviewing an NDA includes animal or preclinical testing data, chemistry, drug-drug interaction data, manufacturing controls data and clinical safety and efficacy data.

Future human clinical testing and marketing outside the United States will be subject to foreign regulatory requirements. These requirements vary by jurisdiction, differ from those in the United States and may require us to perform additional preclinical or clinical testing regardless of whether FDA approval has been obtained. The amount of time required to obtain necessary approvals from foreign regulatory agencies may be longer or shorter than that required for FDA approval. In many countries outside of the United States, coverage, pricing and reimbursement approvals are also required.

We have an ongoing Phase 3 program for vidofludimus calcium in RMS, and ongoing Phase 2 trials for vidofludimus calcium in PMS and UC. We are also considering whether to conduct another clinical trials in CD and PSC. For our lead indications RMS and IBD, marketing approval would require completion of two successful, well-controlled Phase 3 trials. Completing such trials would require substantial financial and resource investments and may take several years to complete. In parallel, additional preclinical and clinical investigations need to be conducted in preparation for filing applications for regulatory approval, including additional pharmacological studies in special populations or drug-drug interaction studies. There are also additional steps required to develop and validate large-scale manufacturing capabilities as well as manufacturing controls.

The FDA may grant accelerated approval for drugs that address life-threatening diseases without effective therapies, based on findings from surrogate endpoints reasonably expected to predict clinical outcomes. Additionally, the FDA may grant

orphan status for drugs that address high unmet medical needs in rare diseases. Accordingly, due to its relatively low prevalence, PSC may have the potential for an accelerated path toward commercial approval. Based on the rarity of PSC, the life-threatening nature of the disease and the lack of effective therapies, the FDA and other regulatory agencies may agree to an abbreviated development plan, including the possibility of only one single open-label pivotal trial. However, any such development path needs to be discussed with and approved by regulatory agencies and we have not yet had any such discussions.

Vidofludimus Calcium Manufacturing and Formulation

Vidofludimus calcium is provided as a white, uncoated immediate release tablet. Dose strengths for clinical trials are 5 mg, 15 mg, 22.5 mg, 30 mg and 45 mg, compared with placebo. The tablets are packaged in polyethylene bottles. Vidofludimus calcium has been synthesized in several batches of approximately 80 kg each of active pharmaceutical ingredient ("API") and a drug product batch size of 500,000 tablets has been produced by manufacturers under contract with us. Our existing manufacturers have the capacity for batch sizes of up to several million units.

Vidofludimus Calcium Intellectual Property, Licenses and Royalties

Vidofludimus calcium is covered by several layers of patents and applications, all either granted or filed in the United States, the European Union and other territories. Initially, vidofludimus calcium is protected by a granted patent claiming the composition of matter of vidofludimus calcium's active moiety, vidofludimus, the free acid form of vidofludimus calcium. This patent is granted in most major markets and expires in 2022 in most of these jurisdictions. Additionally, a second layer of applications was filed to cover vidofludimus calcium's active ingredient, the calcium salt of vidofludimus. These applications are granted in some jurisdictions and cover vidofludimus calcium until 2031, and U.S. Patent Term Extension and/or European Supplementary Protection Certificates could provide prolonged protection from generic entry up to 2036, depending on NDA submission time and IND filing in the United States and analogous filings in the European Union. Another layer consists of patent applications filed in early 2018 and directed to composition of matter of a newly-identified, specific polymorph of vidofludimus calcium and a related method of production of the clinical material for vidofludimus calcium, which is now the active ingredient of the currently used vidofludimus calcium formulation. In addition, a patent application covering a dosing scheme currently used with vidofludimus calcium was filed in 2017, based on unexpected findings from Phase 1 and preclinical investigations. If issued, this patent could extend patent protection for vidofludimus calcium to 2038.

Vidofludimus calcium and IMU-935 were acquired in a transaction with the originator 4SC in September 2016. We have subsequently submitted additional patent applications for independently developed intellectual property relating to each of vidofludimus calcium and IMU-935. On March 31, 2021, our German subsidiary, Immunic AG, and 4SC entered into a Settlement Agreement, pursuant to which Immunic AG settled its remaining obligation of a 4.4% royalty on net sales for $17.25 million. The payment was made 50% in cash and 50% in shares of our common stock.

IMU-935 – Targeting RORγt and Th17

Mechanism of Action and Key Mechanistic Data

IMU-935 is a highly potent and selective inverse agonist of a transcription factor called RORγt. We believe that the nuclear receptor RORγt is the main driver for the differentiation of Th17 cells and the release of cytokines involved in various inflammatory and autoimmune diseases. The target RORγt (RORC) has three known main functions in T cells: (i) it is a key regulator of Th17 cell differentiation, (ii)it is the crucial transcription factor for the genes encoding IL-17A and IL-17F, and (iii) it drives normal thymocyte maturation. We believe this target is an attractive alternative to approved antibodies for targets, such as IL-23, the IL-17 receptor and IL-17 itself.

Preclinical results confirm that IMU-935 is a highly potent and selective inverse agonist of RORγt with an IC_{50} (the concentration of drug that inhibits 50% of the activity of the target) of around 24 nM in reporter assays and 20 nM in a microscale thermophoresis ("MST") binding assay to the protein. The resulting effect of RORγt inhibition by IMU-935 *in vitro* on IL-17A, IL-17F and IFNγ cytokine release from stimulated human lymphocytes is in the low single-digit nanomolar range, showing IC_{90} levels of 5-6 nM. Furthermore, IMU-935 potently inhibits Th17 differentiation and has demonstrated dose dependent activity in several cellular test systems and *in vivo* in psoriasis/IL-17, graft versus host disease, experimental autoimmune encephalomyelitis ("EAE")and IBD animal models.

One of the potential risks of drugs targeting RORγt was identified in prior research suggesting that RORγt knockout or inhibition impacts Th17 differentiation, IL-17 transcription and thymocyte maturation to the same extent. More recent research published in Nature Immunology (2017) suggests that these functions are differentially mediated by small structural changes of the RORγt protein impacting the interaction with co-factors and other proteins.

Preclinical experiments indicated that, while leading to a potent inhibition of Th17 differentiation and cytokine secretion, IMU-935 did not affect thymocyte maturation, one of the important physiological functions that should be maintained. Based on these preclinical data and the selectivity of the effect maintaining important physiological functions while providing the desired anti-Th17 effect, we believe that IMU-935 has potential to be a best-in-class therapy for various autoimmune diseases. Newly obtained data from acute and chronic treatment of mice corroborated *in vivo* that IMU-935 is the first molecule observed to impact neither thymus size, thymocyte numbers, nor the maturation status of thymocytes, in contrast to two other known inhibitors of RORγt.

The preclinical effect of targeting RORγt has been demonstrated in several preclinical experiments of competing RORγt modulators. Some molecules progressed to clinical stage. However, to date, only a limited number of product candidates have reached clinical Phase 2 studies.

Indication: Psoriasis

Diagnosis and Prevalence

Psoriasis is a chronic inflammatory disease of the skin with unknown etiology that leads to hyperproliferation of keratinocytes and endothelial cells. Most mechanistic data support the hypothesis that psoriasis is an autoimmune disease driven by activated T-lymphocytes which then release cytokines, chemokines and pro-inflammatory molecules into the dermis and epidermis.

Psoriasis is characterized clinically by development of red, scaly, itchy, symmetrical, dry plaques typically located on skin overlying the elbows, knees, lumbar area and scalp. Plaques vary from a few millimeters in diameter to several centimeters and can be localized to a specific area or extend over most of the body surface.

Psoriasis is one of the most common chronic inflammatory skin diseases (Di Meglio et al. 2014). The disease prevalence varies between geographic regions. Studies of psoriasis suggest an overall prevalence of 2% to 3% of the world's population, with a higher prevalence in U.S. and Canadian populations (4.6% and 4.7%, respectively). Psoriasis is considered equally prevalent between genders and can occur at any age. However, there seems to be a bimodal distribution of the age of disease onset, with a first peak between 15 and 30 years, and a second peak between 50 and 60 years of age.

Current Treatment Options

Current treatments for patients with psoriasis include topical therapies, oral therapies and biologics. Topical therapies, such as corticosteroids and vitamin D3 analogues, reduce inflammation, which slows the proliferation of keratinocytes and reduces itching. Oral therapies, such as methotrexate, cyclosporine, apremilast and tofacitinib, target anti-inflammatory processes. Biologics block proteins produced by keratinocytes, dendritic cells, Th17 lymphocytes or other immune cells. Examples of biologics include anti-TNFα therapies, such as infliximab, etanercept and adalimumab. Monoclonal antibodies, such as secukinumab, ixekizumab and brodalumab, have been developed to target the pro-inflammatory cytokine IL-17. Anti-IL-23 agents, such as risankizumab, guselkumab and tildrakizumab, are further treatment options. Of note, therapies targeting the IL-17/IL-23 axis have largely revolutionized the treatment of patients with moderate to severe psoriasis as they have achieved highly successful skin clearance rates.

We intend to develop IMU-935 as an oral and more convenient treatment option for patients with moderate to severe psoriasis with a mechanism of action and efficacy that approximates those of IL-17 antibodies.

Indication: Castration-Resistant Prostate Cancer

Diagnosis and Prevalence

Prostate cancer is the most common malignancy in men (Siegel RL et al., CA CANCER J CLIN 2021;71:7–33). Castration-resistant prostate cancer ("CRPC") is defined by disease progression despite androgen depletion therapy and may

present as either a continuous rise in serum prostate-specific antigen (“PSA”) levels, the progression of pre-existing disease, and/or the appearance of new metastases (Saad et al., CAN UROL ASSOC J 2010;4(6):380-4).

Among patients whose prostate cancer is metastatic at the time of diagnosis, bone pain may be the leading symptom. Bone is the predominant site of disseminated prostate cancer, and pain is the most common manifestation of bone metastases. Other symptoms with metastatic disease may include hematuria, inability to void, incontinence, erectile dysfunction, weight loss, weakness or pain due to spinal cord compression, pain due to pathologic fractures, fatigue caused by anemia, or symptoms associated with chronic renal failure. Clinical signs associated with prostate cancer include an elevated PSA on laboratory testing and an abnormal prostate finding on digital rectal examination.

Current Treatment Options and Unmet Need

While docetaxel is still considered a reference chemotherapy for patients with CRPC, cabazitaxel, abiraterone acetate and enzalutamide are commonly prescribed for the majority of patients with CRPC based on the ability to improve overall survival in men who progress after docetaxel. However, *de novo* and acquired resistance to these therapies seem to be inevitable, meaning that almost all show disease progression despite treatment with these agents (Chopra S and Rashid P, Aust Fam Physician 2015 May;44(5):302-5).

On July 12, 2021, we presented new preclinical data highlighting IMU-935's therapeutic potential in CRPC. Recently published third-party studies have shown that RORγ plays an important pro-tumor role by driving expression of the androgen receptor (“AR”), leading to tumor growth. AR has been shown to be mutated in a constitutively active form called AR-V7 in 18% of untreated patients and up to 95% of patients treated with abiraterone acetate and enzalutamide. This mutation leads to resistance of AR-axis-targeted therapies and is associated with poor outcomes of progression free survival and overall survival for patients on AR-axis-targeted therapies (Sciarra et al. 2019 May; 98(19): e15608). In preclinical studies, IMU-935 was observed to inhibit the expression of mutated AR-V7, and the tumor growth of prostate cancer cell lines *in vitro*. We believe IMU-935's potency in inhibiting tumorigenesis-promoting IL-17 and Th17 cells *in vitro* may result in further antitumoral activity in humans.

Indication: Guillain-Barré Syndrome

Diagnosis and Prevalence

Historically, Guillain-Barré Syndrome (“GBS”) was considered a single disease entity. It is now known to be a heterogeneous syndrome with several variant forms. Acute inflammatory demyelinating polyradiculopathy is the most common form in North America, Europe and most of the developed world, where it accounts for approximately 90% of cases. GBS is thought to result from an immune response to a preceding infection that cross-reacts with peripheral nerve components. The exact mechanisms are unknown. However, cellular and humoral immune responses are of relevance in the pathogenesis of GBS.

The clinical manifestation of GBS is characterized by an acute or subacute onset of a progressive, symmetric weakness in limbs or cranial nerve-innervated muscles, accompanied by absent or depressed deep tendon reflexes, and a characteristic profile in the cerebrospinal fluid and electrodiagnostic studies (Hughes et al. 2005). Patients usually present a few days to a week after onset of symptoms. The weakness can vary from mild difficulty with walking to nearly complete paralysis of all extremity, facial, respiratory, and bulbar muscles.

GBS occurs worldwide with an overall incidence of 0.16 to 3.0 per 100,000 person-years (McGrogan et al. 2009). Thus, it is considered a rare disease. The incidence increases by approximately 20% with every 10-year increase in age beyond the first decade of life (Sejvar et al. 2011). In addition, the incidence is slightly greater in males than in females.

Current Treatment Options

Current treatments for patients with GBS include plasma exchange (also called plasmapheresis) and administration of intravenous immune globulin (“IVIg”). Over the past three decades, no other therapies have been found to be effective for GBS.

IMU-935 Clinical Development Plan and Ongoing/Planned Clinical Studies

Our current development plan for IMU-935 focuses on two initial goals: (i) to rapidly obtain human safety and pharmacokinetic data for IMU-935 in order to evaluate the safety profile of this development candidate, and (ii) to obtain preliminary clinical activity data using safe doses.

We are currently performing a Phase 1 clinical trial with IMU-935 through its Australian subsidiary. Immunic believes that this development approach allows it to accelerate the program due to certain unique regulatory requirements and processes in Australia. In the third quarter of 2019, our Australian subsidiary received clearance from the Bellberry Human Research Ethics Committee in Australia to begin Phase 1 trials of IMU-935 under the Clinical Trial Notification scheme of the Australian Therapeutic Goods Administration.

The Phase 1 clinical trial of IMU-935 is comprised of three parts:

Part A: Single Ascending Dose Part

The first part of the Phase 1 trial was a single ascending dose, double-blind, placebo-controlled study of IMU-935 in healthy human subjects. This part was designed to evaluate the drug's safety and pharmacokinetic profile and also included the evaluation of food effects.

On December 14, 2021, we announced that unblinded data from the single ascending dose part of the ongoing phase 1 clinical trial of a new powder-in-capsule formulation of IMU-935, in which healthy human subjects were treated with 100 mg, 200 mg, 300 mg and 400 mg of this new formulation or placebo, found these single ascending daily doses of IMU-935 to be safe and well-tolerated, and no maximum tolerated dose was reached. No serious adverse events occurred. A dose-proportional pharmacokinetic profile was observed across the investigated dose range.

Part B: Multiple Ascending Dose Part

Following the single ascending dose part, we initiated a second portion of the Phase 1 trial which was a multiple ascending dose, double-blind, placebo-controlled study in healthy human subjects with IMU-935 given daily for 14 consecutive days. This part assessed the safety and pharmacokinetic properties of IMU-935.

On December 14, 2021, we also announced unblinded data from the multiple ascending dose part of the ongoing phase 1 clinical trial, in which healthy human subjects were dosed for 14 days with 150 mg either once or twice daily doses of IMU-935 or placebo, found these multiple ascending doses of IMU-935 to be safe and well-tolerated, and no maximum tolerated dose was reached. Treatment emergent adverse events were generally mild in severity, with moderate treatment emergent adverse events reported in one of eleven IMU-935 treated subjects, compared with one of four subjects on placebo. No serious adverse events were reported. No dose-dependent changes in laboratory values (including no effects on liver enzymes or in hematological parameters), vital signs or in electrocardiographic evaluations were found. Pharmacokinetic analysis showed that stable steady-state plasma concentrations were achieved within the first week of dosing with an accumulation factor for IMU-935 allowing predictable trough levels during daily dosing.

Part C: Psoriasis Patients

In light of the favorable safety and tolerability data observed in healthy human subjects, we announced on October 27, 2021 that it has initiated part C of the ongoing phase 1 clinical trial, where moderate to severe psoriasis patients are to be randomized to 28-day treatment with IMU-935 or placebo. Planned assessments include safety, tolerability, pharmacokinetic and pharmacodynamic markers, as well as skin evaluations. Recruitment of part C depends on several external factors which are not under our direct control, including, in particular, the relatively restrictive COVID-19-related rules in effect in Australia and New Zealand. This situation has and may further influence our ability to enroll study participants and/or perform on-site monitoring at clinical sites in those locations. In light of this, we have already initiated remedial measures, including the potential addition of sites outside of Australia and New Zealand, for the ongoing part C of IMU-935 in psoriasis patients. As a result, initial results from the third portion of the Phase 1 clinical trial in patients with moderate-to-severe psoriasis are now expected to be available in the second half of 2022, instead of at the end of the second quarter of 2022, as previously announced.

Further information regarding our Phase 1 clinical trial can be found on anzctr.org.au under the registration number ACTRN12619001544167.

Phase 1 Clinical Trial of IMU-935 in mCRPC

Based on these strong preclinical results, the Company has initiated an open-label Phase 1 dose-escalation trial designed to evaluate the safety and tolerability of increasing doses of IMU-935 to establish the maximum tolerated dose and the recommended phase 2 dose. The trial will also evaluate the anti-tumor activity of IMU-935 by means of PSA levels, circulating tumor cell numbers, and radiographic response assessments of tumor progression. The trial's Principal Investigator is Johann Sebastian de Bono, MD, PhD, Regius Professor of Cancer Research and Professor in Experimental Cancer Medicine, The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, London, United Kingdom. The trial was approved by the Medicines and Healthcare products Regulatory Agency ("MHRA"), the Research Ethics Committee ("REC") and the Health Research Authority ("HRA") in the United Kingdom. The first patient was enrolled in December 2021. Initial clinical data are expected to be available in the third quarter of 2022.

Further information regarding Immunic's Phase 1 clinical trial in mCRPC can be found on ClinicalTrials.gov under the identifier NCT05124795.

Potential Phase 2 Trial of IMU-935 in GBS

Immunic believes that the mechanism of action of IMU-935 may also support its evaluation for the treatment of potential orphan indications. Immunic anticipates that it may also begin a Phase 2a proof-of-concept clinical trial of IMU-935 in an orphan autoimmune indication, if the full Phase 1 clinical trial results support such a study. This orphan approach may allow for an accelerated path to approval, in parallel to IMU-935's previously planned development in psoriasis. After a thorough review of suitable autoimmune conditions, Immunic has targeted GBS as additional indication for IMU-935, as previously announced. GBS is an acute neurological disorder in which the body's immune system attacks its peripheral nervous system, and for which very few therapies exist. The Company plans to announce additional details as soon as design and timing of the envisaged trial are further defined.

IMU-935 Manufacturing and Formulation

IM105935, the API of the IMU-935 drug product, is a small molecule compound and is currently synthesized at up to 30 kg scale. Clinical trials are supplied with a powder-in-capsule formulation produced by manufacturers under contract with us.

IMU-935 Intellectual Property, Licenses and Royalties

On February 2, 2022 the Company announced that it received a Notice of Allowance from the U.S. Patent and Trademark Office ("USPTO") for patent application 16/644581, entitled, "IL-17 and IFN-gamma inhibition for the treatment of autoimmune diseases and chronic inflammation". The company also received notice of allowance of patent application EP18762111.5 in Europe, and notice of grant of patent application 2018330633 in Australia. All three patents cover composition of matter of IMU-935 and related formulations, and are expected to provide protection into at least 2038, without accounting for potential Patent Term Extension ("PTE") in the United States or Supplementary Protection Certificates ("SPC") in Europe, respectively.

IP related to IMU-838 and IMU-935 was acquired in a transaction with the originator 4SC in September 2016. Immunic has subsequently submitted additional patent applications for independently developed intellectual property relating to each of IMU-838 and IMU-935. On March 31, 2021, Immunic AG, our German subsidiary, and 4SC entered into a Settlement Agreement, pursuant to which Immunic AG settled its remaining obligation of a 4.4% royalty on net sales for $17.25 million. The payment was made 50% in cash and 50% in shares of our common stock.

IMU-856 – Targeting Intestinal Barrier Function

Mechanism of Action and Key Mechanistic Data

IMU-856, which we believe could have a highly advantageous potential for multiple diseases, is an orally available small molecule modulator that targets a protein which serves as a transcriptional regulator of the intestinal barrier function and regeneration of bowel epithelium. Immunic has not yet disclosed the molecular target for IMU-856. Based on preclinical data,

Immunic believes this compound may represent a new treatment approach, as the mechanism of action targets the restoration of the intestinal barrier function and regeneration of bowel epithelium in patients suffering from gastrointestinal diseases such as IBD, IBS-D, celiac disease and other intestinal barrier function associated diseases. Immunic believes that because IMU-856 has been shown in preclinical investigations to avoid suppression of immune cells, it may therefore maintain immune surveillance for patients during therapy, which would be an important advantage versus chronic treatment with potentially immunosuppressive medications.

Importance of Targeting Bowel Permeability in Multiple Diseases

Bowel permeability is suspected to be involved in the initiation of many chronic inflammatory or autoimmune conditions, as the impaired intestinal barrier function may be one of the preconditions for antigens of the microbiome to be recognized by the body's immune system. This is not only true for diseases of the bowel; the interaction of the immune system with components of the microbiome is suspected for many diseases throughout the body. To date, there are no good treatment strategies to ameliorate impaired bowel permeability.

IBD is a chronic, inflammatory disorder characterized by transmural inflammation of a part of the GI tract (UC) or the entire GI tract (CD). IBD is defined by relapsing and remitting episodes with progression over time to complications, including intestinal ulcers and bleeding. The current hypothesis regarding the onset of IBD involves an impaired bowel wall barrier function as the central element of the pathophysiology. In healthy bowel walls, bacteria cannot pass from the lumen to the lamina propria because tightness is maintained between the epithelial cells in what resembles an intact barrier function of the bowel wall. However, in response to environmental or genetic factors, bowel wall barrier function may be weakened, allowing bacteria to pass through and enter the bowel wall, where immune cells recognize the bacteria. This would trigger an initial inflammation event. It is hypothesized that in IBD patients, the initial inflammatory response is abnormally sustained from lack of efficient apoptosis of immune cells, but this mechanism is not yet fully understood. Ultimately, patients develop a chronic and systemic immune response. The presence of certain "bad bacteria", which may contain certain epitopes in the microbiota, or the overall makeup of the microbiome, which lack "good bacteria", are also known to contribute to the sustained and overshooting inflammation in IBD. Additionally, it was shown that IBD patients in endoscopic remission still display IBD symptoms if bowel tightness is not normalized. Episodes of impaired bowel wall barrier function are also correlated with relapse weeks later.

Irritable bowel syndrome is a common GI disorder in which the underlying pathophysiology is poorly understood. However, increased intestinal permeability in IBS-D patients has been reported. Studies have shown that IBS-D patients have increased intestinal membrane permeability. This increased intestinal permeability may be due to a number of factors, including low-grade inflammation, which has been reported in mucosal biopsies of some diarrhea-predominant and post-infectious patients, but not constipation-predominant patients. It has been established that patients with inflammatory conditions, such as celiac sprue and acute alcoholic gastroenteritis, also have increased gut permeability. Acute symptoms usually coincide with the acute inflammation that leads to chronic abdominal pain, diarrhea and bloating.

Celiac disease is an autoimmune and chronic inflammatory condition of the small intestine involving an inappropriate immune response to the gluten-derived protein gliadin in genetically susceptible individuals. It is characterized by small intestinal epithelial injury, elevated intestinal permeability, and nutrient malabsorption. The prevalence of celiac disease is 0.5–1% in the general population, with an increasing incidence since the second half of the 20th century. Celiac disease causes debilitating symptoms and serious medical complications. Many patients suffer from gastrointestinal symptoms and have abnormal bowel epithelial lining (mucosal atrophy and crypt enlargement). Small bowel damage often leads to nutrient malabsorption that can result in a range of further clinical manifestations (anemia, osteopenia, failure to thrive in children). In addition, extra-intestinal symptoms and systemic manifestations are often present, such as dermatitis, infertility, or neurological and skeletal disorders. Patients with persistent villous atrophy show an increased risk of lymphoproliferative malignancy. The intestinal epithelia barrier, physiologically impermeable to macromolecules such as gliadin, is recognized to play an important role in the pathogenesis of celiac disease.

Targeting the Disease-Causing and Sustaining Processes

Current treatments of many conditions of the bowel are aimed at inhibiting inflammation, but they do not target the impaired bowel wall barrier function. IMU-856 is designed to target pathways impacting the bowel wall barrier function and is aimed to normalize such function. Immunic believes that normalized bowel wall barrier function may avoid bacterial triggers, which may lead to the achievement and maintenance of remission without significantly influencing the immune competency of the patient.

Clinical Development Plan and Planned Studies

Immunic is currently performing early clinical trials of IMU-856, including Phase 1 single and multiple ascending dose trials, through its Australian subsidiary. Immunic believes that this development approach will allow it to accelerate the studies due to certain unique regulatory requirements and processes in Australia. The development activities for IMU-856 are intended to largely follow established processes and service provider relationships established for the IMU-935 development program. This may lead to operational and financial synergies in study preparation and execution.

In the third quarter of 2020, Immunic's Australian subsidiary received clearance from the Bellberry Human Research Ethics Committee in Australia to begin Phase 1 trials of IMU-856 under the Clinical Trial Notification scheme of the Australian Therapeutic Goods Administration. The first healthy volunteer in the Phase 1 clinical trial of IMU-856 was dosed in August 2020. The trial is currently ongoing and progressing. Unblinded safety data from the single and multiple ascending dose parts in healthy human subjects is expected to be available in the third quarter of 2022.

The Phase 1 clinical trial of IMU-856 is comprised of three parts:

Part A: Single Ascending Dose Part

The first part of the Phase 1 trial is a single ascending dose, double-blind, placebo-controlled study in healthy human subjects designed to assess safety, pharmacodynamic and pharmacokinetic properties of IMU-856. One dose level evaluates intra-individual differences between fasted and fed conditions. All planned single ascending dose cohorts for the current tablet formulation of IMU-856 have been completed but have not yet been unblinded.

Part B: Multiple Ascending Dose Part

Based on the favorable data available so far, the Ethics Committee in Australia has agreed to proceed to the multiple ascending dose part of the Phase 1 trial which is currently being dosed. This is a multiple ascending dose, double-blind, placebo-controlled study in healthy human subjects with two ascending dose levels of IMU-856 and the study drug given daily for 14 consecutive days. This part is designed to assess safety, pharmacodynamic and pharmacokinetic properties of IMU-856.

Part C: Patients with Conditions Involving Impaired Bowel Barrier Function

The Company plans to extend these single and multiple ascending dose studies in the first half of 2022 to include patients with intestinal barrier function associated diseases. This would be a double-blind, placebo-controlled study with partial parallel group design. The study drug would be given daily over 28 consecutive days to patients with a model disease which would allow to potentially provide initial evidence of activity of IMU-856.

IMU-856 Manufacturing and Formulation

SPIM-15, the API of the IMU-856 drug product, is a small molecule compound and is currently synthesized at up to 8 kg scale. It is formulated as an immediate release tablet. Although the IMU-856 tablets are produced in different countries by manufacturers under contract with us, the final release for clinical trials is done by a vendor in Australia

IMU-856 Intellectual Property, Licenses and Royalties

On November 5, 2018, Daiichi Sankyo and Immunic AG, our German subsidiary, entered into an option and license agreement that granted Immunic AG an exclusive global option to exclusively license a group of compounds, designated by us as IMU-856. Under this agreement, ImmunicAG has the exclusive rights to commercialization of IMU-856 in all countries, including the United States, Europe and Japan. The license also includes exclusivity on a patent application filed by Daiichi Sankyo in early 2018, covering IMU-856's composition of matter. Immunic AG exercised the option on January 5, 2020.

Concurrent with the option exercise, Immunic AG paid to Daiichi Sankyo a one-time upfront licensing fee. Going forward, Daiichi Sankyo is eligible to receive future development, regulatory and sales milestone payments, as well as royalties related to IMU-856.

Government Regulation - All Products

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (“FDCA”), and its implementing regulations. All of Immunic’s drug development candidates require approval from the FDA and corresponding agencies in other countries before they can be marketed for sale. The activities required before drugs or biologics may be marketed in the United States include:

- preclinical laboratory tests, *in vitro* and *in vivo* preclinical studies and formulation and stability studies;
- the submission to the FDA of an application for human clinical testing, which is known as an IND application;
- adequate and well-controlled human clinical trials to demonstrate the safety and effectiveness of the drug;
- the submission to the FDA of a New Drug Application ("NDA") for a drug; and
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current GMP (“cGMP”), requirements to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity;
- the approval by the FDA of an NDA.

The FDA reviews all available data relating to safety, efficacy and quality and assesses the risk/benefit profile of a product candidate before granting approval. The data assessed by the FDA in reviewing an NDA includes animal or preclinical testing data, chemistry, drug-drug interaction data, manufacturing controls data and clinical safety and efficacy data.

Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. Preclinical trials must also be conducted in accordance with FDA and comparable foreign authorities’ legal requirements, regulations or guidelines, including Good Laboratory Practice (“GLP”), an international standard meant to harmonize the conduct and quality of non-clinical studies and the archiving and reporting of findings. Before human clinical testing can begin, a sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND, which is a request for authorization from the FDA to administer an IND product candidates to humans in clinical trials. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may impose a clinical hold at any time before or during clinical trials due to safety concerns about proposed or ongoing clinical trials or non-compliance with FDA requirements, and the trials may not commence or continue until the FDA notifies the sponsor that the hold has been lifted.

All clinical trials must be conducted under the supervision of one or more qualified investigators pursuant to protocols detailing, among other things, the objectives of the trial, dosing procedures, subject selection, inclusion/exclusion criteria and the safety and effectiveness criteria to be evaluated. The trial sponsor submits the protocol, as well as any subsequent protocol amendments, to the FDA as part of the IND. Sponsors must also provide all participating investigators and FDA safety reports of any serious and unexpected adverse events and any findings from laboratory tests in animals that suggests a significant risk for human subjects. For each institution where a clinical trial will be conducted, an Institutional Review Board ("IRB") must review and approve the clinical trial protocol and informed consent form required to be provided to each trial subject or his or her legal representative prior to a clinical trial commencing, and conduct ongoing monitoring of the study until completed or termination to assure that appropriate steps are taken to protect the human subjects participating in the research.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

Phase 1: In Phase 1 studies, the product candidate is initially introduced into healthy human subjects and tested for safety, dosage and tolerability, absorption, distribution, metabolism, excretion, and effect on the body.

Phase 2: Phase 2 studies are conducted in a limited patient population. These studies continue to evaluate safety while gathering preliminary data on effectiveness in patients with the targeted disease or condition.

Phase 3: Phase 3 trials further evaluate efficacy and safety in an expanded patient population, generally at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

Post-approval studies, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval from the FDA. These studies are used to gather additional information about a product’s safety and/or efficacy in patients affected by the therapeutic indication. The FDA may require Phase 4 studies as a condition of approval of an NDA.

Clinical trials must also be conducted in accordance with legal requirements, regulations or guidelines of the FDA and comparable foreign authorities, including human subject protection requirements and current good clinical practice ("cGCP" or "GCP"). In addition, clinical trials must be conducted using product candidates produced under cGMP requirements. The FDA or the sponsor may suspend a clinical trial at any time for various reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB may suspend or terminate approval of a clinical trial at an institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts, known as a data safety monitoring board or committee, which monitors data from the trial to ensure patient safety and data integrity and may also make recommendations to alter or terminate a trial based on concerns for patient safety.

Before obtaining marketing approval for the commercial sale of any drug product, a sponsor must demonstrate in preclinical studies and well-controlled clinical trials that the product is safe and effective for its intended use and that the manufacturing facilities, processes and controls are adequate to preserve the drug's identity, strength, quality and purity. The results of these preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees ($3,117,218 for 2022); under certain limited circumstances, a waiver of such fees may be obtained. After the submission of an NDA, but before approval of the NDA, the manufacturing facilities used to manufacture a product candidate must be inspected by the FDA to ensure compliance with the applicable cGMP requirements. The FDA may also inspect clinical trial sites and audit clinical study data to ensure that the sponsor's studies were properly conducted in accordance with the IND regulations, human subject protection regulations, and cGCP.

Under the current Prescription Drug User Fee Act ("PDUFA") guidelines, the FDA goal for acting on the submission of an NDA for a new molecular entity is ten months from the date of "filing." The FDA conducts a preliminary review of an NDA within 60 days after submission to determine whether it is sufficiently complete to permit substantive review, before accepting the NDA for filing. This two month preliminary review effectively extends the typical NDA review period to twelve months. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Following the FDA's evaluation of an NDA, it will issue an approval letter or a complete response letter ("CRL"). An approval letter authorizes the sponsor to begin commercial marketing of the drug for specific indications. A CRL indicates that the review cycle of the application is complete and the application will not be approved in its present form. A CRL describes the specific deficiencies in the NDA identified by the FDA. When possible, a CRL will recommend actions that the applicant might take, including providing additional clinical data, such as an additional Phase 3 trial or other significant and time consuming requirements related to clinical trials, nonclinical studies or manufacturing, to place the application in condition for approval. If a CRL is issued, the sponsor must resubmit the NDA addressing all of the deficiencies identified in the letter, or withdraw the application. Even if the sponsor submits the recommended data and information, the FDA may decide that the NDA does not satisfy the criteria for approval.

As condition to a product's regulatory approval, the FDA may require a sponsor to conduct Phase 4 studies designed to further assess the drug's safety and effectiveness after NDA approval, or may require other testing and surveillance programs to monitor the safety of the approved product. The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy ("REMS") to assure the safe use of the drug. A REMS could include medication guides, communication plans to healthcare professionals or other activities to assure safe use, such as provider certification or training, restricted distribution methods, and patient registries.

Research and Development

We recognized $61.1 million and $38.6 million in research and development expenses in the years ended December 31, 2021 and 2020, respectively.

Geographic Information

Substantially all of our long-lived assets were located within both the United States and Germany in 2021 and 2020.

Employees

As of February 18, 2021, we had 55 employees, six of whom held M.D. degrees. Of the employees, 38 were engaged in research and development and 17 in administration. We consider our employee relations to be good.

Corporate Information and Website

We maintain a website at www.imux.com. The information contained on, or that can be accessed through, the website is not a part of this Annual Report on Form 10-K.

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act are available free of charge through the investor relations page of our internet website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. Before deciding to invest in our company or deciding to maintain or increase your investment, you should consider carefully the risks and uncertainties described below. The risks and uncertainties described below and in our other filings with the SEC are not the only risks we face. If one or more of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the market price for our common stock could decline, and you may lose your entire investment.

Risk Factor Summary

The following is a summary of certain important factors that may make an investment in our Company speculative or risky. You should carefully consider the fuller risk factor disclosure set forth in this Annual Report, in addition to the other information herein, including the section of this report titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes.

- The coronavirus pandemic has caused interruptions or delays of our business plan and may have a significant adverse effect on our business.
- Our clinical trials could be delayed or suspended as a result of the threatened invasion of Ukraine by Russia.
- We have a limited operating history with our current business plan, have incurred significant losses since 2016, anticipate that we will continue to incur significant and increasing losses for the foreseeable future and may never achieve or maintain profitability. The absence of any commercial sales and our limited operating history make it difficult to assess our future viability.
- We currently have no source of product sales revenue and may never be profitable.
- We will require substantial additional funding, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or future commercialization efforts.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.
- The marketing approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our product candidates, our business will be substantially harmed.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome.
- Clinical failure can occur at any stage of clinical development. Because the results of earlier clinical trials are not necessarily predictive of future results, any product candidate we advance through clinical trials may not have favorable results in later clinical trials or receive marketing approval.
- Our product candidates may cause undesirable adverse effects or have other properties that could delay or prevent their marketing approval, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if obtained.

- We are heavily dependent on the success of our product candidates, which are in the early stages of clinical development. We cannot give any assurance that we will generate data for any of our product candidates sufficient to receive regulatory approval in our planned indications, which will be required before they can be commercialized.

- Due to our limited resources and access to capital, we must decide to prioritize development of our current product candidates for certain indications and at certain doses. These decisions may prove to have been wrong and may materially adversely affect our business, financial condition, results of operations and prospects.

- If we fail to attract and retain key management and scientific personnel, we may be unable to successfully develop or commercialize our product candidates.

- Even if we obtain the required regulatory approvals in the United States and other territories, the commercial success of our product candidates will depend on market awareness and acceptance of our product candidates.

- We currently have limited marketing and sales experience. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

- If we fail to enter into strategic relationships or collaborations, our business, financial condition, commercialization prospects and results of operations may be materially adversely affected.

- We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

- The size of the potential market for our product candidates is difficult to estimate and, if any of our assumptions are inaccurate, the actual markets for our product candidates may be smaller than our estimates.

- We may be unable to realize the potential benefits of any collaboration.

- Our proprietary rights may not adequately protect our technologies and product candidates.

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

- Intellectual property rights do not protect against all potential threats to our competitive advantage.

- We incur significant costs and demands upon management as a result of complying with the laws and regulations affecting public companies.

- The market price of our common stock is volatile.

- We do not anticipate that we will pay any cash dividends in the foreseeable future.

Risks Related to COVID-19

The coronavirus pandemic has caused interruptions or delays of our business plan and may have a significant adverse effect on our business.

In an effort to contain and mitigate the spread of COVID-19, many countries, including the United States (and some states and cities), Canada, the European Union and China, have imposed unprecedented restrictions on travel, quarantines, vaccine mandates and other public health safety measures. Legal challenges to some of these restrictions have been successful, others are currently pending, with additional challenges expected. As a result, there is uncertainty about the legality and enforceability of many of these restrictions. The timing and efficacy of the vaccination programs in the jurisdictions in which we operate, and the actions implemented to contain the impact of COVID-19 by Federal, state and local governments, limit determining the foreseeable resulting economic effects with any level of predictability.

The extent to which the pandemic may continue to impact our business will depend on future developments, which are highly uncertain and cannot be predicted, but the development of clinical supply materials could be delayed and enrollment of patients in our ongoing studies may be delayed or suspended, as hospitals and clinics in areas where we are conducting trials have shifted resources to cope with the COVID-19 pandemic and may limit access or close clinical facilities due to the COVID-19 pandemic. Additionally, if our trial participants are unable to travel to our clinical study sites as a result of

quarantines, vaccine mandates, travel bans or other restrictions resulting from the COVID-19 pandemic, we may experience higher discontinuation rates or delays in our clinical studies, as occurred in our investigator-sponsored trial of vidofludimus calcium in PSC that was conducted at the Mayo Clinic. Government-imposed quarantines and restrictions may also require us to temporarily terminate our clinical sites. Furthermore, if we determine that our trial participants may suffer from exposure to COVID-19 as a result of their participation in our clinical trials, we may voluntarily terminate certain clinical sites as a safety measure until we reasonably believe that the likelihood of exposure has subsided. As a result, our expected development timelines for our product candidates may be negatively impacted. In addition, the COVID-19 pandemic has affected and may continue to affect the operations of the U.S. Food and Drug Administration and other regulatory authorities, which could result in delays of reviews and approvals with respect to our product candidates. We cannot predict the continuing impact of the COVID-19 pandemic, as consequences of such an event are highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts that have affected and may continue to affect our business, or our clinical studies in general. The COVID-19 pandemic has already adversely affected our operations and may further materially disrupt or delay our business operations, further divert the attention and efforts of the medical community to coping with COVID-19, disrupt the marketplace in which we operate, and/or have continuing material adverse effects on our operations.

Additionally, Phase 1 trials are ongoing for drug candidates IMU-935 and IMU-856 in Australia. Such Phase 1 trials are customarily conducted in healthy volunteers who have no potential benefits from participation in such trials. Hence, Phase 1 trials usually are subject to more strict evaluation and assessments during pandemic periods. Such Phase 1 trials may for that reason be interrupted or delayed.

Moreover, the various precautionary measures taken by many governmental authorities throughout the world in order to limit the spread of COVID-19 have had and may continue to have an adverse effect on the global markets and global economy generally, including on the availability and pricing of employees, resources, materials, manufacturing and delivery efforts and other aspects of the global economy. There have been business closures and a substantial global reduction in economic activity as a result of COVID-19. Significant uncertainty remains as to the full impact of the COVID-19 pandemic on the global economy. We cannot currently predict the duration of the pandemic or its impact on global or regional economic activity. The COVID-19 pandemic could continue to disrupt our business and operations, interrupt our sources of supply, hamper our ability to raise additional funds or sell our securities, continue to slow down the overall economy or curtail consumer spending.

Our clinical trials could be delayed or suspended as a result of the threatened military action by Russia in the Ukraine.

We are currently conducting several clinical trials of vidofludimus calcium at more than 60 sites in total for both Ukraine and Russia, currently involving a total of approximately 100 participants. Over 100,000 Russian military troops are reportedly massed on the Ukraine border and prepared for an invasion of Ukraine. Any invasion or military conflict----or even its threat and continued uncertainty----could materially disrupt our clinical trials, increase our costs and may disrupt future planned clinical development activities in these two countries. Although the route, length and impact of any military action are highly unpredictable, clinical trial sites in Ukraine could suspend or terminate trials, and patients could be forced to evacuate or voluntarily choose to relocate far from clinical trial sites, making them unavailable for further dosing or necessary follow-up. The United States and other nations have also threatened to impose economic and other sanctions on Russia for aggression in Ukraine. Any such sanctions could adversely affect clinical trials we are currently conducting or are planning to be conducted in Russia by delaying or preventing their completion and increasing our costs. Alternative sites to fully and timely compensate for our clinical trial activities in Ukraine or Russia may not be available. If our clinical trials are interrupted, we may have insufficient data to support regulatory approvals of vidofludimus calcium, and any commercialization may be delayed, which could limit our potential revenue and hurt the competitive position of our products.

Risks Related to Our Business and Financial Condition

We have a limited operating history with our current business plan, have incurred significant losses since 2016, anticipate that we will continue to incur significant and increasing losses for the foreseeable future and may never achieve or maintain profitability. The absence of any commercial sales and our limited operating history make it difficult to assess our future viability.

We are a development-stage pharmaceutical company with a limited operating history with our current business plan. Our net losses were $92.9 million and $44.0 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $196.9 million to date and have not generated any revenue from our current product candidates. Moreover, Immunic AG, the company's operating subsidiary, has only a limited operating history upon which stockholders can evaluate our business and prospects, is not profitable and has incurred losses in each year since its inception in 2016. In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biotechnology industry.

We have devoted substantially all of our financial resources to identify, acquire and develop our product candidates, including providing general and administrative support for our operations. We expect our losses to increase as we continue to conduct clinical trials and continue to develop our lead product candidates. We expect to invest significant funds into the research and development of our current product candidates to determine the potential to advance these product candidates to seek regulatory approval. To date, we have financed our operations primarily through the sale of equity securities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations or grants.

We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for, and successfully commercialize, any current or future product candidate. However pharmaceutical product development is an extremely costly and highly speculative undertaking and involves a substantial degree of risk. In addition, if we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive regulatory approval, and our ability to achieve sufficient market acceptance, pricing, reimbursement from third-party payors, and adequate market share for our product candidates. Even if we eventually obtain adequate market share for our product candidates, to the extent they receive regulatory and market approval, the potential markets for our product candidates may not be large enough for us to become profitable.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, and our expenses will increase substantially if and as we:

- continue the clinical development of our product candidates;
- continue efforts to discover, develop and/or acquire new product candidates;
- undertake the manufacturing of our product candidates for clinical development and, potentially, commercialization, or increase volumes manufactured by third parties;
- advance our programs into larger, more expensive clinical trials;
- initiate additional preclinical, clinical, or other trials or studies for our product candidates;
- seek regulatory and marketing approvals and reimbursement for our product candidates;
- experience any delays or encounter issues with the development and process for regulatory approval of our product candidates such as safety issues, clinical trial accrual delays, longer follow-up for planned studies, additional major studies or supportive studies necessary to support marketing approval;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval and market for our self;
- make milestone, royalty or other payments under any third-party license agreements;
- seek to maintain, protect and expand our intellectual property portfolio;
- seek to retain current skilled personnel and attract additional personnel; and
- add operational, financial and management, and information systems personnel, including personnel to support our product development and commercialization efforts.

Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. Failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, expand our pipeline of product candidates or continue our operations.

We currently have no source of product sales revenue and may never be profitable.

We have not generated any revenues from commercial sales of any of our current product candidates. Our ability to generate product revenue depends upon our ability to successfully commercialize these product candidates or other product candidates that we may develop, in-license or acquire in the future. We do not anticipate generating revenue from the sale of products for the foreseeable future. Our ability to generate revenue from our current or future product candidates also depends on a number of additional factors, including our ability to:

- successfully complete research and clinical development of current and future product candidates;
- establish and maintain supply and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of product candidates;
- obtain regulatory approval from relevant regulatory authorities in jurisdictions where we intend to market our product candidates;
- launch and commercialize any product candidates for which we obtain marketing approval, and if launched independently, successfully establish a sales force and marketing and distribution infrastructure;
- obtain coverage and adequate product reimbursement from third-party payors, including government payors;
- achieve market acceptance for any approved products;

- establish, maintain and protect our intellectual property rights; and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with clinical product development, including that our product candidates may not advance through development or achieve regulatory approval, we are unable to predict the timing or amount of any potential future product sale revenues. Our expenses also could increase beyond expectations if we decide to or are required by the FDA or comparable foreign regulatory authorities, to perform studies or trials in addition to those that we currently anticipate. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing any product candidates that may be approved.

We will require substantial additional funding, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or future commercialization efforts.

Since the inception of Immunic AG, substantially all of our resources have been dedicated to the clinical development of our product candidates. Developing pharmaceutical products, including conducting preclinical and non-clinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We have consumed substantial amounts of cash since our inception. For example, in the years ended December 31, 2021 and December 31, 2020, we used net cash of $83.8 million and $46.1 million, respectively, in our operating activities, substantially all of which related to development of our current product candidates. We believe that we will continue to expend substantial resources for the foreseeable future toward the completion of clinical development and regulatory preparedness of our product candidates, preparations for a commercial launch of any approved product candidates, and development of any other current or future product candidates we may choose to further develop. These expenditures will include costs associated with research and development, conducting preclinical studies and clinical trials, seeking marketing approvals, and manufacturing and supply as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of any drug development process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any current or future product candidates that may be approved for marketing.

Our operating plan may change as a result of factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations. Such financing may result in dilution to our stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements through the first quarter of 2023. Our estimate as to how long we expect our existing cash and cash equivalents to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume cash and cash equivalents significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing our current product candidates, future product candidates and related preclinical and clinical trials;
- the cost of commercialization activities if our current product candidates and future product candidates are approved for sale, including marketing, sales and distribution costs and preparedness of our corporate infrastructure;
- the cost of manufacturing current product candidates and future product candidates that we may obtain approval for and successfully commercialize;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such agreements;
- the number and characteristics of any additional product candidates we may develop or acquire;
- any product liability or other lawsuits related to our products or otherwise commenced against us;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property rights, including litigation costs and the outcome of any such litigation; and
- the timing, receipt and amount of sales of, or royalties on, any future approved products.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate:

- preclinical studies, clinical trials or other development activities for our current product candidates or any future product candidates;
- our research and development activities; or
- our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our future product candidates.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic collaborations and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of such equity or convertible debt securities may include liquidation or other preferences that adversely affect the rights of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, acquire or license intellectual property rights, redeem stock or declare dividends, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic collaborations and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

Risks Related to the Clinical Development and Marketing Approval of Our Product Candidates

The marketing approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our product candidates, our business will be substantially harmed.

None of our current product candidates have gained marketing approval for sale in the United States or any other country, and we cannot guarantee that we will ever have marketable products. Our business is substantially dependent on our ability to complete the development of, obtain marketing approval for, and successfully commercialize our product candidates in a timely manner. We cannot commercialize our product candidates in the United States without first obtaining approval from the FDA to market each product candidate. Similarly, we cannot commercialize our product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Our product candidates could fail to receive marketing approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- the FDA or comparable foreign regulatory authorities may find the human subject protections for our clinical trials inadequate and place a clinical hold on (i) an IND application at the time of its submission, precluding commencement of any trials, or (ii) one or more clinical trials at any time during the conduct of such trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an application to obtain marketing approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may find inadequate the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies of our product candidates; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner that would delay marketing approval.

Before obtaining marketing approval for the commercial sale of any drug product for a target indication, we must demonstrate in preclinical studies and well-controlled clinical trials and, with respect to approval in the United States, to the satisfaction of the FDA, that the product is safe and effective for its intended use and that the manufacturing facilities, processes and controls are adequate to preserve the drug's identity, strength, quality and purity. In the United States, it is necessary to submit and obtain approval of a new drug application ("NDA") from the FDA. The submission of an NDA is subject to the payment of substantial user fees ($3,117,218 for 2022); under certain limited circumstances, a waiver of such fees may be

obtained. An NDA must include extensive preclinical and clinical data and supporting information to establish the product safety and efficacy for each desired indication. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the product. After the submission of an NDA, but before approval of the NDA, the manufacturing facilities used to manufacture a product candidate must be inspected by the FDA to ensure compliance with the applicable current good manufacturing practice (“cGMP”) requirements. The FDA, the competent authorities of the member states of the European Economic Area, and comparable foreign regulatory authorities may also inspect our clinical trial sites and audit clinical study data to ensure that our studies are properly conducted in accordance with the IND regulations, human subject protection regulations, and current good clinical practice (“cGCP”).

Under the current Prescription Drug User Fee Act (“PDUFA”) guidelines, the FDA goal for acting on the submission of an NDA for a new molecular entity is ten months from the date of “filing.” The FDA conducts a preliminary review of an NDA within 60 days after submission to determine whether it is sufficiently complete to permit substantive review, before accepting the NDA for filing. This two month preliminary review effectively extends the typical NDA review period to twelve months. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Obtaining approval of an NDA is a lengthy, expensive and uncertain process, and approval may not be obtained. We cannot be certain that any submissions will be accepted for filing and reviewed by the FDA, or ultimately be approved. If an application is not accepted for review, the FDA may require that we conduct additional clinical studies or preclinical testing, or take other actions before it will reconsider our application. If the FDA requires additional studies or data, we would incur increased costs and delays in the marketing approval process, which may require us to expend more resources than we have available. In addition, the FDA may not consider any additional information to be complete or sufficient to support the filing or approval of the NDA.

Regulatory authorities outside of the United States, such as in Europe and Japan and in emerging markets, also have requirements for approval of drugs for commercial sale with which we must comply prior to marketing in those jurisdictions. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates into the relevant markets. Clinical trials conducted in one country may not be accepted or the results may not be found adequate by regulatory authorities in other countries, and obtaining regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. However, the failure to obtain regulatory approval in one jurisdiction could have a negative impact on our ability to obtain approval in a different jurisdiction. Approval processes vary among countries and can involve additional product candidate testing and validation and additional administrative review periods. Seeking foreign regulatory approval could require additional non-clinical studies or clinical trials, which could be costly and time-consuming. Foreign regulatory approval may be subject to all of the risks associated with obtaining FDA approval. For all of these reasons, we may not obtain foreign regulatory approvals on a timely basis, if at all.

The process to develop, obtain marketing approval for, and commercialize product candidates both inside and outside of the United States is long, complex and costly, and approval is never guaranteed. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary between jurisdictions. Even if our product candidates were to successfully obtain approval from regulatory authorities, any such approval might significantly limit the approved indications for use, including conditioning approval on the requirement of (i) more limited patient populations, (ii) precautions, warnings or contraindications on the product labeling, including “black box” warnings, (iii) expensive and time-consuming post-approval clinical studies, risk evaluation and mitigation strategies ("REMS"), or surveillance, or (iv) limiting the claims that the product label may make, any of which may impede the successful commercialization of our product candidates. Following any approval for commercial sale of our product candidates, certain changes to the product, such as changes in manufacturing processes and additional labeling claims, as well as new safety information, may require new studies and will be subject to additional FDA notification, or review and approval. Also, marketing approval for any of our product candidates may be withdrawn. If we are unable to obtain and maintain marketing approval for our product candidates in one or more jurisdictions, or any approval contains significant limitations, our ability to market our product candidates to our full target market will be reduced and our ability to realize the full market potential of our product candidates will be impaired. Furthermore, we may not be able to obtain sufficient funding or generate sufficient revenue and cash flows to continue or complete the development of any of our current or future product candidates.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. The FDA and comparable foreign regulatory authorities have substantial discretion when and if to grant approval to our product candidates. Even if we believe the data collected from clinical trials of our current product candidates are promising, such data may not be sufficient to support approval by the FDA or comparable foreign regulatory authorities. Our future clinical trial results also may not be successful.

It is impossible to predict the extent to which the clinical trial process may be affected by existing or prospective legislative and regulatory developments. Due to these and other factors, our current or future product candidates could take significantly longer than expected to gain marketing approval, if at all. This could delay or eliminate any potential product revenue by delaying or terminating the potential commercialization of our current product candidates.

Preclinical studies must also be conducted in accordance with FDA and comparable foreign regulatory authorities' legal requirements, regulations or guidelines, including Good Laboratory Practice ("GLP"), an international standard meant to harmonize the conduct and quality of non-clinical studies and the archiving and reporting of findings. Preclinical studies, including long-term toxicity studies and carcinogenicity studies in experimental animals, may require further evaluation, which could affect the risk-benefit evaluation of clinical development, or which may even lead the regulatory agencies to delay, prohibit the initiation of or halt clinical trials or delay or deny marketing authorization applications. Failure to adhere to the applicable GLP standards or misconduct during the course of preclinical studies may invalidate the data and require repeating one or more studies or conducting additional testing.

Clinical trials must also be conducted in accordance with legal requirements, regulations or guidelines of the FDA and comparable foreign regulatory authorities, including human subject protection requirements and GCP. Clinical trials are subject to further oversight by these governmental agencies and institutional review boards ("IRBs") at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our current product candidates produced under cGMP and other requirements. Our clinical trials are conducted at multiple sites, including some sites in countries outside the United States and the European Union, which may subject us to further delays and expenses as a result of increased shipment costs, additional regulatory requirements and the engagement of foreign and non-European Union contract research organizations ("CROs"), as well as expose us to risks associated with clinical investigators who are unknown to the FDA or European regulatory authorities, and with different standards of diagnosis, screening and medical care.

To date, we have not completed all clinical trials required for the approval of any of our current product candidates. The commencement and completion of clinical trials for our current 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 a clinical trial at a prospective trial site;
- changes in regulatory requirements, policies and guidelines;
- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- failure to reach agreement on acceptable terms with prospective CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in patient enrollment and variability in the number and types of patients available for clinical trials;
- the inability to enroll a sufficient number of patients in trials to ensure adequate statistical power to detect statistically significant treatment effects;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- clinical sites deviating from trial protocols or dropping out of a trial;
- adding new clinical trial sites;
- negative or inconclusive results, which may require us to conduct additional preclinical or clinical trials or to abandon projects that we expect to be promising;
- safety or tolerability concerns, which could cause us to suspend or terminate a trial if we find that participants are 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;
- our third-party research and manufacturing contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- third-party researchers becoming debarred or otherwise penalized by FDA or other regulatory authorities for violations of regulatory requirements, which could call into question data collected by such researcher and potentially affecting our ability rely on some or all of the data in support of our marketing applications;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;

- delays in establishing the appropriate dosage levels;
- the quality or stability of our current product candidates falling below acceptable standards;
- the inability to produce or obtain sufficient quantities of our current product candidates to complete clinical trials; and
- exceeding budgeted costs due to difficulty in accurately predicting the costs associated with clinical trials.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, and competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating.

There are significant requirements imposed on us and on clinical investigators who conduct clinical trials that we sponsor. Although we are responsible for selecting qualified clinical investigators, providing them with the information they need to conduct the clinical trial properly, ensuring proper monitoring of the clinical trial, and ensuring that the clinical trial is conducted in accordance with the general investigational plan and protocols contained in the IND, we cannot ensure that clinical investigators will maintain compliance with all regulatory requirements at all times. The pharmaceutical industry has experienced cases where clinical investigators have been found to incorrectly record, omit, or even falsify data. We cannot ensure that the clinical investigators in our trials will not make mistakes or otherwise compromise the integrity or validity of data, any of which would have a significant negative effect on our ability to obtain marketing approval, our business, and our financial condition.

We could encounter delays if a clinical trial is suspended or terminated by us, the IRBs or ethics committees of the institutions in which such trial is being conducted, the independent steering committee, the data safety monitoring board ("DSMB"), for such trial, or the FDA or comparable foreign regulatory authorities. We or such authorities may impose a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, safety issues or adverse side effects, failure to demonstrate a benefit from using the drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Delay or termination of clinical trials of our current product candidates will harm their commercial prospects and impair our ability to potentially generate revenues from such product candidates. In addition, any delays in completion of our clinical trials will increase our costs, slow our development and approval process and jeopardize our ability to commence product sales and generate revenues.

Moreover, clinical investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. We are required to report certain financial relationships with clinical investigators to the FDA and, where applicable, take steps to minimize the potential for bias resulting from such financial relationships. The FDA may evaluate the reported information and conclude that a financial relationship between us and a clinical investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site, and the utility of the clinical trial itself may be jeopardized. The FDA may refuse to accept our marketing applications, and other delays or even denial of marketing approval could result.

Preclinical testing or clinical trials of any development candidate may also show new and unexpected findings regarding safety and tolerability. Such findings may harm the ability to conduct further development of product candidates, delay such development, require additional expensive tests, harm our ability to partner these development candidates, or delay or prevent marketing approval by regulatory agencies. Such findings may also harm the ability to compete in the market with other products or to achieve certain pricing thresholds.

Any of these occurrences could materially adversely affect our business, financial condition, results of operations, and prospects. In addition, many of the factors that could cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval of our product candidates. Significant clinical trial delays could also allow our competitors to bring products to market before we can, shorten any periods during which we may have the exclusive right to commercialize any approved product candidates, and impair our ability to commercialize any approved product candidates, which may harm our business, financial condition, results of operations and prospects.

Use of patient-reported outcomes in our clinical trials may delay the development of our product candidates or increase development costs.

In recent years, due to regulatory changes, patient-reported outcomes ("PROs"), may have an important role in the development and regulatory approval of any of our product candidates. PROs involve patients' subjective assessments of efficacy, and this subjectivity increases the uncertainty in determining achievement of clinical endpoints. Such assessments can be influenced by factors outside of our control, and can vary widely from day-to-day for a particular patient, and from patient-to-patient and site-to-site within a clinical trial. Use of PROs may make the outcome of trials more uncertain and may increase our costs and time to finish regulatory approval trials.

Clinical failure can occur at any stage of clinical development. Because the results of earlier clinical trials are not necessarily predictive of future results, any product candidate we advance through clinical trials may not have favorable results in later clinical trials or receive marketing approval.

Clinical failure can occur at any stage of clinical development. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of pharmaceutical companies have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical or preclinical testing. Data obtained from trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent marketing approval of our product candidates. In addition, the design of a clinical trial can determine whether its results will support approval of a product, or approval of a product for desired indications, and flaws or shortcomings in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to properly design and execute a clinical trial to support marketing approval for our desired indications. Further, clinical trials of product candidates often reveal that it is not practical or feasible to continue development efforts. If one of our product candidates is found to be unsafe or lack efficacy, we will not be able to obtain marketing approval for such product candidate and our business would be harmed. For example, if the results of our clinical trials of our product candidates do not achieve pre-specified endpoints, we are unable to provide primary or secondary endpoint measurements deemed acceptable by the FDA or comparable foreign regulators, or we are unable to demonstrate an acceptable level of safety relative to the efficacy associated with our proposed indications, the prospects for approval of our product candidates would be materially and adversely affected. A number of companies in the pharmaceutical industry, including those with greater resources and experience than we, have suffered significant setbacks in Phase 2 and Phase 3 clinical trials, even after seeing promising results in earlier clinical trials.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including differences in trial protocols and design, the size and type of the patient population, adherence to the dosing regimen and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we may conduct will demonstrate consistent and/or adequate efficacy and safety to obtain marketing approval for our product candidates.

Marketing approval may be substantially delayed or may not be obtained for one or all of our product candidates if regulatory authorities require additional or more time-consuming studies to assess the safety and efficacy of our product candidates.

We may be unable to initiate or complete development of our product candidates on schedule, if at all. The completion of the studies for our product candidates will require additional funding. In addition, if regulatory authorities require additional or more time-consuming studies to assess the safety or efficacy of our product candidates, we may not have or be able to obtain adequate funding to complete the necessary steps for approval for any or all of our product candidates. Additional delays may result if the FDA, an FDA advisory committee (if one is convened to review our NDA) or other regulatory authority indicates that the product candidate should not be approved or there should be restrictions on approval, such as the requirement for a REMS, to ensure safe use of the drug. Delays in marketing approval or rejections of applications for marketing approval in the United States or other markets may result from many factors, including:

- the FDA or comparable foreign regulatory authorities disagreeing with the design or implementation of our clinical trials;
- regulatory requests for additional analyses, reports, data, non-clinical and preclinical studies and clinical trials;
- the FDA or comparable regulatory authorities questioning or disagreeing with our interpretations of data and results;
- the emergence of new information regarding our current or future product candidates or the field of research;

- unfavorable or inconclusive results of clinical trials and supportive non-clinical studies, including unfavorable results regarding safety or efficacy of our product candidates during clinical trials;
- failure to meet the level of statistical significance required for approval;
- inability to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- lack of adequate funding to commence or continue our clinical trials due to unforeseen costs or other business decisions;
- regulatory authorities may find inadequate the manufacturing processes or facilities of the third-party manufacturers with which we contract for clinical and commercial supplies;
- we may have insufficient funds to pay the significant user fees required by the FDA upon the filing of an NDA; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner that would delay marketing approval.

The lengthy and unpredictable approval process, as well as the unpredictability of future clinical trial results, may result in our failure to obtain marketing approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

Our product candidates may cause undesirable adverse effects or have other properties that could delay or prevent their marketing approval, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if obtained.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or other comparable foreign regulatory authorities. If any of our current or future product candidates is associated with serious adverse, undesirable or unacceptable side effects, we may need to abandon such candidate's development or limit development to certain uses or sub-populations in which such side effects are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many drug candidates that initially showed promise in early-stage or clinical testing have later been found to cause side effects that prevented their further development. Results our trials could reveal a high and unacceptable prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Drug-related side effects could also adversely affect patient recruitment or the ability of enrolled patients to complete the trial, or could result in potential product liability claims.

If our product candidates receive 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:

- regulatory authorities may withdraw approvals of such products;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing process for the product or any component thereof;
- regulatory authorities may require the addition of labeling statements, such as a precaution, "black box" warning or other warnings or a contraindication;
- we or our collaborators may be required to implement a REMS or create a medication guide outlining the risks of such side effect for distribution to patients;
- we or our collaborators could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation would suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of any approved product candidates, and could materially adversely affect our business, financial condition, results of operations and prospects.

We are heavily dependent on the success of our product candidates, most of which are in the early stages of clinical development. We may not be able to generate data for any product candidates sufficient to receive regulatory approval in its planned indications, which will be required before it can be commercialized.

We have invested substantially all of our efforts and financial resources to identify, acquire and develop our portfolio of product candidates. Our future success is dependent on our ability to successfully further develop, obtain regulatory approval for, and commercialize one or more product candidates. We currently generate no revenue from sales of any products, and we may never be able to develop or commercialize a product candidate.

Our most advanced product candidate, vidofludimus calcium, had the first patient enrolled in a Phase 3 program for RMS in November 2021. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA 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 trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

We may use our financial and operational resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and operational resources, we may forego or delay pursuit of opportunities in some programs, product candidates or indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or more profitable market opportunities. Our spending on current and future research and development programs and future product candidates for specific indications may not yield any commercially viable products. We may also enter into additional strategic collaboration agreements to develop and commercialize some of our programs and potential product candidates in indications with potentially large commercial markets. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may (i) relinquish valuable rights to that product candidate through strategic collaborations, licensing or other royalty arrangements when it would have been more advantageous to retain sole development and commercialization rights to such product candidate, or (ii) allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a collaborative arrangement.

We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates are being studied. Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates.

Identifying and qualifying sufficient numbers of eligible patients to participate in clinical trials of our product candidates is essential to our success. The timing of our clinical trials depends in part on the rate at which we can recruit eligible patients to participate in clinical trials of our product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment.

The specific eligibility criteria of our planned clinical trials may further limit the population of available eligible trial participants. We may not be able to identify, recruit, and enroll a sufficient number of eligible patients to initiate or complete our clinical trials in a timely manner because of the perceived risks and benefits of the product candidate under study, the availability and efficacy of competing therapies and clinical trials, and the willingness of physicians to participate in our planned clinical trials. If patients are unwilling to participate in our clinical trials for any reason, the timeline for conducting trials and obtaining regulatory approval of our product candidates may be delayed.

If we experience delays in the completion of, or experiences termination of, any clinical trials of our product candidates, the commercial prospects of our product candidates could be harmed, and our ability to generate product revenue from product candidates could be delayed or impaired. In addition, any delays in initiating or completing clinical trials would likely increase our overall costs, impair product candidate development and impair our ability to obtain regulatory approval. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Even if we receive marketing approval for any of our product candidates, such approved products will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, any approved product candidates could be subject to labeling and other restrictions, and we may be subject to penalties and legal sanctions if we fail to comply with regulatory requirements or experience unanticipated problems with any of our approved products.

If the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, packaging, distribution, adverse event reporting, storage, labeling, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP regulations and GCP for any clinical trials that we conduct post-approval. Any marketing 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 subject to conditions of approval, or contain requirements for potentially costly post-approval studies, including Phase 4 clinical trials,

and surveillance to monitor safety and efficacy. The FDA may also require us to implement a Risk Evaluation and Mitigation Strategy drug safety program as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools

Later discovery of previously unknown problems with an approved product, including adverse events of unanticipated severity or frequency, or problems with manufacturing operations or processes, or failure to comply with regulatory requirements, or evidence of acts that raise questions about the integrity of data supporting the product approval, may result in, among other things:

- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- 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, untitled letters, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay marketing approval, manufacturing or commercialization of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or other jurisdictions. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or not able to maintain regulatory compliance, we may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

The occurrence of any event described above may limit our ability to commercialize any approved product candidates and harm our business, financial condition, and prospects significantly.

If we fail to obtain regulatory approval in jurisdictions outside the United States, we will not be able to market our products in those jurisdictions.

We intend to market any approved product candidates in international markets, either ourselves or in conjunction with collaborators. Such marketing will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The approval procedures vary from country to country and may require testing in addition to what is required for a marketing application in the United States. Moreover, the time required to obtain approval in other countries may be different than in the United States. In addition, in many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval in another jurisdiction. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval and additional or different risks. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market, which would significantly harm our business, results of operations and prospects.

Agencies like the FDA and national competition regulators in European countries strictly regulate the marketing and promotion of drugs. If we are found to have improperly promoted any of our product candidates for uses beyond those that are approved, we may become subject to significant liability.

Regulatory authorities like the FDA and national competition laws in Europe strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or comparable foreign regulatory authorities as reflected in the product's approved labeling, known as "off-label" use, nor may a product be promoted prior to marketing approval. If we receive marketing approval for a product candidate for its proposed indication(s), physicians may nevertheless prescribe the product for their patients in a manner that is inconsistent with the approved label if the physicians personally believe in their professional medical judgment it could be used in such manner. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

In addition, the FDA requires that promotional claims not be "false or misleading" as such terms are interpreted by the FDA. For example, the FDA requires substantial evidence, which generally consists of two adequate and well-controlled head-

to-head clinical trials, for a company to make a claim that its product is superior to another product in terms of safety or effectiveness. Generally, unless we perform clinical trials meeting that standard comparing our product candidates to competing products and these claims are approved for our product labeling, we will not be able promote our product candidates as superior to competing products.

In the United States, regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted our product, including for an off-label use, we may become subject to significant liability. Numerous drug manufacturers have been the subject of investigations related to off-label promotion resulting in multi-billion dollar settlements, consent decrees, and on-going monitoring under corporate integrity agreements or deferred prosecution agreements. In addition, the FDA could also seek permanent injunctions under which specified promotional conduct is monitored, changed or curtailed.

Our current and future relationships with healthcare professionals, investigators, consultants, collaborators, actual customers, potential customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, physician payment transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to sanctions.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any drug candidates for which we may obtain marketing approval. Our current and future arrangements with healthcare professionals, investigators, consultants, collaborators, actual customers, potential customers and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act ("FCA"), which may constrain the business or financial arrangements and relationships through which we sell, market and distribute any drug candidates for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy and security regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct business. The applicable federal, state and foreign healthcare laws that may affect our ability to operate include the following:

- The federal 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, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid. Remuneration has been interpreted broadly to include anything of value. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and those activities may be subject to scrutiny or penalty if they do not qualify for an exemption or safe harbor. A conviction for violation of the Anti-Kickback Statute results in mandatory exclusion from participation in federal healthcare programs. This statute has been applied to arrangements between pharmaceutical manufacturers and those in a position to purchase products or refer others including prescribers, patients, purchasers and formulary managers. In addition, the Affordable Care Act amended the Social Security Act to provide that the U.S. government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute also constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act, the penalties for which are described below.

- Federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or for making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties (tied to inflation) of $11,803 to $23,607 (after December 13, 2021) per false claim or statement.
- The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal healthcare 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 Health Insurance Portability and Accountability Act of 1996 ("HIPAA") imposes criminal and civil penalties for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters.

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and its implementing regulations impose obligations on covered entities, including healthcare providers, health plans, and healthcare clearinghouses, as well as their respective business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.
- The federal Open Payments program, created under the Physician Payment Sunshine Act, also known as Section 6002 of the Patient Protection and Affordable Care Act (the "Affordable Care Act"), and its implementing regulations, impose annual reporting requirements for certain manufacturers of drugs, devices, biologicals and medical supplies for payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. The SUPPORT for Patients and Communities Act expanded the scope of reporting such that companies must also report payments and transfers of value provided to other types of healthcare professionals. Failure to submit timely, accurately and completely the required information for all covered payments, transfers of value and ownership or investment interests may result in civil monetary penalties.
- There are many analogous state and foreign laws, such as: state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.
- The Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it.

Efforts to ensure that our future business arrangements with third parties comply with applicable healthcare laws and regulations may 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. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to it, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could significantly harm our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including current and any future collaborators, are found not to be in compliance with applicable laws, those persons or entities may be subject to criminal, civil or administrative sanctions, including exclusion from participation in government healthcare programs, which could also negatively affect our business.

We are subject to the U.S. Foreign Corrupt Practices Act and other anti-corruption laws, as well as import and export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties and other remedial measures, and incur legal expenses, which could adversely affect our business, financial condition, results of operations, stock price and prospects.

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act ("FCPA"), and other anti-corruption laws that apply in countries where we do, or may in the future do, business. The FCPA and these other laws generally prohibit us and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We also may participate in collaborations and relationships with third parties whose actions, if non-compliant, could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing or future laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States and authorities in the European Union, including applicable import and export control regulations, economic sanctions on countries and persons, anti-money laundering laws, customs requirements and currency exchange regulations, collectively referred to as trade control laws.

We may not be effective in ensuring our compliance with all applicable anti-corruption laws or other legal requirements, including trade control laws. If we are not in compliance with applicable anti-corruption laws or trade control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and incur legal expenses, which could have an adverse impact on our business, financial condition, results of operations, stock price and prospects. Likewise, any investigation of any potential violations of these anti-corruption laws or trade control laws by U.S. or other authorities could also have an adverse impact on our reputation, business, financial condition, results of operations, stock price and prospects.

The impact on us of recent and future healthcare reform legislation and other changes in the healthcare industry and healthcare spending is currently unknown, and may adversely affect our business model.

In the United States and some foreign jurisdictions, legislative and regulatory changes and proposed changes regarding the healthcare system could prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any drug candidates for which we obtain marketing approval.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and other jurisdictions. We operate in a highly regulated industry and new laws, regulations, judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery of, or payment for, healthcare products and services could negatively impact our business, financial condition, results of operations and prospects. There continues to be significant interest in promoting healthcare reform, as evidenced by the enactment in the United States of the Affordable Care Act and efforts to repeal, invalidate or modify portions of the act. Among other things, the Affordable Care Act contains provisions that may reduce the profitability of drug products, including, for example, revising the methodology by which rebates owed by manufacturers for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated, extending Medicaid rebates to individuals enrolled in Medicaid managed care plans, imposing mandatory discounts for certain Medicare Part D beneficiaries who fall into a coverage gap, and subjecting drug manufacturers to payment of an annual fee based on its market share of prior year total sales of branded programs to certain federal healthcare programs.

There have been judicial and congressional challenges to the Affordable Care Act, as well as efforts to repeal or replace certain aspects of the Affordable Care Act. If a new law is enacted, or if the Affordable Care Act is overturned, repealed or modified, in whole or in part, by judicial or legislative action, many if not all of the provisions of the Affordable Care Act may no longer apply to prescription drugs. While we are unable to predict what changes may ultimately be enacted, to the extent that future changes affect how any future prescription drug products are paid for and reimbursed by government and private payors, our business could be adversely impacted.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year, which started in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, also reduced Medicare payments to several categories of healthcare providers. The Biden administration and Congress may announce initiatives intended to result in lower drug prices. We are not in a position to know at this time whether such initiatives will become law or what impact they may potentially have on our business.

We expect that additional healthcare reform measures and drug pricing regulations that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the revenue that we may potentially receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue or commercialize our drug candidates.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any drug products for which we may obtain marketing approval;
- our ability to set a price for our products that we believe is fair;
- our ability to obtain coverage and reimbursement approval for a product approved for marketing;
- our ability to generate revenues and achieve or maintain profitability; and

- the level of taxes that we are required to pay.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business, financial condition or results of operations.

Our research and development activities and the activities of our contract manufacturers and suppliers involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at facilities of we and our manufacturers, pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, or the risk of environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our contract manufacturers and suppliers for handling and disposing of these materials generally comply with the standards prescribed by applicable laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In the event of contamination of injury, we may be held liable for any resulting damages, which could exceed our resources or result in government-imposed restrictions on our use of specified materials or interruptions of our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have generally tended to become more stringent over time. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

Other Risks Related to Our Business

If governing bodies in the United States or elsewhere implement a waiver on patents on COVID-19 vaccines, there could be a significant adverse effect on our business.

On May 5, 2021, the Biden Administration announced that it supports a waiver for patents on vaccines protecting against the coronavirus. The World Trade Organization supports a similar proposal. Any actions by governments of the United States or other countries or by international governing organizations that limit the ability of companies to enforce their patents or other technology could limit the value of our intellectual property and revenue potential for our product candidates.

Due to our limited resources and access to capital, we must decide to prioritize development of our current product candidates for certain indications and at certain doses. These decisions may prove to have been wrong and may materially adversely affect our business, financial condition, results of operations and prospects.

Because we has limited resources and access to capital to fund our operations, we must decide which dosages and indications to pursue for the clinical development of our current product candidates and the amount of resources to allocate to each. Our decisions concerning the allocation of research, collaboration, management and financial resources toward dosages or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from better opportunities. If we make incorrect determinations regarding the market potential of our current product candidates or if we misread trends in the pharmaceutical industry, our business, financial condition, results of operations and prospects could be materially adversely affected.

We may not be able to win contracts or grants from governments, academic institutions or non-profits.

From time to time, we may apply for contracts or grants from government agencies, non-profit entities and academic institutions. Such contracts or grants can be highly attractive because they provide capital to fund the ongoing development of our product candidates without diluting our stockholders. However, there is often significant competition for these contracts or grants. Entities offering contracts or grants may have requirements to apply for, or to otherwise be eligible for, certain contracts or grants that our competitors may be able to satisfy that we cannot satisfy. In addition, such entities may make arbitrary decisions as to whether to offer contracts or make grants, to whom the contracts or grants may or will be awarded and the conditions and size of the contracts or grants to each awardee. Even if we are able to satisfy the award requirements, we may not be able to win any contracts or grants in a timely manner, if at all.

In addition, even if we enter into contracts with or receives grants from government agencies, non-profit entities or academic institutions, we may lose such contracts or grants due to failure to comply with applicable terms, limitations, or government regulations. As a result, our business, results of operations, financial condition and prospects could be harmed.

If we fail to attract and retain key management and scientific personnel, we may be unable to successfully develop or commercialize our product candidates.

Our success as a biotechnology company depends on our continued ability to attract, retain and motivate highly qualified management and scientific and clinical personnel. The loss of the services of any such personnel could delay or prevent obtaining marketing approval or commercialization of our product candidates.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for a limited number of qualified personnel among biotechnology, pharmaceutical and other companies. Our failure to attract, hire, integrate and retain qualified personnel could impair our ability to achieve our business objectives.

If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of applicable insurance coverage, we could be forced to pay substantial damage awards.

The use of any of our product candidates in clinical trials and the sale of any approved products may expose us to product liability claims. We currently maintain a limited amount of product liability insurance. We intend to monitor the amount of coverage we maintain as the size and design of our clinical trials evolve and seek to adjust the amount of coverage we maintain accordingly. However, we may not maintain insurance coverage that adequately protects us against some or all of the claims to which we might become subject. We might not be able to maintain adequate insurance coverage at a reasonable cost or in sufficient amounts or scope to protect us against potential losses. In the event a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as uncovered damages awards resulting from a claim brought against us. Furthermore, whether or not we are ultimately successful in defending any such claims, we might be required to divert substantial financial and managerial resources to such defense, and adverse publicity could result, all of which could harm our business.

We could have liability if our employees, independent contractors, investigators, CROs, consultants, collaborators and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees and other parties with which we do business may engage in fraudulent conduct or other illegal activity. Misconduct by employees and other parties could include intentional, reckless and/or negligent conduct or violation of FDA regulations and laws that require reporting true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare fraud and abuse laws and regulations, or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commissions, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee and other third-party 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 be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate. Even if we are ultimately successful in defending any such actions, we could be required to divert financial and managerial resources to such action and adverse publicity could result, all of which could harm our business.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

We currently have approximately 55 employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial, legal and other resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing our growth. As we advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these

capabilities. As our operations expand, we expect that we will need to manage additional relationships with such third parties, as well as additional collaborators and suppliers.

We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure and internal controls, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Our internal computer systems, or those of our development collaborators, third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future strategic collaborators, vendors, and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, cybersecurity threats, war and telecommunication and electrical failures. We may experience cyber-attacks on our information technology systems by threat actors of all types (including but not limited to nation states, organized crime, other criminal enterprises, individual actors and/or advanced persistent threat groups). In addition, we may experience intrusions on our physical premises by any of these threat actors. If any such cyber-attack or physical intrusion were to cause interruptions in our operations, such as a material disruption of our development programs or our manufacturing operations, whether due to a loss of our trade secrets or other proprietary information, it would have a material and adverse effect on us. For example, the loss of clinical trial data from one or more ongoing or completed or future clinical trials could result in delays in our regulatory approval efforts, significantly increase our costs to recover or reproduce the data and expose us to liability. In addition, any breach of our computer systems or physical premises could result in a loss of data or compromised data integrity across more than one of our programs in different stages of development. Any such breach, loss, or compromise of clinical trial participant personal data may also subject us to civil fines and penalties or claims for damages, either under the General Data Protection Regulation and relevant member state law in the European Union, other foreign laws, and HIPAA, and other relevant state and federal privacy laws in the United States including the California Consumer Privacy Act. On May 13, 2020, the Federal Bureau of Investigation ("FBI") and Cybersecurity and Infrastructure Security Agency announced that the FBI is investigating the targeting and compromise of U.S. organizations conducting COVID-19-related research by People's Republic of China-affiliated cyber actors. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, including but not limited to information related to our vidofludimus calcium product candidate, we could incur liability, our competitive and reputational position could be harmed, and the further development and commercialization of our investigational medicines could be delayed. On July 31, 2020 we discovered that an email account at the Company was subject to attempted unauthorized access for a period of up to 24 hours and we hired an investigator to ascertain what, if any, Company or patient information was impacted. We do not believe any confidential or proprietary information was compromised and have taken steps to prevent unauthorized action in the future such as implementing two factor authentication for our email accounts. While we believe that our insurance policies include liability coverage for security breaches, we could be subject to indemnity claims or other damages that exceed, or are outside the scope of, our insurance coverage. As a result, the ramifications of a potential security breach could have a material adverse effect on our business, financial condition, results of operations and prospects, as well as cause a decline in the trading price of our common stock.

Risks Related to Commercialization of Our Product Candidates

Even if we obtain the required regulatory approvals in the United States and other territories, the commercial success of our product candidates will depend on market awareness and acceptance of our product candidates.

Even if we obtain marketing approval for our current product candidates or any other product candidates that we may develop or acquire in the future, our products may not gain market acceptance among physicians, key opinion leaders, healthcare payors, patients and the medical community. Market acceptance of any approved products depends on a number of factors, including:

- the timing of market introduction;
- the efficacy and safety of the product, as demonstrated in clinical trials;
- the clinical indications for which the product is approved and the label approved by regulatory authorities for use with the product, including any precautions, warnings or contraindications that may be required on the label;
- acceptance by physicians, key opinion leaders and patients of the product as a safe and effective treatment;
- the cost, safety and efficacy of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement and pricing by third-party payors and government authorities;

- the number, cost and clinical profile of competing products;
- the growth of drug markets in our various indications;
- relative convenience and ease of administration;
- marketing and distribution support;
- the prevalence and severity of adverse side effects; and
- the effectiveness of our sales and marketing efforts.

Market acceptance is critical to our ability to generate revenue. Any approved and commercialized product candidate may be accepted in only limited capacities or not at all. If any approved products are not accepted by the market to the extent that we expect, we may not be able to generate sufficient revenue and our business would suffer.

We currently have limited marketing and sales experience. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

We have never commercialized a product candidate, and we currently have no marketing and sales organization. To the extent our product candidates are approved for marketing, if we are unable to establish marketing and sales capabilities or enter into agreements with third parties to effectively market and sell our product candidates, we may not be able to successfully market and sell our product candidates or generate product revenue.

In addition, we currently do not have marketing, sales or distribution capabilities for our product candidates. In order to commercialize any of our products that receive marketing approval, we would have to build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In the event of successful development of our product candidates, if we elect to build a targeted specialty sales force, such an effort would be expensive and time consuming. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may choose to collaborate with third parties that have their own sales forces and established distribution systems, in lieu of or to augment any sales force and distribution systems we may create. If we are unable to enter into collaborations with third parties for the commercialization of any approved products on acceptable terms or at all, or if any such collaborator does not devote sufficient resources to the commercialization of our product or otherwise fails in commercialization efforts, we may not be able to successfully commercialize our product candidates even if we receive marketing approval. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future revenue will be materially and adversely impacted.

If we fail to enter into strategic relationships or collaborations, 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 current product candidates will require substantial additional cash to fund expenses. Therefore, in addition to financing the development of our product candidates through additional equity financings or through debt financings, we may decide to enter into collaborations with pharmaceutical or biopharmaceutical companies for the development and potential commercialization of our product candidates in the United States or foreign markets.

We face significant competition in seeking appropriate collaborators. Collaborations are complex and time-consuming to negotiate and document. We may also be restricted under existing and future collaboration agreements from entering into agreements on certain terms with other potential collaborators. We may not be able to negotiate collaborations on acceptable terms, or at all. Any of these contingencies may require us to curtail the development of a particular product, reduce or delay one or more of our development programs, delay our 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. 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 any approved product candidates to market and generate product revenue. If we do enter into a new collaboration agreement, 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 or timing of resources that the collaborator devotes to the product development program;
- the collaborator may experience financial difficulties and thus not commit sufficient financial resources or personnel to the product development program;
- we may be required to relinquish important rights such as marketing, distribution and intellectual property rights;

- a collaborator 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 collaborator's business strategy may adversely affect our or the collaborator's willingness to complete our respective obligations under any arrangement.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our products profitably.

The pricing, coverage, and reimbursement of any of our approved products must be sufficient to support our commercial efforts and other development programs, and the availability and adequacy of coverage and reimbursement by third-party payors, including governmental and private insurers, are essential for most patients to be able to afford expensive treatments. Sales of any of our approved product candidates will depend substantially, both domestically in other jurisdictions, on the extent to which the costs of any of our approved products will be paid for or reimbursed by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or government payors and private payors. If coverage and reimbursement are not available, or are available only in limited amounts, we may have to subsidize or provide products for free or we may not be able to successfully commercialize our products.

In addition, there is significant uncertainty related to the insurance coverage and reimbursement for newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services ("CMS"), an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for our novel product candidates and what reimbursement codes our product candidates may receive if approved. There also may be delays in obtaining coverage for newly-approved drugs. Obtaining coverage and reimbursement approval is time-consuming and costly, requiring us to provide payors with scientific, clinical, and cost-effectiveness data. Further, eligibility for coverage does not necessarily signify that a drug will be reimbursed in all cases or at a rate that covers our costs. Thus, even if we succeed in bringing a product to market, it may not be considered medically necessary or cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis.

Outside the United States, international operations are generally subject to extensive governmental price controls and other price-restrictive regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of products. In many countries, the prices of products are subject to varying price control mechanisms as part of national health systems. Price controls or other changes in pricing regulation could restrict the amount that we may be able to charge for any of our products. Accordingly, the potential revenue and profits from markets outside the United States may be commercially inadequate.

Moreover, increasing efforts by governmental and private payors in the United States and other jurisdictions to limit or reduce healthcare costs may result in restrictions on coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with products due to the increasing trend toward managed healthcare, including the increasing influence of health maintenance organizations, pharmacy benefit management organizations and additional legislative changes. The downward pressure on healthcare costs in general, and prescription drugs in particular, has and is expected to continue to increase in the future. For instance, government and private payors who reimburse patients or healthcare providers are increasingly seeking greater upfront discounts, additional rebates and other concessions to reduce prices for pharmaceutical products. As a result, it may be difficult for any of our products to achieve profitability, even if they receive regulatory approval.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide with respect to our product candidates that we may seek to develop or commercialize in the future. Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in preclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies, and other public and private organizations

conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors.

In particular, the field of inflammatory bowel disease, including ulcerative colitis and Crohn's disease, are highly competitive. Our competitors in the United States and elsewhere include major pharmaceutical, biotechnology and biosimilar manufacturers. Some of these competitors may have more extensive research and development, regulatory compliance, manufacturing, marketing and sales capabilities than we have. Many competitors also have significantly greater financial resources. These companies may succeed in developing products that are more effective or more economical than any of our product candidates and may also be more successful than we in manufacturing, developing and obtaining regulatory approvals and reimbursement for products. In addition, technological advances or different approaches developed by one or more of our competitors may render our products obsolete, less effective or uneconomical.

If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than we do, they could establish a strong market position before we are able to enter the market. Third-party payors, including governmental and private insurers, also may encourage the use of generic products. Failure of any approved product candidates of ours to effectively compete against established treatment options or to compete in the future with new products currently in development would harm our business, financial condition, results of operations and prospects.

The size of the potential market for our product candidates is difficult to estimate and, if any of our assumptions are inaccurate, the actual markets for our product candidates may be smaller than our estimates.

The potential market opportunities for our product candidates are difficult to estimate and will depend on a number of factors beyond our control. Our estimates of potential market opportunities are predicated on many assumptions, which may include industry knowledge and publications, third-party research reports, and other surveys. Although we believe that our internal assumptions are reasonable based on currently available information, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain, and their reasonableness has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be substantially smaller than our estimates.

Negative developments in the field of oral therapies for chronic inflammatory and autoimmune diseases could damage public perception of our product candidates and negatively affect our business.

The commercial success of our product candidates will depend in part on public acceptance of the use of oral therapies for the treatment of chronic inflammatory and autoimmune diseases. Adverse events in clinical trials of our product candidates or in clinical trials of others developing similar products and the resulting publicity, as well as any other negative developments that may occur in the future, including in connection with competitors' therapies, could result in a decrease in demand for our product candidates. These events could also result in the suspension, discontinuation, or clinical hold of, or modifications to, our clinical trials. Our product candidates may not be accepted by the general public or the medical community and potential clinical trial subjects may be discouraged from enrolling in our clinical trials. As a result, we may not be able to continue, or may be delayed in conducting, our development programs.

Price controls may be imposed in foreign markets, which may adversely affect our future profitability.

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

Risks Related to Third Parties

We 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 do not currently own or operate manufacturing facilities for clinical or commercial production of our product candidates. We lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. Instead, we rely on, and expect to continue to rely on, third parties for the supply of raw materials and manufacture of drug supplies necessary to conduct our preclinical studies and clinical trials. Our reliance on third parties for manufacturing exposes us to additional risks. Delays in production by third parties could delay our clinical trials or have an adverse impact on any commercial activities. In addition, our dependence on third parties for the manufacture of and formulation of our product candidates subjects us to the risk that such products may have manufacturing defects that we has limited ability to prevent or control. Although we oversee these activities to ensure compliance with our quality standards, budgets and timelines, we have, and will continue to have, less control over the manufacturing of our product candidates than if we were to manufacture our product candidates. Further, the third parties we contract with could have staffing difficulties, might undergo changes in priorities or may become financially distressed, any of which would adversely affect the manufacturing and production of our product candidates. In addition, a third party could be acquired by, or enter into an exclusive arrangement with, one of our competitors, which would adversely affect our ability to access the formulations we require for the manufacturing of our product candidates.

The facilities used by our current contract manufacturers and any future manufacturers to manufacture our product candidates must be inspected by the FDA after we submits our NDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, the FDA may refuse to approve our NDA. If the FDA does not approve our NDA because of concerns about the manufacture of our product candidates, or if significant manufacturing issues arise in the future, we may need to find alternative manufacturing facilities, which would significantly delay and adversely impact our ability to develop our product candidates, obtain marketing approval of our NDA or to continue to market any approved product candidates. Although we are ultimately responsible for ensuring compliance with these regulatory requirements, we do not have day-to-day control over a contract manufacturing organization's ("CMO"), or other third-party manufacturer's compliance with applicable laws and regulations, including cGMPs and other laws and regulations, such as those related to environmental, health and safety matters. 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. In addition, third-party contractors, such as our CMOs, may elect not to continue to work with us due to factors beyond our control. They may also refuse to work with us because of their own financial difficulties, business priorities or other reasons, at a time that is costly or otherwise inconvenient for us. If we was unable to find adequate replacement or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed.

Problems with the quality of the work performed by third parties may lead us to seek to terminate our working relationships and use alternative service providers. However, making this change may be costly and may substantially delay clinical trials. In addition, it may be very challenging, and in some cases impossible, to find replacement service providers that can develop and manufacture our drug candidates in an acceptable manner and at an acceptable cost and on a timely basis. The sale of products containing any defects or any delays in the supply of necessary products or services could adversely affect our business, financial condition, results of operations, and prospects.

Growth in the costs and expenses of components or raw materials may also adversely affect our business, financial condition, results of operations, and prospects. Supply sources could be interrupted from time to time and, if interrupted, supplies may not be resumed (whether in part or in whole) within a reasonable timeframe and at an acceptable cost or at all.

We currently rely on and plan to continue to rely on third parties to conduct clinical trials for our product candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, it may cause delays in commencing and completing clinical trials of our product candidates or we may be unable to obtain marketing approval for or commercialize our product candidates.

Clinical trials must meet applicable FDA and foreign regulatory requirements. We do not have the ability to independently conduct clinical trials for any of our product candidates. We rely and expect to continue relying on third parties, such as CROs,

medical institutions, clinical investigators and contract laboratories, to conduct all of our clinical trials of our product candidates; however, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with our investigational plan and protocol. Moreover, the FDA and other foreign regulatory authorities require us to comply with IND and human subject protection regulations and cGCPs for conducting, monitoring, recording, and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. Our reliance on third parties does not relieve us of these responsibilities and requirements. Regulatory authorities enforce eGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable eGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There is no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with eGCPs. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the marketing approval process.

There are significant requirements imposed on us and on clinical investigators who conduct clinical trials that we sponsor. Although we are responsible for selecting qualified CROs or clinical investigators, providing them with the information they need to conduct the clinical trials properly, ensuring proper monitoring of the clinical trials, and ensuring that the clinical trials are conducted in accordance with the general investigational plan and protocols contained in the IND, we cannot ensure that the CROs or clinical investigators will maintain compliance with all regulatory requirements at all times. The pharmaceutical industry has experienced cases where clinical investigators have been found to incorrectly record data, omit data, or even falsify data. We cannot ensure that the CROs or clinical investigators in our trials will not make mistakes or otherwise compromise the integrity or validity of data, any of which would have a significant negative effect on our ability to obtain marketing approval, our business, and our financial condition.

We or the third parties we rely on may encounter problems in clinical trials that may cause us or the FDA or foreign regulatory agencies to delay, suspend or terminate our clinical trials at any phase. These problems could include the possibility that we may not be able to manufacture sufficient quantities of materials for use in our clinical trials, conduct clinical trials at our preferred sites, enroll a sufficient number of patients for our clinical trials at one or more sites, or begin or successfully complete clinical trials in a timely fashion, if at all. Furthermore, we, the FDA or foreign regulatory agencies may suspend clinical trials of our product candidates at any time if we or they believe the subjects participating in the trials are being exposed to unacceptable health risks, whether as a result of adverse events occurring in our trials or otherwise, or if we or they find deficiencies in the clinical trial process or conduct of the investigation. The FDA or foreign regulatory agencies could also require additional clinical trials before or after granting marketing approval for any products, which would result in increased costs and significant delays in the development and commercialization of such products and could result in the withdrawal of such products from the market even if marketing approval has already been obtained. Our failure to adequately demonstrate the safety and efficacy of a product candidate in clinical development could delay or prevent marketing approval of the product candidate. Even if market approval has already been obtained, adverse data from post-approval studies could result in the product being withdrawn from the market. Any of these occurrences would likely have a material adverse effect on our business.

We may be unable to realize the potential benefits of any collaboration.

Even if we are successful in entering into a collaboration with respect to the development and/or commercialization of one or more product candidates, the collaboration may not be successful. Collaborations pose a number of risks, including:

- collaborators often have significant discretion in determining the extent of efforts and resources that they will apply to the collaboration, and may not commit sufficient attention and financial or other resources to the development, marketing or commercialization of the product or products that are subject to the collaboration;
- collaborators may not perform their obligations as expected;
- any such collaboration may significantly limit our share of potential future profits from the associated program, and may require us to relinquish potentially valuable rights to our current product candidates, potential product candidates or proprietary technologies, or to grant licenses on terms that are not favorable to us;
- collaborators may cease to devote sufficient resources to the development or commercialization of our product candidates if the collaborators view our product candidates as competitive with their own products or product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the course of development, might cause delays or termination of the development or commercialization of product candidates, and might result in legal proceedings, which would be time-consuming, distracting and expensive;
- collaborators may be impacted by changes in their strategic focus or available funding, or business combinations involving them, which could cause them to divert resources away from the collaboration;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the collaborations may not result in our achieving revenues to justify such transactions; and
- collaborations may be terminated, which may require us to raise additional capital to pursue further development or commercialization of the applicable product candidate.

As a result, a collaboration may not result in the successful development or commercialization of our product candidates.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sublicensees' exercise of rights under the agreements.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

If our contract manufacturers fail to comply with continuing regulations, resulting enforcement action could adversely affect us.

If any of our contract manufacturers fail to comply with regulatory requirements or if previously unknown problems with products, manufacturers or manufacturing processes are discovered, we or the manufacturer could be subject to administrative or judicially imposed sanctions, including restrictions on the products or the manufacturers or manufacturing processes we use, warning letters, untitled letters, civil or criminal penalties, fines, injunctions, product seizures or detentions, import bans, voluntary or mandatory product recalls and publicity requirements, suspension or withdrawal of regulatory approvals, total or partial suspension of production, and refusal to approve pending applications for marketing approval of new products.

Risks Related to Our Intellectual Property

Our proprietary rights may not adequately protect our technologies and product candidates.

Our commercial success will depend in part on our ability to obtain additional patents and protect our existing patent position as well as our ability to maintain adequate protection of other intellectual property for our technologies, product candidates, and any future products in the United States and other countries. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. The laws of some foreign countries, in particular China and India, do not protect our proprietary rights to the same extent or in the same manner as U.S. laws, and we may encounter significant problems in protecting and defending our proprietary rights in these countries. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary technologies, product candidates and any future products are covered by valid and enforceable patents or are effectively maintained as trade secrets.

We apply for patents covering both our technologies and product candidates as we deem appropriate. However, we may fail to apply for patents on important technologies or product candidates in a timely fashion, or at all. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or developing competing products and technologies. We cannot be certain that our patent applications will be approved or that any patents issued will adequately protect our intellectual property.

Moreover, the patent positions of pharmaceutical companies are highly uncertain and involve complex legal and factual questions for which important legal principles are evolving and remain unresolved. As a result, the validity and enforceability of patents cannot be predicted with certainty. In addition, we do not know whether:

- we or our licensors were the first to make the inventions covered by each of our issued patents and pending patent applications;
- we or our licensors were the first to file patent applications for these inventions;

- any of the patents that cover our product candidates will be eligible to be listed in the FDA's compendium of "Approved Drug Products with Therapeutic Equivalence Evaluations," sometimes referred to as the FDA's Orange Book;
- others will independently develop similar or alternative technologies or duplicate any of our technologies;
- any of our or our licensors' pending patent applications will result in issued patents;
- any of our or our licensors' patents will be valid or enforceable;
- any patents issued to us or our licensors and collaborators will provide us with any competitive advantages, or will be challenged by third parties;
- we will develop additional proprietary technologies that are patentable;
- governmental authorities will exercise any of their statutory rights to our intellectual property that was developed with government funding; or
- our business may infringe the patents or other proprietary rights of others.

The actual protection afforded by a patent varies based on products or processes, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory related extensions, the availability of legal remedies in a particular country, the validity and enforceability of the patents and our financial ability to enforce our patents and other intellectual property rights. Our ability to maintain and solidify our proprietary rights to our product candidates and future products will depend on our success in obtaining effective claims and enforcing those claims once granted. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, narrowed, invalidated or circumvented, and the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar products. Due to the extensive amount of time required for the development, testing and regulatory review of a product candidate, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

We may also rely on trade secrets to protect some of our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to maintain. While we use reasonable efforts to protect our trade secrets, our or any of our collaborators' employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our proprietary information to competitors and we may not have adequate remedies in respect of such disclosure. Enforcement of claims that a third party has illegally obtained and is using trade secrets is expensive, time consuming and uncertain. In addition, foreign courts are sometimes less willing than U.S. courts to protect trade secrets. If our competitors independently develop equivalent knowledge, methods or know-how, we would not be able to assert our rights to trade secrets and our business could be harmed.

We are a party to license agreements under which we license intellectual property and receive commercialization rights relating to certain of our product candidates. If we fail to comply with obligations in such agreements or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business; any termination of such agreements would adversely affect our business.

We are a party to license agreements that give us various commercialization rights, the loss of which (whether due to our actions or inactions or those of the respective counterparties) may adversely affect our business. For instance, in November 2018, Immunic AG and Daiichi Sankyo entered into a license and option agreement that grants us an exclusive global option to license IMU-856 and related molecules. In January 2020, we exercised this option and acquired the rights to commercialization of IMU-856 in all countries including the U.S., Europe and Japan.

The loss of (i) the licenses granted to us under our agreements with Daiichi Sankyo and other licensors, or (ii) the rights provided under such agreements, would prevent us from developing, manufacturing or marketing products covered by the license or subject to supply commitments, and could materially harm our business, financial condition, results of operations and prospects.

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 United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our technologies in all countries outside the United States, or from selling or importing products made using our technologies in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where

we have not obtained patent protection, to develop their own products and further, may export otherwise infringing products to territories where we have patent protection but enforcement rights are weaker than in the United States. These products may compete with our product candidates in jurisdictions where we do not have any issued patents and our patent claims or other intellectual rights may not be effective or sufficient to prevent such competition.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries do not favor the enforcement of patents and other intellectual property rights, which could make it difficult for us to stop the infringement of our patents generally. Proceedings to enforce our patent rights in foreign jurisdictions 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 put 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 throughout the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, we may be unable to extend the term of marketing exclusivity for our product candidates and our business may be materially harmed.

Depending on the timing, duration and specifics of any FDA marketing approval of any of our product candidates, one of the U.S. patents covering each such approved product or the use thereof may be eligible for up to five years of patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act allows extension of a maximum of one patent per FDA-approved product. Patent term extension or special protection certificates also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, among other things, failing to apply prior to applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension afforded as well as the scope of patent protection during any such extension could be less than we request.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we or our collaborators request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following expiration of our patent, and our potential revenue could be materially reduced.

We may not identify relevant patents or may incorrectly interpret the relevance, scope or expiration of a patent, which could adversely affect our ability to develop and market our product candidates.

Our patent searches or analyses (including, but not limited to, the identification of relevant patents, the scope of patent claims or the expiration of relevant patents) might not be accurate, complete or thorough, and could fail to identify each and every patent and pending application in the United States and other jurisdictions that is or may potentially be relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

The scope of a patent claim is determined by legal interpretation, the written disclosure in a patent and the patent's prosecution history. If our interpretation of the relevance or the scope of a patent or a pending application is not accurate and we incorrectly determine that our product candidates are not covered by a third-party patent, we could be potentially liable for infringement, prevented from marketing our product candidate, or required to seek costly licenses from patent holders.

Many patents may cover a marketed product, including but not limited to patents covering the composition, methods of use, formulations, production processes and purification processes of or for the product. The identification of all patents and their expiration dates relevant to the production and sale of a therapeutic product is extraordinarily complex and requires sophisticated legal knowledge in the relevant jurisdiction. It may be impossible to identify all patents in all jurisdictions relevant to a marketed product. Our determination of the expiration date of any patent in the United States or other jurisdictions that we consider relevant may be incorrect, which could negatively impact our ability to develop and market our product candidates.

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

The United States Patent and Trademark Office ("USPTO"), and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent prosecution

process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on any issued patent and/or pending patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of a patent or patent application. We employ an outside firm and rely on outside counsel to pay these fees. While an inadvertent lapse may sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, there are many 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. If we fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market sooner, which would have a material adverse effect on our business.

The patent protection for our product candidates may expire before we are able to maximize their commercial value, which may subject us to increased competition and reduce or eliminate our opportunity to generate product revenue.

The patents for our product candidates have, and any patents issued in the future will have, varying expiration dates and, when these patents expire, we may be subject to increased competition and we may not be able to recover our development costs or market any of our approved products profitably. In some of the larger potential markets, such as the United States and Europe, patent term extension or restoration may be available to compensate for time taken during aspects of the product's development and regulatory review. However, extensions might not be granted or, if granted, the applicable time period or the scope of patent protection afforded during any extension period could be inadequate. In addition, even though some regulatory authorities may provide some other exclusivity for a product under their own laws and regulations, we may not be able to qualify the product or obtain exclusivity. If we are unable to obtain patent term extension, restoration or some other exclusivity, we could be subject to increased competition and our opportunity to establish or maintain product revenue could be substantially reduced or eliminated. Furthermore, we may not have sufficient time to recover our development costs prior to the expiration of our U.S. and foreign patents.

We may become involved in lawsuits or interference proceedings to protect our patents or other intellectual property rights, which could be expensive, time-consuming and ultimately unsuccessful.

Competitors may infringe our patents or other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, directly or through our licensors, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of our licensor is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of the patents we license at risk of being invalidated or interpreted narrowly and could put our licensors' patent applications at risk of not issuing.

Interference proceedings brought by the USPTO may be necessary to determine the priority of inventions with respect to patents and patent applications of our licensors or those of our current or future collaborators. An unfavorable outcome could require us to cease using the technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if a prevailing party does not offer us a license on terms that are acceptable to us. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distraction of our management and other employees. We may not be able to prevent, alone or with our collaborators, misappropriation of our proprietary rights, particularly in countries whose laws do not grant the same protections to intellectual property as fully as the United States.

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

Third-party claims of intellectual property infringement or misappropriation may adversely affect our business and could prevent us from developing or commercializing our product candidates.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation and other challenges, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, ex-parte review, inter party review and post-grant review proceedings before the USPTO and foreign patent offices. Numerous U.S. and foreign patents and patent applications exist in the fields in which we are developing and may develop our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to third-party claims of patent infringement. Third-party claims that we infringe on their products or technology could present a number of issues, including:

- infringement and other intellectual property claims, whether with or without merit, can be extremely expensive and time-consuming to litigate and can divert management's attention from our core business;
- the risk of substantial court-imposed damages for past infringement;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it would not be required to do;
- even if a license is available from the patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- we may need to redesign our processes to avoid further infringement, which may not be possible or could require expenditure of substantial funds and time.

Third parties may assert that we are employing their proprietary technology without authorization. We may be unaware of third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. For example, applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the United States, remain confidential until issued as patents. Except for the preceding exceptions, patent applications in the United States and elsewhere are generally published only after a waiting period of approximately 18 months after the earliest filing. Therefore, patent applications covering our product candidates may have been filed by others without the knowledge of us or our licensors. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use or manufacture of our product candidates. We may also face misappropriation claims if a third party believes that we inappropriately obtained and used its trade secrets. If the third-party prevails on such claims, we may be prevented from further using such trade secrets, limiting our ability to develop our product candidates, and may be required to pay damages.

If a court of competent jurisdiction held that any third-party patents covers aspects of our materials, formulations, methods of manufacture or methods for treatment, the holders of any such patents would be able to block our ability to develop and commercialize the applicable product candidate until such patent expired or unless we obtain a license. A license may not be available on acceptable terms, if at all. Even if we were able to obtain a license, the rights could be nonexclusive, which could result in our competitors having access to our licensed intellectual property.

Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms or at all. In addition, during the course of any patent or other intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our product candidates, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time-consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company 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 to obtain or require substantial expenditure of time and money. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into collaborative arrangements that would help us bring our product candidates to market.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents and patent rights. Obtaining and enforcing patents and patent rights in the biotechnology industry involves both technological and legal complexity and, therefore, is costly, time-consuming and inherently uncertain. In addition, some patent reform legislation and court rulings in the United States have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents and patent rights, once obtained.

For our U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act ("the AIA"), was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and reviewed after issuance, and may also affect patent litigation. USPTO regulations and procedures govern administration of the AIA and many of the substantive changes to patent law associated with the AIA. It is not clear what other, if any, impact the AIA will have on the operation of our business. Moreover, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of patent rights, all of which could have a material adverse effect on our business and financial condition.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-inventor-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date, but before we or our licensor files a patent application, could therefore be awarded a patent covering an invention of ours even if we or our licensor had made the invention before the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patent rights depends on whether the differences between the licensor’s or our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain if we (or our licensor) was the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

Among other changes, the AIA limits where a patentee may file a patent infringement suit and provides opportunities for third parties to challenge any issued patent in the USPTO. This applies to all U.S. patents, even those issued before March 16, 2013. Because the evidentiary standard to invalidate a patent claim in USPTO proceedings is lower than for a procedure in U.S. federal court, a challenger may attempt to use the USPTO procedures to invalidate our patent rights that would not have been invalidated in federal court.

Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that, even if a third party is infringing our patents or our licensors’ patents or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of us or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

Intellectual property rights do not protect against all potential threats to our potential competitive advantage.

The degree of future protection afforded by our intellectual property rights is highly uncertain because intellectual property rights have limitations and may not adequately protect our business, or permit us to maintain any competitive advantage we may gain. The following examples are illustrative:

- Others may be able to make products that are similar to our product candidates but that are not covered by the claims of the patents that we license from others or may license or own in the future.
- Others may independently develop similar or alternative technologies or otherwise circumvent any of our technologies without infringing our intellectual property rights.
- Any of our collaborators might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we license or may, in the future, own or license.
- Any of our collaborators might not have been the first to file patent applications covering certain of the patents or patent applications that we license or may, in the future, license.
- Issued patents that have been licensed to us may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in countries where we does not have license rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.
- Ownership of patents or patent applications licensed to us may be challenged by third parties.

- The patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Confidentiality agreements with employees, consultants and others may not adequately prevent disclosure of trade secrets and protect other proprietary information.

Trade secrets and/or confidential know-how can be difficult to maintain as confidential. In an effort to protect this type of information against disclosure or appropriation by competitors, we require our employees, consultants, contractors and advisors to enter into confidentiality agreements with us. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party obtained illegally and is using trade secrets and/or confidential know-how is challenging, expensive, time-consuming and unpredictable. The extent to which confidentiality agreements may be enforced does vary from jurisdiction to jurisdiction.

Failure to obtain or maintain trade secrets and/or trade protection of our confidential know-how could adversely affect our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection of that information. If successful in obtaining such patent protection, our competitors could limit our use of our trade secrets and/or confidential know-how.

We may need to license certain intellectual property from third parties, and such licenses may not be available on commercially reasonable terms, or at all.

A third party may hold intellectual property, including patent rights that are important or necessary to the development or commercialization of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from such third parties. Such a license may not be available on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates.

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

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise improperly used or disclosed to us or others confidential information of their former employers or other owners of confidential information.

Further, we may be subject to ownership disputes in the future arising from, among other things, consultants or third-parties who are involved in developing our product candidates. We may also be subject to claims that former employees, consultants, independent contractors, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging our right to, and use of, confidential and proprietary information. If we fail in defending any such claims, in addition to paying monetary damages, we may lose our rights to certain intellectual property. Such an outcome could have a material adverse effect on our business.

Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents and other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who have been involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. 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 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 be extremely costly and distract our management and other employees.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to assist with research and development and to manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements are intended to limit the rights of the third parties to use, disclose or publish our confidential information, including our trade secrets. Despite these contractual restrictions, the need to share trade secrets and other confidential information increases the risk that such trade secrets could become known to our competitors, could be inadvertently incorporated into the technology of others, or could be disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development, or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

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 and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or 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 collaborators or customers in our markets of interest. If we cannot adequately protect our trademarks and trade names, then we may not be able to build name recognition in our markets of interest and our business would be harmed. At times, competitors may adopt trade 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 successfully register and protect our trademarks and trade names and 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, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Being a Public Company

We incur significant costs and demands upon management as a result of complying with the laws and regulations affecting public companies.

We incur significant legal, accounting and other expenses that we would not incur as a private company, including costs associated with public company reporting requirements. We also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), as well as new rules implemented by the SEC and The Nasdaq Stock Market ("Nasdaq"). These rules and regulations increase the company's legal and financial compliance costs and make some activities more time-consuming and costly. Not all members of our management have previously managed and operated a public company. These executive officers and other personnel will need to devote substantial time to gaining expertise regarding operations as a public company and compliance with applicable laws and regulations. These rules and regulations may also make it difficult and expensive for us to obtain directors' and officers' liability insurance. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers of our company, which may adversely affect investor confidence in us and could cause our business and stock price to suffer.

Effective December 31, 2019, we are no longer an "emerging growth company," and the reduced disclosure requirements applicable to "emerging growth companies" no longer apply, which will increase our costs as a public company and increase the demands on management.

Effective December 31, 2019, the fiscal year-end following the fifth anniversary of the completion of our initial public offering, we are no longer an "emerging growth company" as defined in the Jumpstart Our Business Startups Act. As a result, we are incurring significant additional expenses in complying with certain provisions of the Sarbanes-Oxley Act and rules implemented by the SEC. Moreover, 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 stock 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 us may suffer if, in the future, material weaknesses are found, and this could cause a decline in the market price of our stock. Any failure of our internal control over financial reporting could have a material adverse effect on the company's stated operating results and harm our reputation. If we are unable to implement these changes effectively or efficiently, it could harm our operations, financial reporting and financial results and could result in an adverse opinion on internal control from our independent registered public accounting firm.

In addition, we are no longer eligible for reduced disclosure requirements applicable to emerging growth companies regarding executive compensation and exemptions from the requirements of holding advisory say-on-pay votes on executive compensation. These increased disclosure requirements require additional attention from management and increased costs to the company, including higher legal fees, accounting fees and fees associated with investor relations activities, among others.

Risks Related to Our Common Stock

The market price of our common stock is volatile.

The market price of our common stock has been, and is expected to continue to be, subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- reports on or the perception of clinical trial progress, or the lack thereof;
- our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals;
- failure of any of our approved product candidates to achieve commercial success;
- failure to maintain our existing third-party license, supply and manufacturing agreements;
- failure by us or our licensors to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations (or their interpretation) applicable to our product candidates;
- any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices;
- adverse regulatory authority decisions or delays;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial and development projections that we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- the perception of the pharmaceutical industry in general, and companies addressing our disease indications in particular, by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic collaborations, joint ventures, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent, product liability or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue negative or misleading opinions regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- sales of common stock by the company or our stockholders in the future;
- trading volume of our common stock;
- announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships or capital commitments;
- adverse publicity relating to the markets in which we operate, including with respect to other products and product candidates in such markets;
- the introduction of technological innovations or new therapies that compete or might compete with our product candidates;
- changes in the structure of healthcare payment systems; and
- period-to-period fluctuations in our financial results.

Moreover, stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations have had, and can be expected to continue to have, adverse effects on the trading price of our common stock.

In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

Additionally, a decrease in our stock price may cause our common stock to no longer satisfy the continued listing standards of The Nasdaq Global Select Market. If we are not able to maintain the requirements for listing on The Nasdaq Global Select Market, we could be delisted, which would likely result in an immediate and significant decline in the trading price and liquidity of our stock, and would have a materially adverse effect on our ability to raise additional funds.

Anti-takeover provisions in our organizational documents and Delaware law might discourage or delay acquisition attempts for the company that stockholders might consider favorable.

Our Amended and Restated Certificate of Incorporation, and Amended and Restated Bylaws, contain provisions that may delay or prevent an acquisition or change in control of the company. Our certificate of incorporation and bylaws include provisions that:

- authorize our board of directors to issue without further action by the stockholders, up to 20,000,000 shares of undesignated preferred stock;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum; and
- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered terms.

Further, as a Delaware corporation, we are subject to provisions of Delaware corporations law, which may impair a takeover attempt that our stockholders may find beneficial. These anti-takeover provisions and other provisions under Delaware law could discourage, delay or prevent a transaction involving a change in control of our company, including actions that our stockholders may deem advantageous, or could negatively affect the trading price of our common stock. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors of their choosing and to cause us to take other corporate actions they desire.

We may experience adverse consequences because of required indemnification of officers and directors.

Provisions of our certificate of incorporation and bylaws provide that we will indemnify any director and officer as to liabilities incurred in their capacity as a director or officer and on those terms and conditions set forth therein to the fullest extent of Delaware law. Further, we have purchased directors and officers insurance on behalf of any such persons whether or not we would have the power to indemnify such person against the liability insured against. The foregoing could result in substantial expenditures by us and prevent any recovery from our officers, directors, agents and employees for losses incurred by the company as a result of their actions.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

The current expectation is that we will retain any future earnings to fund the development and growth of our business. As a result, any capital appreciation of the common stock of the company will be stockholders' sole source of any gain for the foreseeable future.

The ownership of our common stock is highly concentrated, which may prevent stockholders from influencing significant corporate decisions and may result in conflicts of interest that could cause our stock price to decline.

Our executive officers and directors and their affiliates and entities that are related to such officers and directors beneficially own or control approximately 16% of the total outstanding shares of common stock of the company. Accordingly, these executive officers, directors and their affiliates, acting as a group, have substantial influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or

substantially all of our assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of our company, even if such a change of control would benefit the other stockholders of the company. The significant concentration of stock ownership also may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise, and may adversely affect the liquidity of our common stock.

General Risk Factors

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and Nasdaq rules and regulations. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. We must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Annual Report on Form 10-K for each year, as required by Section 404 of the Sarbanes-Oxley Act ("Section 404"). This requires significant management efforts and requires us to incur substantial professional fees and internal costs to expand our accounting and finance functions. Any failure to implement 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, as and when required, conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal controls over financial reporting that are deemed to be significant deficiencies or material weaknesses or that may require prospective or retroactive changes to our financial statements, or may identify other areas for further attention or improvement. Furthermore, we cannot be certain that our efforts will be sufficient to remediate or prevent future material weaknesses or significant deficiencies from occurring.

If we are not able to comply with the requirements of Section 404, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our common stock would likely decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities.

Our business and stock price could be negatively affected as a result of actions of activist stockholders, and such activism could impact the trading value of our securities.

Stockholders may, from time to time, engage in proxy solicitations or put forth stockholder proposals, or otherwise attempt to effect changes and assert influence on our board of directors and management. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition and divert management's attention. A proxy contest would require us to incur significant legal and advisory fees, proxy solicitation expenses and administrative and associated costs and require significant time and attention by our board of directors and management, diverting their attention from the pursuit of our business strategy. Any perceived uncertainties as to our future direction and control, our ability to execute on our strategy, or changes to the composition of our board of directors or management team arising from a proxy contest or initiatives of activist stockholders could lead to the perception of a change in the direction of our business or instability, which may result in the loss of potential business opportunities, make it more difficult to pursue strategic initiatives, or limit our ability to attract and retain qualified personnel and business partners, any of which could adversely affect our business and operating results and the trading price of our stock. If individuals are ultimately elected to our board of directors with a specific agenda, our ability to effectively implement our business strategy and create additional value for our stockholders may be adversely effected. We may choose to initiate, or may become subject to, litigation as a result of a proxy contest or matters arising from a proxy contest, which would serve as a further distraction to our board of directors and management and would require us to incur significant additional costs. In addition, actions such as those described above could cause significant negative or other fluctuations in our stock price based upon temporary or speculative market perceptions or other factors that do not necessarily reflect the underlying fundamentals and prospects of our business.

An active trading market for our common stock may not be sustained and our stockholders may not be able to resell their shares of common stock for a profit, if at all.

An active trading market for our shares of common stock may not be sustained. If an active market for our common stock is not sustained, it may be difficult for stockholders to sell their shares at an attractive price or at all.

Future sales of shares by existing stockholders could cause our stock price to decline.

If existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, whether after legal restrictions on resale lapse or at other times, the trading price of our common stock could decline.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. If we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our common stock could substantially decline immediately if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports onus regularly, demand for our common stock could decrease, which in turn could cause our stock price and trading volume to decline.

If we become profitable, our ability to use our net operating loss carryforwards and other tax attributes to offset future taxable income or taxes may be subject to limitations.

We have incurred net losses since our inception, and expect to continue to incur operating losses for the foreseeable future. If we become profitable in the future, our ability to use net operating loss carryforwards, or NOLs, and other tax attributes to offset future taxable income or reduce taxes may be subject to limitations. In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" (generally defined as a greater than 50% cumulative change by value in its equity ownership of certain stockholders over a rolling three-year period) is subject to an annual limitation on its ability to utilize its pre-change NOLs and other tax attributes (including any research and development credit carryforwards). Similar provisions of state tax law may also apply to limit the use of our state NOLs and other tax attributes.

We have not performed an analysis to determine whether our past issuances of stock and other changes in our stock ownership may have resulted in one or more ownership changes within the meaning of Sections 382 and 383 of the Code. In addition, we may experience an ownership change in connection with this offering or in the future as a result of subsequent changes in our stock ownership, some of which are outside our control; and we are not intending to take any steps to prohibit any subsequent changes in our stock ownership in order to avoid such an ownership change. If an ownership change has occurred in the past or occurs in the future, we may not be able to use a material portion of our NOLs and other tax attributes to offset future taxable income or taxes if we attain profitability.

In addition to any limitation imposed by Section 382 of Code, the use of NOLs arising after December 31, 2017 generally is limited to a deduction of 80% of taxable income for the corresponding taxable year. NOLs arising after December 31, 2017, with certain exceptions may not be carried back to previous taxable years, but may be carried forward indefinitely.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

As of December 31, 2021, we lease approximately 10,400 square feet in Germany in Gräfelfing and approximately 3,300 of office space in the U.S. in New York City.

The New York City lease, which we entered into in November 2019, expires in April 2023 and provides the principal location for our U.S. operations. The Gräfelfing, Germany lease, which was effective July 1, 2020 and then adjusted on March 1, 2021 to add more square footage, expires in June 2025.

We may look to expand the space available to us in our German facilities.

Item 3. Legal Proceedings.

We are not currently a party to any litigation, nor are we aware of any pending or threatened litigation against us that we believe would materially affect our business, operating results, financial condition or cash flows. Our industry is characterized by frequent claims and litigation including securities litigation, claims regarding patent and other intellectual property rights and claims for product liability. As a result, in the future, we may be involved in various legal proceedings from time to time.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock is listed on the Nasdaq Global Select Market under the symbol "IMUX".

Holders

As of February 12, 2022, there were 34 holders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the 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 by other entities.

Dividend Policy

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Unregistered Sales of Equity Securities

None.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data.
Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this Annual Report. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in "Risk Factors" included elsewhere in this Annual Report. As used in this report, unless the context suggests otherwise, "we," "us," our" or "the Company" refer to Immunic, Inc. and its subsidiaries.

Overview

We are a clinical-stage biopharmaceutical company with a pipeline of selective oral immunology therapies focused on treating chronic inflammatory and autoimmune diseases, including relapsing multiple sclerosis ("RMS"), ulcerative colitis ("UC"), Crohn's disease ("CD") and psoriasis. We are headquartered in New York City with our main operations in Gräfelfing near Munich, Germany. We currently have approximately 55 employees.

We are currently pursuing three development programs. These include the vidofludimus calcium (IMU-838) program, which is focused on the development of oral formulations of a small molecule inhibitor of the enzyme dihydroorotate dehydrogenase ("DHODH"); the IMU-935 program, which is focused on an inverse agonist of retinoic acid receptor-related orphan nuclear receptor gamma truncated ("RORγt"), an immune cell-specific isoform of RORγ; and the IMU-856 program, which involves the development of a drug targeting the restoration of intestinal barrier function and regeneration of bowel epithelium. These product candidates are being developed to address diseases such as RMS, UC, CD, and psoriasis. In addition to these large markets, these products are also being developed to address certain rare diseases with high unmet medical needs, such as primary sclerosing cholangitis ("PSC"), as well as metastatic castration-resistant prostate cancer ("mCRPC").

We have incurred net losses since inception of $196.9 million through December 31, 2021. We anticipate that we will continue to incur losses for at least the next several years. Due to the uncertainties involved with therapeutic product development and the clinical trial process, we cannot predict the timing or level of future expenses with certainty, when product approval might occur, if ever, or when profitability may be achieved or sustained.

Recent Events

1. CALDOSE-1 Baseline Characteristics

On February 18, 2022, we announced the main blinded baseline characteristics of our CALDOSE-1 trial of vidofludimus calcium in moderate-to-severe UC, including:

- 263 moderate-to-severe UC patients were enrolled in 78 study sites with the Ukraine and Poland representing the countries with highest number of patients and U.S. sites contributing 12.5% of the overall enrollment.
- Of the 263 patients, 148 (56.3%) were male and 115 (43.7%) were female patients. The mean age at baseline was 41.7 (18-77) years.
- All patients had to have failed at least one prior therapy option. Of the 263 patients, 83% were biologically naïve and 17% were biologically experienced (received at least 1 prior treatment with any biological agent approved in the UC indication).
- Enrolled patients had to show evidence of active moderate-to-severe UC disease. This is reflected in their baseline characteristics for patient-reported outcomes:
    - The baseline Mayo stool frequency scores were: (i) score of 3 for 59% of patients, (ii) score of 2 for 36% of patients and (iii) score of 1 for 5% of patients.
    - The Mayo rectal bleeding scores were: (i) score of 3 in 10% of patients, (ii) score of 2 for 54% of patients and (iii) score of 1 for 31% of patients.
    - The average value for fecal calprotectin at baseline was approximately 1,320 µg/g for currently available, yet incomplete data.
- The trial employed a central independent reader to evaluate the endoscopic eligibility criteria and the following modified Mayo endoscopic scores were assessed at baseline:
    - 55% of patients with a score of 3; and
    - 45% of patients with a score of 2.
- At week 10 (the time point of the primary efficacy analysis), an adjudication procedure was used for endoscopy assessments. In the case of disagreement between two independent readers, a third independent reader was used for adjudication.

We believe that these blinded baseline characteristics of randomized patients and the methodology regarding endoscopic assessments contributes to ensuring an optimized study read-out.

2. IMU-935 Composition-of-Matter patents Granted

On February 2, 2022, we received a Notice of Allowance from the U.S. Patent and Trademark Office (USPTO) for patent application 16/644581, entitled, “IL-17 and IFN-gamma inhibition for the treatment of autoimmune diseases and chronic inflammation”. We also received notice of allowance of patent application EP18762111.5 in Europe, and notice of grant of patent application 2018330633 in Australia. All three patents cover composition-of-matter of IMU-935 and related formulations, and are expected to provide protection into at least 2038, without accounting for potential Patent Term Extension (PTE) in the United States or Supplementary Protection Certificates (SPC) in Europe, respectively.

3. Other Product updates

For status updates on our product candidates in development, please see "Business - Key Status Updates."

4. Equity Financings

July 2021 Public Equity Offering

On July 15, 2021, we entered into an underwriting agreement with Piper Sandler & Co., as representative of the several underwriters listed on Schedule A thereto, in connection with our public offering of 4,500,000 shares of our common stock, $0.0001 par value per share, at a public offering price of $10.00 per share. Under the terms of the underwriting agreement, we granted the underwriters an option, exercisable for 30 days, to purchase up to an additional 675,000 shares of Common Stock at the public offering price, less underwriting discounts and commissions.

On July 19, 2021, we closed the offering. The net proceeds to us from the offering were approximately $42.0 million, after deducting underwriting discounts and commissions and estimated offering expenses. The underwriters did not exercise the option to purchase additional shares.

ATM Issuances

On December 29, 2020, we entered into a sales agreement with SVB Leerink LLC under which we may issue and sell up to $50 million of our common stock from time to time, through SVB Leerink as our sales agent, in what is deemed to be an “at the market offering” under applicable securities rules (the “December 2020 ATM”). In the year ended December 31, 2021, we raised gross proceeds of $0.8 million pursuant to the December 2020 ATM through the sale of 73,221 shares of common stock at a weighted average price of $10.27 per share. The net proceeds in 2021 from the December 2020 ATM were $0.7 million after deducting underwriter commissions of $22,555. To date in 2022, we have raised gross proceeds of $16.7 million pursuant to the December 2020 ATM through the sale of 1,568,487 shares of common stock at a weighted average price of $10.62 per shared. The net proceeds were $16.2 million after deducting underwriter commissions of $0.5 million. As of February 18, 2022, $32.6 million in capacity remains under the December 2020 ATM.

5. License Agreement with the University Medical Center Goettingen

On September 22, 2021, we announced the execution of an in-license agreement with the University Medical Center Goettingen, Germany, covering the combination of DHODH inhibitors and nucleoside analogues to treat viral infections (COVID-19 and Influenza). Terms of the agreement were not disclosed.

Preclinical research completed by the parties and their collaborators has shown that certain DHODH inhibitors, including vidofludimus calcium, strongly synergize with selected nucleoside analogues to inhibit SARS-CoV-2 replication *in vitro*. For instance, in an *in vitro* test system, vidofludimus calcium alone showed an up to 99.9% reduction in viral RNA at concentrations of 5 µM, which is well within the exposure levels seen in prior clinical trials. Likewise, NHC, the active metabolite of molnupiravir, alone, was associated with an up to 99% reduction in viral RNA at concentrations of 100 nM. Compared to single agent activity, the combination of vidofludimus calcium and NHC achieved an extra-ordinary reduction in viral RNA, down to the limit of detection, reducing SARS-CoV-2 RNA by up to seven log units (corresponding to 0.00001% viral RNA remaining). This powerful reduction of virus replication *in vitro* was demonstrated across multiple SARS-CoV-2 variants, including alpha, beta and delta, highlighting the independence of this approach to mutant virus forms. In addition to molnupiravir, we are exploring alternate nucleoside analogues, some of which have shown very promising antiviral activity *in vitro*.

Recalling vidofludimus calcium's clinical activity against COVID-19 in our Phase 2 CALVID-1 trial published in February 2021, and in light of recent exacerbations in COVID-19 worldwide, we are very excited to have in-licensed this technology to incorporate into our pandemic preparedness effort. However, with the extra-ordinary wealth of activity already ongoing at the company in other programs, we intend to evaluate and pursue the best possible strategic option for this program, including potential partnership, collaboration or external funding.

6. Settlement Agreement with 4SC AG

On March 31, 2021, Immunic AG, our wholly-owned subsidiary, and 4SC AG entered into a settlement agreement, pursuant to which Immunic AG settled its remaining obligation of the 4.4% royalty on net sales for $17.25 million. The payment was made 50% in cash and 50% in shares of our common stock. Pursuant to the Agreement, we filed a resale shelf registration statement on Form S-3 covering the resale of the shares. With the execution of the agreement, no further payment obligations remain between Immunic AG and 4SC AG.

7. Other

Changes to Executive Team

Appointment of Inderpal Singh as General Counsel

On June 1, 2021, we announced the appointment of Inderpal Singh as our General Counsel. In his role, Mr. Singh is responsible for legal and compliance matters and has become part of our executive management team.

Appointment of Patrick Walsh as Chief Business Officer

On October 14, 2021, we announced the appointment of Patrick Walsh as Chief Business Officer. In this newly created role, Mr. Walsh is responsible for business development, including strategic partnering opportunities, and has become part of our executive management team.

Executive Chairman Agreement with Duane Nash

On April 15, 2020, the compensation committee of our Board of Directors independently reviewed and approved entering into an employment agreement with the current Chairman of the Board, Duane Nash, MD, JD, MBA and pursuant to such approval, on April 17, 2020, we and Dr. Nash entered into the Executive Chairman Agreement. The Executive Chairman Agreement establishes an "at will" employment relationship pursuant to which Dr. Nash serves as Executive Chairman and contemplated a term that ends on October 15, 2020, which was subsequently extended to April 15, 2021. On April 15, 2021, we and Dr. Nash entered into an addendum to extend the term of the Executive Chairman Agreement to April 15, 2022. In connection with the Agreement, we made a one-time award to Dr. Nash of an option to purchase 90,000 shares of Company common stock, which vest monthly commencing on May 15, 2021, and increased Dr. Nash's monthly base salary to $27,960 from $25,417.

Critical Accounting Policies and Estimates

The preparation of financial statements in conformity with generally accepted accounting principles in the United States ("US"), or GAAP, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. On an on-going basis, management makes its best estimate of the ultimate outcome for these items based on historical trends and other information available when the financial statements are prepared. Changes in estimates are typically recognized in the period when new information regarding estimates becomes available to management. Actual results could differ from those estimates.

Our significant accounting policies are described in more detail in Note 2, "Summary of Significant Accounting Policies," in the notes to the consolidated financial statements. See below for what we believe are our Critical Accounting Policies.

Foreign Currency Translation and Presentation

Our reporting currency is US dollars. During the twelve months ended December 31, 2021 and 2020, Immunic AG's operations were located in Germany with the euro being its functional currency. Immunic Australia Pty Ltd.'s functional currency is the Australian dollar. All amounts in the financial statements where the functional currency is not the US dollar are translated into US dollar equivalents at exchange rates as follows:

- assets and liabilities at reporting period-end rates;
- income statement accounts at average exchange rates for the reporting period; and
- components of equity at historical rates.

Gains and losses from translation of the financial statements into US dollars are recorded in stockholders' equity net of the anticipated income tax effects as a component of accumulated other comprehensive income (loss). Realized and unrealized gains and losses resulting from foreign currency transactions denominated in currencies other than the functional currency are reflected as general and administrative expenses in the Consolidated Statements of Operations. Foreign currency transaction gains and losses related to long-term intercompany loans that are payable in the foreseeable future are recorded in Other Income. The Consolidated Statements of Cash Flows were prepared by using the average exchange rate in effect during the reporting period which reasonably approximates the timing of the cash flows.

Goodwill

Business combinations are accounted for under the acquisition method. The total purchase price of an acquisition is allocated to the underlying identifiable net assets, based on their respective estimated fair values as of the acquisition date. Determining the fair value of assets acquired and liabilities assumed requires management's judgment and often involves the use of significant estimates and assumptions, including assumptions with respect to future cash inflows and outflows, probabilities of success, discount rates, and asset lives, among other items. Assets acquired and liabilities assumed are recorded at their estimated fair values. The excess of the purchase price over the estimated fair values of the net assets acquired is recorded as goodwill.

Goodwill is tested for impairment at the reporting unit level annually in the fourth quarter, or more frequently when events or changes in circumstances indicate that the asset might be impaired. Examples of such events or circumstances include, but are not limited to, a significant adverse change in legal or business climate, an adverse regulatory action or unanticipated competition.

The Company assesses qualitative factors to determine whether the existence of events or circumstances would indicate that it is more likely than not that the fair value of the reporting unit is less than its carrying amount. If after assessing the totality of events or circumstances, the Company were to determine that it is more likely than not that the fair value of the reporting unit is less than its carrying amount, then the Company would perform a quantitative test that compares the fair value to its carrying value to determine the amount of any impairment. Impairment testing for goodwill is done at the reporting unit level. The Company has determined that it operates in a single operating segment and has a single reporting unit. The Company has determined there was no goodwill impairment as of December 31, 2021.

Research and Development Expenses

Research and development expenses consist of expenses incurred in research and development activities, which include clinical trials, contract research services, certain milestone payments, salaries and related employee benefits, allocated facility costs and other outsourced services. Research and development expenses are charged to operations as incurred.

The Company enters into agreements with CROs to provide clinical trial services for individual studies and projects by executing individual work orders governed by a Master Service Arrangement ("MSA"). The MSAs and associated work orders provide for regular recurrent payments and payments upon the completion of certain milestones. The Company regularly assesses the timing of payments against actual costs incurred to ensure a proper accrual of related expenses in the appropriate accounting period.

Collaboration Arrangements

Certain collaboration and license agreements may include payments to or from the Company of one or more of the following: non-refundable or partially refundable upfront or license fees; development, regulatory and commercial milestone payments; payment for manufacturing supply services; partial or complete reimbursement of research and development costs; and royalties on net sales of licensed products. The Company assesses whether such contracts are within the scope of Financial Accounting Standards Board (FASB) Accounting Standards Update ("ASU") 2014-09 "*Revenue from Contracts with Customers*" and ASU No. 2018-18, "*Collaborative Arrangements*", ("ASU 2018-18"). ASU 2018-18, clarifies that certain elements of collaborative arrangements could qualify as transactions with customers in the scope of ASC 606.

In October 2018, the Company entered into an option and license agreement (the "Daiichi Sankyo Agreement") with Daiichi Sankyo Co., Ltd. ("Daiichi Sankyo") which granted the Company the right to license a group of compounds, designated by the Company as IMU-856, as a potential new oral treatment option for diseases such as inflammatory bowel disease, irritable bowel syndrome with diarrhea, celiac disease and other barrier function associated diseases. During the option period, the Company performed agreed upon research and development activities for which it was reimbursed by Daiichi Sankyo up to a maximum agreed-upon limit. Such reimbursement is recorded as other income.

On January 5, 2020, the Company exercised its option to obtain the exclusive worldwide right to commercialization of IMU-856. Among other things, the option exercise grants Immunic AG the rights to Daiichi Sankyo's patent application related to IMU-856. In connection with the option exercise, the Company paid a one-time upfront licensing fee to Daiichi Sankyo. Under the Daiichi Sankyo Agreement, Daiichi Sankyo is also eligible to receive future development, regulatory and sales milestone payments, as well as royalties related to IMU-856.

Stock-Based Compensation

We measure the cost of employee and non-employee services received in exchange for equity awards based on the grant-date fair value of the award recognized generally as an expense (i) on a straight-line basis over the requisite service period for those awards whose vesting is based upon a service condition, and (ii) on an accelerated method for awards whose vesting is based upon a performance condition, but only to the extent it is probable that the performance condition will be met. Stock-based compensation is estimated (i) at the date of grant based on the award's fair value for equity classified awards and (ii) at the final measurement date for liability classified awards. Forfeitures are recorded in the period in which they occur.

We estimate the fair value of stock options using the Black-Scholes-Merton option-pricing model, which requires the use of estimates and subjective assumptions, including the risk-free interest rate, the fair value of the underlying common stock, the expected dividend yield of our common stock, the expected volatility of the price of our common stock, and the expected term of the option. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future.

Income Taxes

We are subject to corporate income tax laws and regulations in the U.S., Germany and Australia. Tax regulations within each jurisdiction are subject to the interpretation of the related tax laws and regulations and require significant judgment in their application.

We utilize the asset and liability method of accounting for income taxes which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the audited consolidated financial statements. Deferred income tax assets and liabilities are determined based on the differences between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of changes in tax rates on deferred tax assets and liabilities is recognized in operations in the period that includes the enactment date. Deferred taxes are reduced by a valuation allowance when, in the opinion of management, it is more likely than not some portion or the entire deferred tax asset will not be realized. As of December 31, 2021, and December 31, 2020, we maintained a full valuation allowance against the balance of deferred tax assets.

It is our policy to provide for uncertain tax positions and the related interest and penalties based upon management's assessment of whether a tax benefit is more likely than not to be sustained upon examination by tax authorities. We recognize interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense.

Components of Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales. We cannot predict if, when, or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

Research and Development Expenses

Research and development expenses consist of costs associated with our research activities, including our product discovery efforts and the development of our product candidates. Our research and development expenses include:

- external research and development expenses and milestone payments incurred under arrangements with third parties, such as CROs, contract manufacturing organizations, collaborations with partners, consultants, and our scientific advisors; and

- internal personnel expenses.

We expense research and development costs as incurred. Non-refundable advance payments for goods and services that will be used in future research and development activities are capitalized as prepaid expenses and expensed when the service has been performed or when the goods have been received.

Since our inception in March 2016, we have spent a total of approximately $143.5 million in research and development expenses through December 31, 2021.

These costs primarily include external development expenses and internal personnel expenses for the three development programs, vidofludimus calcium, IMU-935 and IMU-856. We have spent the majority of our research and development resources on vidofludimus calcium, our lead development program for clinical trials in MS, UC, COVID-19 and PSC.

In August 2019, Immunic AG received a grant of up to approximately $730,000 from the German Federal Ministry of Education and Research, in support of the InnoMuNiCH (Innovations through Munich-Nippon Cooperation in Healthcare) project. The grant funds will be used to fund a three-year research project relating to autoimmune diseases by us and our three project partners. Since the inception of the grant, we have recorded $356,000, $178,000 and $159,000 of which were recorded in 2021 and 2020, respectively, and which were classified in Other Income in the accompanying consolidated statement of operations.

Our research and development expenses may increase in the foreseeable future as we continue to conduct ongoing regulatory and development activities, initiate new preclinical and clinical trials and build our pipeline. The process of commercialization, conducting clinical trials and preclinical studies necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving regulatory approval for any of our product candidates.

Successful development of product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each product candidate and are difficult to predict. We anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the development and regulatory success of each product candidate, and ongoing assessments as to each product candidate’s commercial potential.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel expenses, professional fees for legal, accounting, tax and business consulting services, insurance premiums and stock-based compensation.

Other Income (Expense), Net

Interest Income

Interest income consists of interest earned on our money market funds and bank accounts which are a portion of our cash and cash equivalents balance. Our interest income has not been significant due to low interest rates earned on invested balances.

Other Income (Expense), Net

Other income (expense) consists primarily of a research and development tax incentive related to clinical trials performed in Australia, foreign currency transaction gains and losses related to long-term intercompany loans that are payable in the foreseeable future and the recognition of deferred revenue related to research and development expenses in connection with our option and licensing agreement with Daiichi Sankyo Co., Ltd.

Results of Operations

Comparison of Fiscal Years Ended December 31, 2021 and 2020

The following table summarizes our operating expenses for the years ended December 31, 2021 and 2020 (dollars in thousands):

	Years Ended December 31,		Change		
	2021	2020	$	%	
Operating expenses:					
Research and development	61,115	38,637	22,478	58	%
General and administrative	13,300	10,334	2,966	29	%
4SC royalty settlement (see note 4)	17,250	—	17,250		NM
Total operating expenses	91,665	48,971	42,694	87	%
Loss from operations	(91,665)	(48,971)	(42,694)	87	%
Total other income (expense)	(1,280)	4,954	(6,234)	(126)	%
Net loss	(92,945)	(44,017)	(48,928)	111	%

Research and development expenses increased by $22.5 million during the twelve months ended December 31, 2021, as compared to the twelve months ended December 31, 2020. The increase reflects (i) a $10.2 million increase in external development costs related to the Phase 3 program of vidofludimus calcium in relapsing multiple sclerosis, (ii) a $7.4 million increase in external development costs related to the Phase 2 trial of vidofludimus calcium in progressive multiple sclerosis, (iii) a $4.7 million increase in external development costs related to the Phase 2 clinical trial of vidofludimus calcium in ulcerative colitis, (iv) a $2.4 million increase in personnel expense in research and development, $1.0 million of which is related to non-cash stock compensation expense and the remainder of which is related to an increase in headcount, (v) a $1.6 million increase in external development costs related to the Phase 1 clinical trial of IMU-935, (vi) a $1.8 million increase in external costs for IMU-856, (vii) a $2.1 million increase in preclinical and drug supply costs related to vidofludimus calcium and (viii) $1.1 million related to increased costs across numerous categories. The increases were partially offset by (i) a $6.9 million decrease in external development costs related to the Phase 2 clinical trial of vidofludimus calcium in COVID-19 and (ii) a decrease of $1.9 million in drug supply costs for IMU-856.

General and administrative expenses increased by $3.0 million during the twelve months ended December 31, 2021, as compared to the twelve months ended December 31, 2020. The increase was primarily due to (i) a $2.2 million increase related to non-cash stock compensation expense and (ii) a $0.8 million increase across numerous categories.

On March 31, 2021, Immunic AG and 4SC AG entered into a Settlement Agreement, pursuant to which Immunic AG settled its remaining obligation of the 4.4% royalty on net sales for $17.25 million (Tranche III of the Agreement). The payment was made 50% in cash and 50% in shares of Immunic’s common stock. No further payment obligations remain between Immunic and 4SC AG.

Other income decreased by $6.2 million during the twelve months ended December 31, 2021, as compared to the twelve months ended December 31, 2020. The decrease was primarily attributable to (i) a $6.9 million change in other income (loss) as a result of a $4.3 million foreign exchange loss in 2021 on a $52.0 million intercompany loan between Immunic, Inc. and

Immunic AG combined with a $2.5 million foreign exchange gain in 2020 on this intercompany loan and (ii) a $1.0 million decrease in recognized deferred income attributable to reimbursements of research and development expenses in connection with the Daiichi Sankyo Agreement realized in 2020. The decrease was partially offset by (i) a $1.2 million research allowance received from the German Federal Ministry of Finance and (ii) a $0.5 million increase in research and development tax incentives for clinical trials in Australia as a result of increased spending on clinical trials in Australia.

Liquidity and Capital Resources

Overview

We have no products approved for commercial sale and have not generated any revenue from product sales. We have never been profitable and have incurred operating losses in each year since our inception in 2016. Our net losses were approximately $92.9 million and $44.0 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of approximately $196.9 million. Substantially all of our operating losses resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We expect to incur significant expenses and increasing operating losses for the foreseeable future as we initiate and continue the preclinical and clinical development of our product candidates and add personnel necessary to operate as a company with an advanced clinical pipeline of product candidates. To the extent additional funds are necessary to meet long-term liquidity needs as we continue to execute our business strategy, we anticipate that they will be obtained through the incurrence of indebtedness, additional equity financings or a combination of these potential sources of funds, although we can provide no assurance that these sources of funding will be available on reasonable terms.

From inception through December 31, 2021, we have raised net cash of approximately $259.5 million from private and public offerings of preferred and common stock. As of December 31, 2021, we had cash and cash equivalents of approximately $86.9 million. We are dependent on financing activities to fund ongoing operations, and due to the inherent uncertainties in successfully completing financing transactions, and with our forecasted cash reach through the first quarter of 2023, these are indicators of an inability to continue as a going concern. However, we have the ability to manage the amount and timing of expenditures to reduce costs, have limited required fixed spend, and can manage working capital as needed and that coupled with the $16.2 million of cash raised so far in 2022 under our At The Market ("ATM") facility alleviates any uncertainty that we will have adequate liquidity to meet our obligations for at least the next 12 months from the financial statement release date.

In November 2020, we filed a shelf registration statement on Form S-3 (the "2020 Shelf Registration Statement"). The 2020 Shelf Registration Statement permits the offering, issuance and sale of up to $250.0 million of common stock, preferred stock, warrants, debt securities, and/or units in one or more offerings and in any combination of the foregoing.

In December 2020, we filed a prospectus supplement for the offering, issuance and sale of up to a maximum aggregate offering price of $50.0 million of common stock that may be issued and sold under an at-the-market sales agreement with SVB Leerink as agent (the "December 2020 ATM"). We intend to use the net proceeds from the December 2020 ATM to continue to fund the ongoing clinical development of our product candidates and for other general corporate purposes, including funding existing and potential new clinical programs and product candidates. The December 2020 ATM will terminate upon the earlier of (i) the issuance and sale of all of the shares through SVB Leerink on the terms and subject to the conditions set forth in the sales agreement for the December 2020 ATM or (ii) termination of the December 2020 ATM as otherwise permitted thereby. The December 2020 ATM may be terminated at any time by either party upon ten days' prior notice, or by SVB Leerink at any time in certain circumstances, including the occurrence of a material adverse effect on us.

In the year ended December 31, 2021, we raised gross proceeds of $0.8 million pursuant to the December 2020 ATM through the sale of 73,221 shares of common stock at a weighted average price of $10.27 per share. The net proceeds from the December 2020 ATM were $0.7 million after deducting underwriter commissions of $22,555. To date in 2022, we have raised gross proceeds of $16.7 million pursuant to the December 2020 ATM through the sale of 1,568,487 shares of common stock at a weighted average price of $10.62 per share. The net proceeds were $16.2 million after deducting underwriter commissions of $0.5 million. As of February 18, 2022, $32.6 million in capacity remains under the December 2020 ATM.

Debt Financing

On October 19, 2020, we and Immunic AG entered into a Finance Contract (the "Loan Agreement") with the European Investment Bank ("EIB"), pursuant to which EIB agreed to provide Immunic AG with a term loan in an aggregate amount of up

to €24.5 million to support the development of our lead product candidate, IMU-838, in moderate coronavirus disease 2019 ("COVID-19"), to be made available to be drawn in three tranches, with the second and third tranches subject to the completion of certain pre-defined milestones. Effective October 20, 2021 we terminated this agreement with the EIB and no funds were drawn under this arrangement.

Public Equity Offerings

July 2021 Public Equity Offering

On July 15, 2021, we entered into an underwriting agreement with Piper Sandler & Co., as representative of the several underwriters listed on Schedule A thereto, in connection with our public offering of 4,500,000 shares of our common stock, $0.0001 par value per share, at a public offering price of $10.00 per share. Under the terms of the underwriting agreement, we granted the underwriters an option, exercisable for 30 days, to purchase up to an additional 675,000 shares of common stock at the public offering price, less underwriting discounts and commissions. This option was not exercised.

On July 19, 2021, we closed the offering. The net proceeds to us from the offering were approximately $42.0 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Cash Flows

The following table shows a summary of our cash flows for the years ended December 31 (in thousands):

	2021	2020
Cash (used in) provided by:		
Operating activities	$ (83,233)	$ (46,124)
Investing activities	(67)	(146)
Financing activities	42,841	144,431

Net cash used in operating activities

During the year ended December 31, 2021, operating activities used $83.2 million of cash. The use of cash related to our net loss of $92.9 million adjusted for non-cash charges of $8.6 million related to common stock issued for the 4SC AG transaction, $5.9 million related to stock-based compensation and a $4.3 million unrealized foreign currency loss as well as a $9.3 million net change in our operating assets and liabilities. Changes in our operating assets and liabilities consisted primarily of an increase of $12.8 million in prepaid expenses and other current assets partially offset by $3.5 million increase in other current liabilities, accrued expenses and accounts payable. The increase in prepaid expenses and other current assets is primarily due to higher prepaid clinical costs and an increased receivable for the Australian research and development credit. The increase in liabilities is primarily due to an increase in clinical costs as a result of the start of our Phase 3 clinical studies for RMS and Phase 2 clinical studies for PMS.

During the year ended December 31, 2020, operating activities used $46.1 million of cash. The use of cash related to our net loss of $44.0 million adjusted for non-cash charges of $2.7 million related to stock-based compensation and was partially offset by a $2.5 million unrealized foreign currency gain as well as a $2.4 million net change in our operating assets and liabilities.

Net cash used in investing activities

During the year ended December 31, 2021, net investing activities used $67,000 of cash, primarily due to purchase of equipment.

During the year ended December 31, 2020, net investing activities used $0.1 million of cash, primarily due to purchase of equipment.

Net cash provided by financing activities

During the year ended December 31, 2021, financing activities provided $42.8 million of cash of consisting of net cash proceeds from the sale of common stock under the July 2021 equity offering and the December 2020 ATM.

During the year ended December 31, 2020, financing activities provided $144.4 million of cash of consisting of net cash proceeds from the sale of common stock under the July 2019 ATM and the April 2020, June 2020, and August 2020 equity offerings.

Our forecast of the period of time through which our financial resources will support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. Our future expenses and capital requirements are difficult to forecast and will depend on many factors, including, but not limited to:

- the timing and structure of any strategic options and transactions, if any;
- the cost, timing and outcome of any future litigation costs;
- personnel-related expenses, including salaries, benefits, stock-based compensation expense and other compensation expenses related to retention and termination of personnel;
- the scope, progress, results and costs of research and development and ongoing clinical trials;
- the cost and timing of future regulatory submissions;
- the cost and timing of developing and validating the manufacturing processes for any potential product candidates;
- the cost and timing of any commercialization activities, including reimbursement, marketing, sales and distribution costs;
- our ability to establish new collaborations, licensing or other arrangements and the financial terms of such agreements;
- the number and characteristics of any future product candidates we pursue;
- the costs involved with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount from the sales of, or royalties on any future products.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of stock offerings, debt financings, strategic alliances, collaborations and licensing arrangements. We do not expect to achieve revenue from product sales prior to the use of the net proceeds from our public and private offerings to date. We do not have any committed external source of funds. Additional funds may not be available on acceptable terms, if at all. To the extent that we raise additional capital through the sale of equity securities, the ownership interest of our stockholders will be diluted and it may be on terms that are not favorable to us or our stockholders. Debt financing, if available, may involve covenants restricting our operations or our ability to incur additional debt or other terms that are not favorable to us or our stockholders. If we raise additional funds through collaborations and licensing arrangements with third parties, we would expect to relinquish substantial rights to our technologies or our future products, or grant licenses on terms that may not be favorable to us. If we were to complete a merger, we may relinquish all control over the organization and could experience detrimental tax effects. If we are unable to raise adequate funds, we may have to liquidate some or all of our assets. Any of these factors could harm our operating results.

Off-Balance Sheet Arrangements

Through December 31, 2021, we have not entered into and did not have any relationships with unconsolidated entities or financial collaborations, such as entities often referred to as structured finance or special purpose entities, established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purpose.

Other Commitments and Obligations

In May 2016, the Company entered into a purchase agreement with 4SC whereby the Company acquired certain assets, including the rights to patents and patent applications, trademarks and know-how. This transaction was accounted for as an asset acquisition under Accounting Standards Update 2017-01 - Business Combinations (Topic 805): Clarifying the Definition of a Business. The Agreement included payments (Tranches III and IV) that were contingent upon the occurrence of certain events and required the Company to pay royalties equal to 4.4% of the aggregated net sales for a certain period as defined in the Agreement (Tranche III) upon commercialization of the acquired assets. Effective April 12, 2019, the parties agreed to settle

Tranche IV by issuing 120,070 shares of the Company's common stock to 4SC at the time, while keeping the obligation to pay Tranche III in effect. Approximately $1.5 million of expense was recorded as a result of the issuance of these shares on April 12, 2019. On March 31, 2021, Immunic AG, a wholly-owned subsidiary of the Company, and 4SC AG entered into a Settlement Agreement, pursuant to which Immunic AG settled its remaining obligation of the 4.4% royalty on net sales for $17.25 million (Tranche III of the purchase agreement). The payment was made 50% in cash and 50% in shares of Immunic's common stock. Pursuant to the Agreement, the Company filed a resale shelf registration statement on Form S-3 covering the resale of the Shares. With the execution of the Agreement, no further payment obligations remain between Immunic AG and 4SC AG.

See Note 4 of Notes to the Financial Statements regarding the Company's obligations under the option agreement with Daiichi Sankyo, which includes the potential payment of future development, regulatory and sales milestone payments, as well as royalties related to IMU-856.

Maturities of the operating lease obligation are as follows as of December 31, 2021 (in thousands):	
2022	$ 457
2023	$ 307
2024	$ 233
2025	$ 116
2026	$ —
Thereafter	$ —
Total lease payments	$ 1,113
Less: interest portion	$ 95
Present value of lease obligation	$ 1,018

Contractual Obligations

As of December 31, 2021, the Company has non-cancelable contractual obligations under certain agreements related to its development programs for vidofludimus calcium, IMU-935 and IMU-856 totaling approximately $2.8 million, all of which is expected to be paid in 2022.

Recently Adopted Accounting Standards

There are no recently issued accounting standards that would have a significant impact on the company's consolidated financial statements.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk.

Interest Rate Sensitivity

We had cash and cash equivalents of $86.9 million as of December 31, 2021, which were held for working capital purposes. We do not enter into investments for trading or speculative purposes. We do not believe that we have any material exposure to changes in the fair value of these investments as a result of changes in interest rates due to their short-term nature. However, $23.6 million of these funds are held in German bank accounts that were earning negative interest of 0.5% as of December 31, 2020 and 2021. There was also $26.9 million held in German banks that are U.S. dollar denominated bank accounts and $36.4 million in U.S. bank accounts that are earning nominal interest. Declines or increases in interest rates, however, will reduce or increase future investment income, respectively, to the extent we have funds available for investment.

Foreign Currency Exchange Risk

Our primary research and development operations are conducted in our facilities in Germany. We have entered and may continue to enter into international agreements, primarily related to our clinical studies. Accordingly, we have exposure to foreign currency exchange rates and fluctuations between the U.S. dollar and foreign currencies, primarily the euro and the Australian dollar, which could adversely affect our financial results, including income and losses as well as assets and liabilities. To date, we have not entered into, and do not have any current plans to enter into, any foreign currency hedging transactions or derivative financial transactions. Our exposure to foreign currency risk will fluctuate in future periods as our research and clinical development activities in Europe and Australia change. We currently maintain a significant amount of our assets outside of the U.S.

The functional currencies of our foreign subsidiaries are the applicable local currencies. Accordingly, the effects of exchange rate fluctuations on the net assets of these operations are accounted for as translation gains or losses in accumulated other comprehensive income (loss) within stockholders' equity. Our German subsidiaries are currently a significant portion of our business and, accordingly, a change of 10% in the currency exchange rates, primarily the euro, could have a material impact on their financial position or results of operations.

Although operating in local currencies may limit the impact of currency rate fluctuations on the results of operations of our German subsidiaries, rate fluctuations may impact the consolidated financial position as the assets and liabilities of our foreign operations are translated into U.S. dollars in preparing our consolidated balance sheets. As of December 31, 2021, our German subsidiaries had net current assets (defined as current assets less current liabilities), subject to foreign currency translation risk, of $63.2 million. The potential decrease in net current assets as of December 31, 2021, from a hypothetical 10% adverse change in quoted foreign currency exchange rates, due primarily to the euro, would be approximately $6.3 million. In addition, a 10% change in the foreign currency exchange rates for the year ended December 31, 2021, would have impacted our net loss by approximately $8.2 million due primarily to the euro.

Effects of Inflation

We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data.

The consolidated financial statements required pursuant to this item are included in Part IV, Item 15 of this Annual Report, and are presented beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Management, with the participation of our Chief Executive Officer and Principal Financial and Accounting Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. The term "disclosure controls and procedures," as defined in Rule 13a-15(e) of the Exchange Act, means controls and other procedures of a company that are designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to provide reasonable assurance that information required to be disclosed is accumulated and communicated to our management, including our Chief Executive Officer and Principal Financial and Accounting Officer, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their desired control objectives, and management necessarily is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer and Principal Financial and Accounting Officer have concluded that, as of December 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rule 13a-15(f) under the Exchange Act. Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our Chief Executive Officer and Principal Financial and Accounting Officer, 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. Our 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 our assets; (ii) provide reasonable assurance (a) that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, (b) that our receipts and expenditures are being made only in accordance with authorizations of our management and directors, and (c) regarding the prevention or timely detection of the unauthorized acquisition, use or disposition of assets that could have a material effect on our 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.

As of December 31, 2021, our management conducted an evaluation of the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control - Integrated Framework (2013). Based on this evaluation, our management concluded that, as of December 31, 2021, our internal control over financial reporting was effective.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the quarter ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item will be contained in our definitive proxy statement (the “Definitive Proxy Statement”), to be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2021, under the headings “Election of Directors,” “Corporate Governance,” “Executive Officers,” and “Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated herein by reference.

We have a written Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer and our principal accounting officer and every other director, officer and employee of Immunic. The Code of Business Conduct and Ethics is available on our Internet website at www.imux.com. A copy of the Code of Business Conduct and Ethics will be provided free of charge by making a written request and mailing it to our corporate headquarters offices to the attention of the Investor Relations Department. If any amendment to, or a waiver from, a provision of the Code of Business Conduct and Ethics that applies to the principal executive officer, principal financial officer and principal accounting officer is made, such information will be posted on our Internet website within four business days at www.imux.com.

Item 11. Executive Compensation.

Information required by this item will be found in our Definitive Proxy Statement under the heading "Executive Compensation" and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item will be found in our Definitive Proxy Statement under the headings "Securities Authorized for Issuance Under Equity Compensation Plans," "Security Ownership of Certain Beneficial Owners" and "Security Ownership of Directors and Executive Officers" and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information required by this item will be found in our Definitive Proxy Statement under the headings "The Board of Directors and Board Committees" and "Certain Relationships and Related-Party Transactions" and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Information required by this item will be found in our Definitive Proxy Statement under the heading "Proposal to Ratify the Appointment of Independent Registered Public Accounting Firm" and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

1. Financial Statements. We have filed the following documents as part of this Annual Report:

2. Financial Statement Schedules. None.

3. Exhibits. The following exhibits are filed herewith or are incorporated by reference to exhibits previously filed with the U.S. Securities and Exchange Commission.

EXHIBITS

Exhibit Number	Exhibit Title	Incorporated by Reference		
		Form	Exhibit	Filing Date
3.1	Amended and Restated Articles of Incorporation.	8-K	3.1	July 17, 2019
3.2	Third Amended and Restated Bylaws.	8-K	3.1	July 17, 2019
4.1	2019 Omnibus Equity Incentive Plan.	S-8	4.1	September 20, 2019
4.2*	Description of Registrant's Securities	10-Q	4.2	February 26, 2020
10.1	Sales Agreement, dated July 17, 2019, between Immunic, Inc. and SVB Leerink LLC.	8-K	10.1	July 17, 2019
10.2	Option and License Agreement, dated September 27, 2018, between Immunic AG and Daiichi Sankyo Company, Ltd.	8-K	10.2	July 17, 2019
10.3	Asset Purchase Agreement, dated May 13, 2016, between Immunic AG and 4SC AG.	8-K	10.3	July 17, 2019
10.4+	Form of Indemnification Agreement.	8-K	10.4	July 17, 2019
10.5+	Employment Agreement between Dr. Daniel Vitt and Immunic AG.	8-K	10.5	July 17, 2019
10.6+	Addendum to Service Agreement between Immunic AG and Dr. Daniel Vitt.	8-K	10.1	September 5, 2019
10.7+	Employment Agreement between Dr. Manfred Groeppel and Immunic AG.	8-K	10.6	July 17, 2019
10.8+	Addendum to Service Agreement between Immunic AG and Dr. Manfred Groeppel.	8-K	10.2	September 5, 2019
10.9+	Employment Agreement dated April 17, 2020, between Immunic, Inc. and Duane Nash.	8-K	10.2	April 20, 2020
10.10+	Addendum to Employment Agreement dated October 15, 2020, between Immunic, Inc. and Duane Nash.	10-Q	10.12	November 6, 2020
10.11	Placement Agency Agreement, dated April 23, 2020, between Immunic, Inc. and Roth Capital Partners, LLC	8-K	10.1	April 20, 2020
10.12	Form of Securities Purchase Agreement, dated April 23, 2020, between Immunic, Inc. and the investors party thereto.	8-K	10.2	April 20, 2020
10.13	Placement Agency Agreement, dated June 10, 2020, between Immunic, Inc. and the Roth Partners, LLC	8-K	10.1	June 12, 2020
10.14	Form of Securities Purchase Agreement, dated June 10, 2020, between Immunic, Inc. and the investors party thereto	8-K	10.2	June 12, 2020
10.15	Underwriting Agreement, dated August 4, 2020, by and between Immunic, Inc. and SVB Leerink LLC.	8-K	1.1	August 10, 2020
10.16	Finance Contract, dated October 19, 2020, between Immunic, Inc., Immunic AG and European Investment Bank	8-K	10.1	October 20, 2020
10.17	Form of Guarantee Agreement between Immunic, Inc., Immunic AG and European Investment Bank.	8-K	10.2	October 20, 2020
10.18	Sales Agreement, dated December 29, 2020 between Immunic, Inc. and SVB Leerink LLC	8-K	10.1	January 4, 2021
10.19	Amendment Letter, dated November 11, 2020	8-K	10.1	November 13, 2020
10.20	Settlement agreement, dated March 31,2021 between Immunic AG and 4SC AG	8-K	10.1	March 31, 2021
10.21+	Addendum No. 2 to Employment Agreement dated April 15, 2021 between Immunic, Inc. and Duane Nash	8-K	10.1	April 15, 2021
10.22+	Second Addendum to Service Agreement between Immunic AG and Dr. Daniel Vitt	8-K	10.1	June 10, 2021
10.23+	Second Addendum, dated June 10, 2021 to Service Agreement between Immunic AG and Dr. Andreas Muehler	8-K	10.2	June 10, 2021
10.24+	Employment Agreement, dated June 10, 2021 between Immunic, Inc. and Dr. Andreas Muehler	8-K	10.3	June 10, 2021

10.25+	Employment Agreement, dated June 10, 2021 between Immunic, Inc. and Glenn Whaley	8-K	10.4	June 10, 2021
10.26+	Underwriting Agreement, dated July 15, 2021, by and between Immunic, Inc. and Piper Sandler & Co	8-K	1.1	July 15, 2021
10.27+	Employment Agreement, dated October 14, 2021, between Immunic, Inc. and Patrick Walsh	8-K	10.1	October 14, 2021
21.1*	List of subsidiaries of the Registrant.			
23.1*	Consent of Baker Tilly U.S. LLP, Independent Registered Public Accounting Firm.			
24.1*	Power of Attorney (included on the signature page).			
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.			
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.			
32.1**	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.			
32.2**	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.			
99.1+	Employment Agreement, dated September 4, 2019, between Immunic, Inc. and Dr. Andreas Muehler.	8-K	99.3	September 5, 2019
99.2+	Addendum, dated September 4, 2019, to Service Agreement between Immunic AG and Dr. Andreas Muehler.	8-K	99.2	September 5, 2019
99.3+	Addendum, dated September 4, 2019, to Service Agreement between Immunic AG and Dr. Hella Kohlhof.	8-K	99.4	September 5, 2019
99.4+	Second Addendum, dated June 10, 2021, to Service Agreement between Immunic AG and Dr. Hella Kohlhof	8-K	99.2	June 10, 2021
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 Database.			
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.			
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.			
104*	Cover Page Interactive Data File			

\+ Indicates a management contract or compensatory plan or arrangement.

* Filed herewith.

** In accordance with Item 601(b)(32)(ii) of Regulation S-K and SEC Release No. 33-8238 and 34-47986, Final Rule: Management's Reports on Internal Control Over Financial Reporting and Certification of Disclosure in Exchange Act Periodic Reports, the certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Exchange Act. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act or the Exchange Act, except to the extent that the registrant specifically incorporates it by reference.

IMMUNIC, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the board of directors of Immunic, Inc.:

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Immunic, Inc. (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows, for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements 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 audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits 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. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Assessment of accrual for research and development costs related to clinical trial activities

Critical Audit Matter Description

As described in Notes 2 and 3 to the consolidated financial statements, the Company records expenses and accruals for estimated costs of research and development activities, including third party contract services costs for clinical research. Clinical trial activities performed by third parties are expensed based upon estimates of work completed in accordance with agreements with the respective Clinical Research Organization. Billing terms and payments are reviewed by management to ensure estimates of outstanding obligations are appropriate as of period end. Tracking the progress of completion for clinical trial activities performed by third parties allows the Company to record the appropriate expense and accruals under the terms of the agreements.

Auditing the accounting for accrued clinical trial expenses is complex because of the high volume of data used in management’s estimates, the assumptions used by management to develop their estimates and the procedures necessary to verify the cost and extent of unbilled work performed during the reporting period.

How We Addressed the Matter in Our Audit

We obtained an understanding of the Company's process and evaluated the design and implementation of internal controls related to the completeness and valuation of accrued clinical trial expenses.

To test the clinical trial accrual, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating and testing the significant assumptions used by management to estimate the accruals. To test the significant assumptions, we corroborated the progress of clinical trials and other research and development projects with the Company's research and development personnel that oversee the clinical trials, and obtained information received directly from third parties, which included the third parties' estimate of costs incurred to date. We also tested subsequent invoicing received from third parties.

Baker Tilly US, LLP

We have served as the Company's auditor since 2019.

Minneapolis, MN

February 24, 2022

IMMUNIC, INC.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

	December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 86,863	$ 127,452
Other current assets and prepaid expenses	18,125	6,293
Total current assets	104,988	133,745
Property and equipment, net	152	203
Goodwill	32,970	32,970
Right of use asset, net	948	901
Other long-term assets	42	42
Total assets	$ 139,100	$ 167,861
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,745	$ 3,700
Accrued expenses	7,071	4,318
Other current liabilities	585	379
Total current liabilities	11,401	8,397
Long-term liabilities:		
Operating lease liabilities	584	679
Total long-term liabilities	584	679
Total liabilities	11,985	9,076
Commitments and contingencies (note 4)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 20,000,000 authorized and no shares issued or outstanding at December 31, 2021 and 2020	—	—
Common stock, $0.0001 par value; 130,000,000 shares authorized and 26,335,418 and 21,168,240 shares issued and outstanding at December 31, 2021 and 2020, respectively	3	2
Additional paid-in capital	324,237	266,823
Accumulated other comprehensive loss	(252)	(4,112)
Accumulated deficit	(196,873)	(103,928)
Total stockholders' equity	127,115	158,785
Total liabilities and stockholders' equity	$ 139,100	$ 167,861

The accompanying notes are an integral part of these consolidated financial statements.

IMMUNIC, INC.

Consolidated Statements of Operations

(In thousands, except share and per share amounts)

	Years Ended December 31,	
	2021	2020
Operating expenses:		
Research and development	$ 61,115	$ 38,637
General and administrative	13,300	10,334
4SC Royalty Settlement (See Note 4)	17,250	—
Total operating expenses	91,665	48,971
Loss from operations	(91,665)	(48,971)
Other income (expense):		
Interest income	66	58
Other income (expense), net	(1,346)	4,896
Total other income (expense)	(1,280)	4,954
Net loss	$ (92,945)	$ (44,017)
Net loss per share, basic and diluted	$ (3.93)	$ (2.81)
Weighted-average common shares outstanding, basic and diluted	23,652,779	15,663,826

The accompanying notes are an integral part of these consolidated financial statements.

IMMUNIC, INC.

Consolidated Statements of Comprehensive Loss

(In thousands)

	Years Ended December 31,	
	2021	**2020**
Net loss	$ (92,945)	$ (44,017)
Other comprehensive income (loss):		
Foreign currency translation income (loss), net of tax	3,860	(2,739)
Total comprehensive loss	$ (89,085)	$ (46,756)

The accompanying notes are an integral part of these consolidated financial statements.

IMMUNIC, INC.

Consolidated Statements of Stockholders' Equity

(In thousands, except shares)

	Shares	Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2019	10,744,806	$ 1	$ 119,646	$ (1,373)	$ (59,911)	$ 58,363
Net loss	—	—	—	—	(44,017)	(44,017)
Foreign exchange translation adjustment	—	—	—	(2,739)	—	(2,739)
Stock-based compensation	—	—	2,747	—	—	2,747
Issuance of common stock - At The Market Sales Agreement net of issuance costs of $339	733,728	—	10,925	—	—	10,925
Issuance of common stock - April registered direct equity offering net of issuance costs of $1,082	1,764,706	—	13,918	—	—	13,918
Issuance of common stock - June public equity offering net of issuance costs of $1,752	2,175,000	—	23,048	—	—	23,048
Issuance of common stock - August public equity offering net of issuance costs of $6,960	5,750,000	1	96,539	—	—	96,540
Balance at December 31, 2020	21,168,240	2	$ 266,823	$ (4,112)	$ (103,928)	$ 158,785
Net loss	—	—	—	—	(92,945)	(92,945)
Foreign exchange translation adjustment	—	—	—	3,860	—	3,860
Stock-based compensation	—	—	5,949	—	—	5,949
Issuance of common stock - July 2021 equity offering net of issuance costs of $2,980	4,500,000	1	42,019	—	—	42,020
Issuance of common stock - At The Market Sales Agreement net of issuance costs of $23	73,221	—	729	—	—	729
Shares issued in connection with the Company's employee stock purchase plan	12,758	—	92	—	—	92
Issuance of common stock in connection with the 4SC royalty settlement (see note 4)	581,199	—	8,625	—	—	8,625
Balance at December 31, 2021	26,335,418	3	$ 324,237	$ (252)	$ (196,873)	$ 127,115

The accompanying notes are an integral part of these consolidated financial statements.

IMMUNIC, INC.

Consolidated Statements of Cash Flows

(In thousands)

	Years Ended December 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (92,945)	$ (44,017)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	85	39
Stock-based compensation	5,949	2,747
Unrealized foreign currency (gain) loss	4,332	(2,528)
Common stock issued in connection with the 4SC royalty settlement (see Note 4)	8,625	—
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(12,800)	(2,779)
Accounts payable	176	1,000
Other liabilities	170	(1,255)
Accrued expenses and other current liabilities	3,175	669
Net cash used in operating activities	(83,233)	(46,124)
Cash flows from investing activities:		
Purchases of property and equipment	(67)	(146)
Net cash used in investing activities	(67)	(146)
Cash flows from financing activities:		
Proceeds from public offering of common stock through At The Market offering, net of issuance costs of $23 and $339, respectively	729	10,925
Proceeds from shares issued in connection with the Company's employee stock purchase plan	92	—
Proceeds from April 2020 registered direct equity offering, net of issuance costs of $1,082	—	13,918
Proceeds from June 2020 public equity offering, net of issuance costs of $1,752	—	23,048
Proceeds from August 2020 public equity offering, net of issuance costs of $6,960	—	96,540
Proceeds from July 2021 public equity offering, net of issuance costs of $2,980	42,020	—
Net cash provided by financing activities	42,841	144,431
Effect of exchange rate changes on cash and cash equivalents	(130)	(78)
Net change in cash and cash equivalents	(40,589)	98,083
Cash and cash equivalents, beginning of year	127,452	29,369
Cash and cash equivalents, end of year	$ 86,863	$ 127,452
Supplemental disclosure of noncash investing and financing activities:		
Common stock issued in connection with the 4SC royalty settlement (see note 4)	$ 8,625	$ —
Operating lease right-of use asset obtained in exchange for lease obligation	$ 435	$ —
Offering costs in accrued expenses	$ —	$ 114

The accompanying notes are an integral part of these consolidated financial statements.

Notes to Consolidated Financial Statements

1. Description of Business and Basis of Financial Statements

Description of Business

Immunic, Inc. ("Immunic" or the "Company") is a clinical-stage biopharmaceutical company with a pipeline of selective oral immunology therapies focused on treating chronic inflammatory and autoimmune diseases, including relapsing multiple sclerosis (“RMS”), ulcerative colitis (“UC”), Crohn’s disease (“CD”) and psoriasis. The Company is headquartered in New York City with its main operations in Gräfelfing near Munich, Germany. The Company currently has approximately 55 employees.

The Company is currently pursuing three development programs. These include the vidofludimus calcium (IMU-838) program, which is focused on the development of oral formulations of a small molecule inhibitor of the enzyme dihydroorotate dehydrogenase (“DHODH”); the IMU-935 program, which is focused on an inverse agonist of retinoic acid receptor-related orphan nuclear receptor gamma truncated (“RORγt”), an immune cell-specific isoform of RORγ; and the IMU-856 program, which involves the development of a drug targeting the restoration of intestinal barrier function and regeneration of bowel epithelium. These product candidates are being developed to address diseases such as RMS, UC, CD, and psoriasis. In addition to these large markets, these products are also being developed to address certain rare diseases with high unmet medical needs, such as primary sclerosing cholangitis (“PSC”), as well as metastatic castration-resistant prostate cancer (“mCRPC”).

The Company’s business, operating results, financial condition and growth prospects are subject to significant risks and uncertainties, including the failure of its clinical trials to meet their endpoints, failure to obtain regulatory approval and needing additional funding to complete the development and commercialization of the Company's three development programs.

Liquidity and Financial Condition

Immunic has no products approved for commercial sale and has not generated any revenue from product sales. Immunic has never been profitable and has incurred operating losses in each year since inception (2016). Immunic has an accumulated deficit of approximately $196.9 million as of December 31, 2021 and approximately $103.9 million as of December 31, 2020. Substantially all of Immunic’s operating losses resulted from expenses incurred in connection with its research and development programs and from general and administrative costs associated with its operations.

Immunic expects to incur significant expenses and increasing operating losses for the foreseeable future as it initiates and continues the preclinical and clinical development of its product candidates and adds personnel necessary to advance its clinical pipeline of product candidates. Immunic expects that its operating losses will fluctuate significantly from quarter-to-quarter and year-to-year due to timing of clinical development programs.

From inception through December 31, 2021, Immunic has raised net cash of approximately $259.5 million from private and public offerings of preferred and common stock. As of December 31, 2021, the Company had cash and cash equivalents of approximately $86.9 million. The Company is dependent on financing activities to fund ongoing operations and due to the inherent uncertainties in successfully completing financing transactions, and with our forecasted cash reach through the first quarter of 2023, these are indicators of an inability to continue as a going concern. However, the Company has the ability to manage the amount and timing of expenditures to reduce costs, has limited required fixed spend, and can manage working capital as needed. These factors coupled with the $16.2 million of cash raised so far in 2022 under it's At The Market ("ATM") facility alleviates any uncertainty that the Company will have adequate liquidity to meet its obligations for at least the next 12 months from the financial statement release date.

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in conformity with United States generally accepted accounting principles, ("U.S. GAAP") and include the accounts of Immunic and its wholly-owned subsidiaries, Immunic AG and Immunic Research GmbH (which both began operations in 2016) and Immunic Australia Pty Ltd. (which began operations in 2018). All intercompany accounts and transactions have been eliminated in consolidation. Immunic manages its operations as a single reportable segment for the purposes of assessing performance and making operating decisions. Certain prior period amounts have been reclassified to conform to the current basis of presentation.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make certain estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and the disclosure of contingent assets and liabilities in the Company's consolidated financial statements. The most significant estimates in the Company's financial statements and accompanying notes relate to clinical trial expenses and share-based compensation. Management believes its estimates to be reasonable under the circumstances. Actual results could differ materially from those estimates and assumptions.

Foreign Currency Translation and Presentation

The Company's reporting currency is United States ("U.S.") dollars. Immunic AG and Immunic Research GmbH's operations are located in Germany with the euro being their functional currency. Immunic Australia Pty Ltd.'s functional currency is the Australian dollar. All amounts in the financial statements where the functional currency is not the U.S. dollar are translated into U.S. dollar equivalents at exchange rates as follows:

- assets and liabilities at reporting period-end rates;
- income statement accounts at average exchange rates for the reporting period; and
- components of equity at historical rates.

Gains and losses from translation of the financial statements into U.S. dollars are recorded in stockholders' equity as a component of accumulated other comprehensive income (loss). Realized and unrealized gains and losses resulting from foreign currency transactions denominated in currencies other than the functional currency are reflected as general and administrative expenses in the Consolidated Statements of Operations. Foreign currency transaction gains and losses related to long-term intercompany loans that are payable in the foreseeable future are recorded in Other Income (Expense). The Consolidated Statements of Cash Flows were prepared by using the average exchange rate in effect during the reporting period which reasonably approximates the timing of the cash flows.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less to be cash equivalents.

Cash and cash equivalents consist of cash on hand and deposits in banks located in the U.S., Germany and Australia. The Company maintains cash and cash equivalent balances denominated in Euro and U.S. dollars with major financial institutions in the U.S. and Germany in excess of the deposit limits insured by the government. Management periodically reviews the credit standing of these financial institutions and believes that the Company is not exposed to any significant credit risk. The Company currently deposits its cash and cash equivalents with two large financial institutions.

Fair Value Measurement

Fair value is defined as the price that would be received to sell an asset or be paid to transfer a liability in an orderly transaction between market participants on the measurement date. Accounting guidance establishes a fair value hierarchy that requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1—Quoted prices in active markets for identical assets or liabilities. Level 1 assets consisted of money market funds for the periods presented. The Company had no Level 1 liabilities for the periods presented.

Level 2— Inputs other than observable quoted prices for the asset or liability, either directly or indirectly; these include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active. The Company had no Level 2 assets or liabilities for the periods presented.

Level 3—Unobservable inputs to the valuation methodology that are significant to the measurement of the fair value of assets or liabilities. The Company had no Level 3 assets or liabilities for the periods presented.

The carrying value of cash and cash equivalents, other current assets and prepaid expenses, accounts payable, accrued expenses, and other current liabilities approximates fair value due to the short period of time to maturity.

Property and Equipment

Property and equipment is stated at cost. Depreciation is computed using the straight-line method based on the estimated service lives of the assets which range from three years to thirteen years. Depreciation and amortization expense was $85,000 and $39,000 for the years ended December 31, 2021 and 2020, respectively.

Impairment of Long-Lived Assets

The Company records impairment losses on long-lived assets used in operations when indicators of impairment are present and the undiscounted cash flows estimated to be generated by those assets are less than the assets' carrying amount. Impaired assets are then recorded at their estimated fair value. There were no impairment losses during the years ended December 31, 2021 and 2020.

Goodwill

Business combinations are accounted for under the acquisition method. The total purchase price of an acquisition is allocated to the underlying identifiable net assets, based on their respective estimated fair values as of the acquisition date. Determining the fair value of assets acquired and liabilities assumed requires management's judgment and often involves the use of significant estimates and assumptions, including assumptions with respect to future cash inflows and outflows, probabilities of success, discount rates, and asset lives, among other items. Assets acquired and liabilities assumed are recorded at their estimated fair values. The excess of the purchase price over the estimated fair values of the net assets acquired is recorded as goodwill.

Goodwill is tested for impairment at the reporting unit level annually in the fourth quarter, or more frequently when events or changes in circumstances indicate that the asset might be impaired. Examples of such events or circumstances include, but are not limited to, a significant adverse change in legal or business climate, an adverse regulatory action or unanticipated competition.

The Company assesses qualitative factors to determine whether the existence of events or circumstances would indicate that it is more likely than not that the fair value of the reporting unit is less than its carrying amount. If after assessing the totality of events or circumstances, the Company were to determine that it is more likely than not that the fair value of the reporting unit is less than its carrying amount, then the Company would perform a quantitative test that compares the fair value to its carrying value to determine the amount of any impairment. Impairment testing for goodwill is done at the reporting unit level. The Company has determined that it operates in a single operating segment and has a single reporting unit. The Company has determined there was no goodwill impairment as of December 31, 2021.

Research and Development Expenses

These costs primarily include external development expenses and internal personnel expenses for the three development programs, vidofludimus calcium, IMU-935 and IMU-856. Immunic has spent the majority of its research and development resources on vidofludimus calcium, the Company's lead development program for clinical trials in RRMS, UC, COVID-19, and PSC.

Research and development expenses consist of expenses incurred in research and development activities, which include clinical trials, contract research services, certain milestone payments, salaries and related employee benefits, allocated facility costs and other outsourced services. Research and development expenses are charged to operations as incurred.

The Company enters into agreements with contract research organizations ("CROs") to provide clinical trial services for individual studies and projects by executing individual work orders governed by a Master Service Arrangement ("MSA"). The MSAs and associated work orders provide for regular recurrent payments and payments upon the completion of certain milestones. The Company regularly assesses the timing of payments against actual costs incurred to ensure a proper accrual of related expenses in the appropriate accounting period.

Collaboration Arrangements

Certain collaboration and license agreements may include payments to or from the Company of one or more of the following: non-refundable or partially refundable upfront or license fees; development, regulatory and commercial milestone payments; payment for manufacturing supply services; partial or complete reimbursement of research and development costs; and royalties on net sales of licensed products. The Company assesses whether such contracts are within the scope of Financial Accounting Standards Board (FASB) Accounting Standards Update ("ASU") 2014-09 "*Revenue from Contracts with Customers*" and ASU No. 2018-18, "*Collaborative Arrangements*", ("ASU 2018-18"). ASU 2018-18, clarifies that certain elements of collaborative arrangements could qualify as transactions with customers in the scope of ASC 606.

In October 2018, the Company entered into an option and license agreement (the "Daiichi Sankyo Agreement") with Daiichi Sankyo Co., Ltd. ("Daiichi Sankyo") which granted the Company the right to license a group of compounds, designated by the Company as IMU-856, as a potential new oral treatment option for diseases such as inflammatory bowel disease, irritable bowel syndrome with diarrhea, immune checkpoint inhibitor induced colitis and other barrier function associated diseases. During the option period, the Company performed agreed upon research and development activities for which it was reimbursed by Daiichi Sankyo up to a maximum agreed-upon limit. Such reimbursement was recorded as other income. There are no more research and development reimbursements expected under this agreement.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, business development and other support functions. Other general and administrative expenses include, but are not limited to, stock-based compensation, insurance costs, professional fees for legal, accounting and tax services, consulting, related facility costs and travel.

Stock-Based Compensation

The Company measures the cost of employee and non-employee services received in exchange for equity awards based on the grant-date fair value of the award recognized generally as an expense (i) on a straight-line basis over the requisite service period for those awards whose vesting is based upon a service condition, and (ii) on an accelerated method for awards whose vesting is based upon a performance condition, but only to the extent it is probable that the performance condition will be met. Stock-based compensation is (i) estimated at the date of grant based on the award's fair value for equity classified awards and (ii) final measurement date for liability classified awards. Forfeitures are recorded in the period in which they occur.

The Company estimates the fair value of stock options using the Black-Scholes-Merton option-pricing model ("BSM"), which requires the use of estimates and subjective assumptions, including the risk-free interest rate, the fair value of the underlying common stock, the expected dividend yield of the Company's common stock, the expected volatility of the price of the Company's common stock, and the expected term of the option. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, the Company's stock-based compensation expense could be materially different in the future.

Leases

The Company leases office space and office equipment. The underlying lease agreements have lease terms of less than 12 months and up to 60 months. Leases with terms of 12 months or less at inception are not included in the operating lease right of use asset and operating lease liability.

The Company has two existing leases for office space. At inception of a lease agreement, the Company determines whether an agreement represents a lease and at commencement each lease agreement is assessed as to classification as an operating or financing lease. The Company's two leases have been classified as operating leases and an operating lease right-of-use asset and an operating lease liability have been recorded on the Company's balance sheet. A right-of-use lease asset represents the Company's right to use the underlying asset for the lease term and the lease obligation represents its commitment to make the lease payments arising from the lease. Right-of-use lease assets and obligations are recognized at the commencement date based on the present value of remaining lease payments over the lease term. As the Company's leases do not provide an implicit rate, the Company has used an estimated incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The right-of-use lease asset includes any lease payments made prior to commencement and excludes any lease incentives. The lease term used in estimating future lease payments may include options to extend when it is reasonably certain that the Company will exercise that option. Operating

lease expense is recognized on a straight-line basis over the lease term, subject to any changes in the lease or changes in expectations regarding the lease term. Variable lease costs such as common area costs and property taxes are expensed as incurred. Leases with an initial term of twelve months or less are not recorded on the balance sheet.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Accumulated other comprehensive income (loss) has been reflected as a separate component of stockholders' equity in the accompanying Consolidated Balance Sheets and consists of foreign currency translation adjustments (net of tax).

Income Taxes

The Company is subject to corporate income tax laws and regulations in the U.S., Germany and Australia. Tax regulations within each jurisdiction are subject to the interpretation of the related tax laws and regulations and require significant judgment in their application.

The Company utilizes the asset and liability method of accounting for income taxes which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the audited consolidated financial statements. Deferred income tax assets and liabilities are determined based on the differences between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of changes in tax rates on deferred tax assets and liabilities is recognized in operations in the period that includes the enactment date. Deferred taxes are reduced by a valuation allowance when, in the opinion of management, it is more likely than not some portion or the entire deferred tax asset will not be realized. As of December 31, 2021 and 2020, the Company maintained a full valuation allowance against the balance of deferred tax assets.

It is the Company's policy to provide for uncertain tax positions and the related interest and penalties based upon management's assessment of whether a tax benefit is more likely than not to be sustained upon examination by tax authorities. The Company recognizes interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense. The Company is subject to U.S. federal, New York, California, Texas, German and Australian income taxes. The Company is subject to U.S. federal or state income tax examination by tax authorities for tax returns filed for the years 2003 and forward due to the carryforward of NOLs. Tax years 2016 through 2020 are subject to audit by German and Australian tax authorities. The Company is not currently under examination by any tax jurisdictions.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss by the weighted-average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss by the weighted-average number of common shares and, if dilutive, common stock equivalents outstanding for the period determined using the treasury-stock method. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to the Company's net loss position.

Potentially dilutive securities, not included in the calculation of diluted net loss per share attributable to common stockholders because to do so would be anti-dilutive, are as follows:

	As of December 31,	
	2021	2020
Options to purchase common stock	2,157,460	1,117,160

Recently Adopted Accounting Standards

There are no recently issued accounting standards that would have a significant impact on the Company's consolidated financial statements.

3. Balance Sheet Details

Prepaid Expenses and Other Current Assets

Prepaid Expense and Other Current Assets consist of (in thousands):

	December 31,	
	2021	2020
Prepaid clinical and related costs	$ 14,853	$ 3,416
VAT receivable	279	295
Australian research and development tax incentive	1,871	1,348
Other	1,122	1,234
Total	$ 18,125	$ 6,293

Accounts Payable

Accounts Payable consist of (in thousands):

	December 31,	
	2021	2020
Clinical and related costs	$ 3,427	$ 3,408
Legal and audit costs	72	139
Other	246	153
Total	$ 3,745	$ 3,700

Accrued Expenses

Accrued Expenses consist of (in thousands):

	December 31,	
	2021	2020
Accrued clinical and related costs	$ 6,214	$ 3,301
Accrued legal and audit costs	96	114
Accrued compensation	674	658
Accrued other	87	245
Total	$ 7,071	$ 4,318

Other Current Liabilities

Other Current Liabilities consist of (in thousands):

	December 31,	
	2021	2020
Lease liabilities	$ 408	$ 297
Other	177	82
Total	$ 585	$ 379

4. Commitments and Contingencies

Operating Lease

The Company leases certain office space under non-cancelable operating leases. The leases terminate on April 30, 2023 for the New York City office and June 30, 2025 for the Gräfelfing, Germany office. The Company formerly leased office space

in Planegg-Martinsried, Germany pursuant to a modified lease that terminated on August 31, 2020. These leases include both lease (e.g., fixed rent) and non-lease components (e.g., common-area and other maintenance costs). The non-lease components are deemed to be executory costs and are therefore excluded from the minimum lease payments used to determine the present value of the operating lease obligation and related right-of-use asset. The New York City lease has renewal options, but they were not included in calculating the right of use asset and liabilities. On April 7, 2020, the Company signed a five year lease for its facility in Gräfelfing, Germany. On March 1, 2021, the Company added additional lease space at the Gräfelfing, Germany office. Renewal options were not included in calculating the right of use asset and liabilities for this facility. The leases do not have concessions, leasehold improvement incentives or other build-out clauses. Further, the leases do not contain contingent rent provisions. The New York City lease had a six month rent holiday at the beginning of the lease. There were net additions to right of use assets of $427,000 as a result of signing the Gräfelfing, Germany lease and shortening the term of the Planegg-Martinsried, Germany lease during the year ended December 31, 2020 and net additions of $435,000 with the signing of additional lease space in March 2021.

The leases do not provide an implicit rate and, due to the lack of a commercially salable product, the Company is generally considered unable to obtain commercial credit. Therefore, the Company estimated its incremental interest rate to be 6%, considering the quoted rates for the lowest investment-grade debt and the interest rates implicit in recent financing leases. Immunic used its estimated incremental borrowing rate and other information available at the lease commencement date in determining the present value of the lease payments.

Immunic's operating lease costs and variable lease costs were $503,000 and $354,000 for the years ended December 31, 2021 and 2020, respectively. Variable lease costs consist primarily of common area maintenance costs, insurance and taxes which are paid based upon actual costs incurred by the lessor.

Maturities of the operating lease obligation are as follows as of December 31, 2021 (in thousands):		
2022	$	457
2023	$	307
2024	$	233
2025	$	116
2026	$	—
Thereafter	$	—
Total lease payments	$	1,113
Less: interest portion	$	95
Present value of lease obligation	$	1,018

Contractual Obligations

As of December 31, 2021, the Company has non-cancelable contractual obligations under certain agreements related to its development programs in vidofludimus calcium, IMU-935 and IMU-856 totaling approximately $2.8 million, all of which is expected to be paid in 2022.

Other Commitments and Obligations

In May 2016, the Company entered into a purchase agreement (the "Agreement") with 4SC AG, whereby the Company acquired certain assets, including the rights to patents and patent applications, trademarks and know-how. This transaction has been accounted for as an asset acquisition under Accounting Standards Update 2017-01 - Business Combinations (Topic 805): Clarifying the Definition of a Business. The Agreement included payments (Tranches III and IV) that were contingent upon the occurrence of certain events and required the Company to pay royalties equal to 4.4% of the aggregated net sales for a certain period as defined in the Agreement (Tranche III) upon commercialization of the acquired assets. Effective April 12, 2019, the parties agreed to settle Tranche IV by issuing 120,070 shares of the Company's common stock, immediately following the Transaction, to 4SC AG while keeping Tranche III in effect. Approximately $1.5 million of expense was recorded as a result of the issuance of these shares on April 12, 2019.

On March 31, 2021, Immunic AG, a wholly-owned subsidiary of the Company, and 4SC AG entered into a Settlement Agreement, pursuant to which Immunic AG settled its remaining obligation of the 4.4% royalty on net sales for $17.25 million (Tranche III of the Agreement). The payment was made 50% in cash and 50% in shares of Immunic's common stock (the

"Shares"). Pursuant to the Agreement, the Company filed a resale shelf registration statement on Form S-3 covering the resale of the Shares. With the execution of the Agreement, no further payment obligations remain between Immunic AG and 4SC AG.

Daiichi Sankyo Agreement

On January 5, 2020, the Company exercised its option to obtain the exclusive worldwide right to commercialization of IMU-856. Among other things, the option exercise grants Immunic AG the rights to Daiichi Sankyo's patent application related to IMU-856. In connection with the option exercise, the Company paid a one-time upfront licensing fee to Daiichi Sankyo. Under the Daiichi Sankyo Agreement, Daiichi Sankyo is also eligible to receive future development, regulatory and sales milestone payments, as well as royalties related to IMU-856.

Legal Proceedings

The Company is not currently a party to any litigation, nor is it aware of any pending or threatened litigation, that it believes would materially affect its business, operating results, financial condition or cash flows. However, its industry is characterized by frequent claims and litigation including securities litigation, claims regarding patent and other intellectual property rights and claims for product liability. As a result, in the future, the Company may be involved in various legal proceedings from time to time.

5. Fair Value

The following fair value hierarchy table present information about each major category of the Company's financial assets and liabilities measured at fair value on a recurring basis (in thousands):

	Fair Value Measurement at December 31, 2021			
	Fair Value	Level 1	Level 2	Level 3
Assets				
Money market funds	$ 31,630	$ 31,630	$ —	$
Total assets at fair value	$ 31,630	$ 31,630	$ —	$

	Fair Value Measurement at December 31, 2020			
	Fair Value	Level 1	Level 2	Level 3
Assets				
Money market funds	$ 39,615	$ 39,615	$ —	$
Total assets at fair value	$ 39,615	$ 39,615	$ —	$

There were no transfers between Level 1, Level 2 or Level 3 assets during the periods presented.

For the Company's money market funds, which are included as a component of cash and cash equivalents on the consolidated balance sheet, realized gains and losses are included in interest income (expense) on the consolidated statements of operations.

The carrying amounts of other current assets and prepaid expenses, accounts payable, accrued expenses, and other current liabilities approximate their fair values due to their short-term nature. The fair value and book value of the money market funds presented in the table above are the same.

6. Common Stock

Shelf Registration Statements

In May 2018, Vital Therapies filed a shelf registration statement on Form S-3 (the "2018 Shelf Registration Statement"), which became effective in June 2018. The 2018 Shelf Registration Statement permitted the offering, issuance and sale of up to $200.0 million of common stock, preferred stock, warrants, debt securities, and/or units in one or more offerings and in any combination. This registration statement expired in June 2021 and is no longer effective.

In November 2020, Immunic filed a shelf registration statement on Form S-3. The 2020 Shelf Registration Statement permits the offering, issuance and sale of up to $250.0 million of common stock, preferred stock, warrants, debt securities, and/or units in one or more offerings and in any combination of the foregoing.

In July 2019, the Company filed a Prospectus Supplement for the offering, issuance and sale of up to a maximum aggregate offering price of $40.0 million of common stock that may be issued and sold under an at-the-market sales agreement ("July 2019 ATM") with SVB Leerink LLC (“SVB Leerink”) as agent. The Company used the net proceeds from the offering to continue to fund the ongoing clinical development of its product candidates and for other general corporate purposes, including funding existing and potential new clinical programs and product candidates. The July 2019 ATM was effectively terminated in June 2021 when the 2018 Shelf Registration Statement expired.

In December 2020, the Company filed another Prospectus Supplement for the offering, issuance and sale of up to a maximum aggregate offering price of $50.0 million of common stock that may be issued and sold under another at-the-market sales agreement ("December 2020 ATM") with SVB Leerink as agent. The Company intends to use the net proceeds from the offering to continue to fund the ongoing clinical development of its product candidates and for other general corporate purposes, including funding existing and potential new clinical programs and product candidates. The December 2020 ATM will terminate upon the earlier of (i) the issuance and sale of all of the shares through SVB Leerink on the terms and subject to the conditions set forth in the December 2020 ATM or (ii) termination of the December 2020 ATM as otherwise permitted thereby. The December 2020 ATM may be terminated at any time by either party upon ten days’ prior notice, or by SVB Leerink at any time in certain circumstances, including the occurrence of a material adverse effect on the Company.

The Company has agreed to pay SVB Leerink a commission equal to 3.0% of the gross proceeds from the sales of common shares pursuant to the ATM and has agreed to provide SVB Leerink with customary indemnification and contribution rights.

For the year ended December 31, 2021, the Company raised gross proceeds of $0.8 million pursuant to the December 2020 ATM through the sale of 73,221 shares of common stock at a weighted average price of $10.27 per share. The net proceeds from the December 2020 ATM were $0.7 million after deducting underwriter commissions of $22,555. During 2022, we raised gross proceeds of $16.7 million pursuant to the December 2020 ATM through the sale of 1,568,487 shares of common stock at a weighted average price of $10.62 per shared. The net proceeds were $16.2 million after deducting underwriter commissions of $0.5 million. As of February 18, 2022, $32.6 million in capacity remains under the December 2020 ATM.

For the year ended December 31, 2020, the Company raised gross proceeds of $11.3 million pursuant to the July 2019 ATM through the sale of 733,728 shares of common stock at a weighted average price of $15.42 per share. The net proceeds from the July 2019 ATM were $11.0 million after deducting underwriter commissions of $339,356.

Public Equity Offerings

July 2021 Public Equity Offering

On July 15, 2021, the Company entered into an underwriting agreement with Piper Sandler & Co., in connection with the Company’s public offering of 4,500,000 shares of the Company’s common stock, $0.0001 par value per share, at a public offering price of $10.00 per share.

On July 19, 2021, the Company closed the Offering. The net proceeds to the Company from the Offering was approximately $42.0 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

August 2020 Offering

On August 4, 2020, the Company entered into an underwriting agreement with SVB Leerink LLC, as representative of the several underwriters in connection with the Company’s public offering of 5,000,000 shares of common stock, at a public offering price of $18.00 per share. Under the terms of the Underwriting Agreement, the Company granted the Underwriters an option, exercisable for 30 days, to purchase up to an additional 750,000 shares of Common Stock at the public offering price, less underwriting discounts and commissions, which was exercised in full on August 6, 2020.

On August 7, 2020, the Company closed the Offering. The net proceeds to the Company from the Offering, after giving effect to the exercise in full by the Underwriters of their option to purchase the Option Shares, was approximately $96.5 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

June 2020 Offering

On June 10, 2020, the Company entered into a placement agency agreement with ROTH Capital Partners, LLC ("RCP") and Ladenburg Thalmann & Co. Inc. relating to the Company's public offering of 2,175,000 shares of common stock. Pursuant to this agreement, the Company agreed to pay the placement agents a cash fee of 6.5% of the gross proceeds from the offering raised from investors and to reimburse the placement agents for certain costs incurred in connection therewith.

In addition, on June 10, 2020, the Company and certain institutional investors entered into securities purchase agreements relating to the issuance and sale of an aggregate of 2,175,000 shares of the Company's common stock. The purchase price per share in the Offering was $11.40 for aggregate gross proceeds to the Company of approximately $25.0 million.

The net proceeds to the Company from this offering, after deducting the Company's offering expenses, were approximately $23.0 million.

April 2020 Registered Direct Offering

On April 23, 2020, the Company entered into an engagement letter with RCP relating to the Company's registered direct offering of common stock to select institutional investors. Pursuant to this agreement, the Company agreed to pay RCP a cash fee of 6.5% of the gross proceeds from the offering raised from investors and to reimburse RCP for certain costs incurred in connection therewith.

In addition, on April 23, 2020, the Company and the investors entered into a securities purchase agreement relating to the issuance and sale of an aggregate of 1,764,706 shares of the Company's common stock. The purchase price per share was $8.50 for aggregate gross proceeds to the Company of approximately $15.0 million. This securities purchase agreement restricted the Company from issuing additional common stock for a period of 75 days from April 27, 2020, subject to certain exceptions.

The net proceeds to the Company from this offering, after deducting the Company's offering expenses, were approximately $13.9 million.

Common Stock

As of December 31, 2021, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 130,000,000 shares of common stock, par value of $0.0001. The voting, dividend and liquidation rights of the holders of the Company's common stock are subject to and qualified by the rights, powers and preferences of any holders of preferred stock.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, if any. Through December 31, 2021, no cash dividends had been declared or paid.

Preferred Stock

The Company's certificate of incorporation, as amended and restated, authorizes the Company to issue 20,000,000 shares of $0.0001 par value preferred stock, rights and preferences to be set by the board of directors. No preferred shares were outstanding as of December 31, 2021.

Stock Reserved for Future Issuance

Shares reserved for future issuance as of December 31, 2021 are as follows:

	Number of Shares
Common stock reserved for issuance for:	
2021 Employee stock purchase plan	187,242
Outstanding stock options	2,157,460
Common stock options available for future grant:	
2014 Equity Incentive Plan	43,311
2017 Inducement Equity Incentive Plan	46,250
2019 Omnibus Equity Incentive Plan	682,590
Total common shares reserved for future issuance	3,116,853

7. Stock-based Compensation Plans

2021 Employee Stock Purchase Plan

On April 25, 2021, the Company adopted the 2021 Employee Stock Purchase Plan ("ESPP"), which was approved by stockholder vote at the 2021 Annual Meeting of Stockholders held on June 10, 2021. The plan provides eligible employees of the Company with an opportunity to purchase common stock of the Company through accumulated payroll deductions, which are included in other current liabilities until they are used to purchase Company shares. Eligible employees participating in the bi-annual offering period can choose to have up to the lesser of 15% of their annual base earnings or the IRS annual share purchase limit of $25,000 in aggregate market value to purchase shares of the Company's common stock. The purchase price of the stock is the lesser of (i) 85% of the closing market price on the date of purchase and (ii) the closing market price at the beginning of the bi-annual offering period. The maximum number of shares reserved for delivery under the plan is 200,000 shares.

The first enrollment period under the plan commenced on August 1, 2021 and the Company recognized $46,000 of expense related to the plan in the twelve months ended December 31, 2021. The Company has issued 12,758 shares under the ESPP for the twelve months ended December 31, 2021.

Stock Option Programs

In July 2019, the Company's stockholders approved the 2019 Omnibus Equity Incentive Plan (the "2019 Plan") which was adopted by the Board with an effective date of June 14, 2019. The 2019 Plan allows for the grant of equity awards to employees, consultants and non-employee directors. An initial maximum of 1,500,000 shares of the Company's common stock are available for grant under the 2019 Plan. The 2019 Plan includes an evergreen provision that allows for the annual addition of up to 4% of the Company's fully-diluted outstanding stock, with a maximum allowable increase of 4,900,000 shares over the term of the 2019 Plan. In accordance with this provision, the shares available for grant were increased in 2020 and 2021 by a total of 1,340,050 shares. The 2019 Plan is currently administered by the Board, or, at the discretion of the Board, by a committee of the Board, which determines the exercise prices, vesting schedules and other restrictions of awards under the 2019 Plan at its discretion. Options to purchase stock may not have an exercise price that is less than the fair market value of underlying shares on the date of grant, and may not have a term greater than ten years. Incentive stock options granted to employees typically vest over four years. Non-statutory options granted to employees, officers, members of the Board, advisors, and consultants of the Company typically vest over three or four years.

Shares that are expired, terminated, surrendered or canceled under the 2019 Plan without having been fully exercised will be available for future awards.

Movements during the year

The following table summarizes stock option activity for the twelve months ended December 31, 2021 and 2020 under the 2019 Plan:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of January 1, 2021	1,117,160	$ 12.96		
Granted	1,193,809	$ 14.08		
Exercised	—	$ —		
Forfeited or expired	(153,509)	$ 13.50		
Outstanding as of December 31, 2021	2,157,460	$ 13.54	8.74	$ 302,155
Options vested and expected to vest as of December 31, 2021	2,157,460	$ 13.54	8.74	$ 302,155
Options exercisable as of December 31, 2021	752,954	$ 13.48	8.15	$ 79,431

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of January 1, 2020	456,645	$ 12.57		
Granted	744,406	$ 13.24		
Exercised	—	$ —		
Forfeited or expired	(83,891)	$ 13.32		
Outstanding as of December 31, 2020	1,117,160	$ 12.96	9.24	$ 2,894,754
Options vested and expected to vest as of December 31, 2020	1,117,160	$ 12.96	9.24	$ 2,894,754
Options exercisable as of December 31, 2020	263,507	$ 13.04	8.92	$ 661,952

Measurement

The weighted-average assumptions used in the BSM option pricing model to determine the fair value of the employee and non-employee stock option grants relating to the 2019 Plan were as follows:

Risk-Free Interest Rate

The risk-free rate assumption is based on U.S. Treasury instruments with maturities similar to the expected term of the stock options.

Expected Dividend Yield

The Company has not issued any dividends and does not expect to issue dividends over the life of the options. As a result, the Company has estimated the dividend yield to be zero.

Expected Volatility

Due to the Company's limited operating history and a lack of company specific historical and implied volatility data, the Company estimates expected volatility based on the historical volatility of a group of comparable companies that are publicly traded. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards.

Expected Term

The expected term of options is estimated considering the vesting period at the grant date, the life of the option and the average length of time similar grants have remained outstanding in the past.

The weighted-average grant date fair value of stock options granted under the 2019 Plan during the years ended December 31, 2021 and 2020 was $10.52 and $9.50, respectively. The following are the underlying assumptions used in the Black-Scholes-Merton option pricing model to determine the fair value of stock options granted to employees and to non-employees under this stock plan:

	2021	2020
Risk-free interest rate	0.93%	0.42%
Expected dividend yield	0%	0%
Expected volatility	93.0%	88.5%
Expected term of options (years)	6.0	5.8

Stock-Based Compensation Expense

Total stock-based compensation expense for all stock awards recognized in the accompanying audited consolidated statements of operations is as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$ 1,760	$ 731
General and administrative	4,189	2,016
Total	$ 5,949	$ 2,747

As of December 31, 2021 there was $12.2 million in total unrecognized compensation expense relating to the 2019 Plan to be recognized over a weighted average period of 2.89 years.

Summary of Equity Incentive Plans Assumed from Vital

Upon completion of the Transaction with Vital on April 12, 2019, Vital's 2012 Stock Option Plan (the "2012 Plan"), Vital's 2014 Equity Incentive Plan (the "2014 Plan") and Vital's 2017 Inducement Equity Incentive Plan (the "Inducement Plan"), were assumed by the Company. All awards granted under these plans have either been forfeited or expired.

There remain 43,311 shares available for grant under the 2014 Plan as of December 31, 2021.

In September 2017, Vital's Board of Directors approved the Inducement Plan, which was amended and restated in November 2017. Under the Inducement Plan 46,250 shares of Vital's common stock were reserved to be used exclusively for non-qualified grants to individuals who were not previously employees or directors as an inducement material to a grantee's entry into employment within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules.

No expense was recorded for the plans assumed from Vital during the twelve months ended December 31, 2021 and 2020, respectively.

8. Income Taxes

Net loss before income tax was subject to tax in the following jurisdictions for the following periods (in thousands):

	Years Ended December 31,	
	2021	2020
United States	$ (11,222)	$ (8,681)
Germany	(78,869)	(33,617)
Foreign	(2,854)	(1,719)
	$ (92,945)	$ (44,017)

The rate reconciliation consists of the following:

	Years Ended December 31,			
	2021		2020	
Federal statutory rate	21.0	%	21.0	%
Foreign rate differential	3.2	%	3.0	%
Stock options	(0.9)	%	(0.9)	%
Tax effect of rate change	0.0	%	(1.9)	%
Other	(0.4)	%	(0.9)	%
Change in valuation allowance	(22.9)	%	(20.3)	%
Effective tax rate	0.0	%	0.0	%

Deferred income taxes result from temporary differences between the tax basis of assets and liabilities and their reported amounts in the financial statements that will result in taxable or deductible amounts in future years. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in years in which those temporary differences are expected to be recovered or settled. As tax laws and rates change, deferred tax assets and liabilities are adjusted through income tax expense. There is no current or deferred income tax expense in the years ended December 31, 2021 and 2020, respectively.

Significant components of the Company's net deferred tax assets are shown below. A valuation allowance has been established as realization of such net deferred tax assets has not met the more likely-than-not threshold requirement. If the Company's judgment changes and it is determined that the Company will be able to realize these net deferred tax assets, the tax benefits relating to any reversal of the valuation allowance on the net deferred tax assets will be accounted for as a reduction to income tax expense.

	December 31,	
	2021	2020
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 18,437	$ 17,3
Stock-based compensation	576	1
Intangible Assets	3,848	
Foreign net operating loss carryforwards	34,819	18,9
Unrealized gain or loss	1,130	
Other, net	9	
Total deferred tax assets	58,819	36,5
Deferred tax liabilities:		
Property, plant and equipment	(2)	
Total deferred tax liability	(2)	
Net deferred tax assets	58,817	36,5
Less valuation allowance	(58,817)	(36,5
	$ —	$

The Company has incurred net operating losses each year since inception due to its history as a development stage company with no realized revenues from its planned principal operations. These cumulative operating losses provide significant negative evidence in the determination of whether or not the Company will be able to realize deferred tax assets such as net operating losses and other favorable temporary differences. There can be no assurance that it will ever generate taxable income. As a result, the Company has maintained a full valuation allowance against the entire balance of its net deferred tax assets since the date of inception. The valuation allowance has increased by $22.3 million and $6.8 million and for the years ended December 31, 2021 and 20, respectively.

As of December 31, 2021, Immunic had available NOLs of approximately $139.9 million in Germany and Australia. These NOLs do not expire.

The U.S. federal NOL carryforwards of $15.6 million were generated prior to 2018 and expire over 20 years beginning in 2023. The $72.2 million of post 2017 federal NOL carryforwards do not expire. Sections 382 of the Internal Revenue Code of 1986 subject the future utilization of net operating losses, to an annual limitation in the event of certain ownership changes, as defined. The Company may have undergone ownership changes and therefore may be limited in the amount of net operating losses available for utilization in the future.

The Company did not have any uncertain tax positions for the years ended December 31, 2021 and 2020, respectively.

Due to the full valuation allowance that the Company has on its net deferred tax asset balance, there are no uncertain tax positions that would impact the effective tax rate if recognized.

The Company is subject to U.S. federal, New York, California, Texas, German and Australian income taxes. The Company is subject to U.S. federal or state income tax examination by tax authorities for tax returns filed for the years 2003 and forward due to the carryforward of NOLs. Tax years 2017 through 2020 are subject to audit by German and Australian tax authorities. The Company is not currently under examination by any tax jurisdictions.

Immunic, Inc. recognizes interest and penalties related to unrecognized tax benefits on the income tax expense line in the accompanying consolidated statement of operations. Accrued interest and penalties are included on the related tax liability line in the consolidated balance sheet. There were no such interest or penalties for any of the years presented.

9. EIB Loan

On October 19, 2020, the Company and Immunic AG, its wholly-owned subsidiary, entered into a Finance Contract (the “Loan Agreement”) with the European Investment Bank (“EIB”), pursuant to which EIB agreed to provide Immunic AG with a

term loan in an aggregate amount of up to €24.5 million to support the development of Immunic's lead asset, vidofludimus calcium, in moderate coronavirus disease 2019 ("COVID-19"), to be made available to be drawn in three tranches, with the second and third tranches subject to the completion of certain pre-defined milestones. Effective October 20, 2021 the Company terminated this agreement with the EIB and no funds were drawn under this arrangement.

10. Related Party Transactions

Executive Chairman Agreement with Duane Nash

On April 15, 2020, the compensation committee of the Board of Directors of the Company independently reviewed and approved entering into an employment agreement with the current Chairman of the Board, Duane Nash, MD, JD, MBA (the "Executive Chairman Agreement") and pursuant to such approval, on April 17, 2020, the Company and Dr. Nash entered into the Executive Chairman Agreement. The Executive Chairman Agreement establishes an "at will" employment relationship pursuant to which Dr. Nash serves as Executive Chairman and contemplated a term that ends on October 15, 2020, which was subsequently extended to April 15, 2021. On April 15, 2021, the Company and Dr. Nash entered into an addendum (the "Agreement") to extend the term of the Executive Chairman Agreement to April 15, 2022. In connection with the Agreement, the Company made a one-time award to Dr. Nash of an option to purchase 90,000 shares of Company common stock, which will vest monthly commencing on May 15, 2021, and to increase Dr. Nash's monthly base salary to $27,960 from $25,417.

11. Selected Quarterly Data (unaudited)

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2021 and 2020 are as follows (in thousands, except per share data):

	For the Quarters Ended				
	March 31	June 30	September 30	December 31	Total Year
2021					
Operating expenses	$ 32,387	$ 19,170	$ 18,387	$ 21,721	$ 91,665
Net loss	$ (34,534)	$ (17,934)	$ (19,292)	$ (21,185)	$ (92,945)
Basic and diluted net loss per share (1)	$ (1.63)	$ (0.82)	$ (0.76)	$ (0.81)	$ (3.93)
2020					
Operating expenses	$ 9,014	$ 12,222	$ 13,545	$ 14,190	$ 48,971
Net loss	$ (8,487)	$ (11,458)	$ (12,913)	$ (11,159)	$ (44,017)
Basic and diluted net loss per share (1)	$ (0.79)	$ (0.90)	$ (0.70)	$ (0.53)	$ (2.81)

(1) Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per share calculations will not necessarily equal the annual per share calculation.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Immunic, Inc.

Date: February 24, 2022

By: /s/ DANIEL VITT
Daniel Vitt
Chief Executive Officer and President

POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Daniel Vitt and Glenn Whaley, and each of them, his or her true and lawful attorneys-in-fact, each with full power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ DANIEL VITT Daniel Vitt	Director, Chief Executive Officer and President	February 24, 2022
/s/ GLENN WHALEY Glenn Whaley	Principal Financial and Accounting Officer	February 24, 2022
/s/ DUANE D. NASH Duane D. Nash	Executive Chairman	February 24, 2022
/s/ TAMAR HOWSON Tamar Howson	Director	February 24, 2022
/s/ JOERG NEERMANN Joerg Neermann	Director	February 24, 2022
/s/ VINCENT OSSIPOW Vincent Ossipow	Director	February 24, 2022
/s/ BARCLAY A. PHILLIPS Barclay A. Phillips	Director	February 24, 2022
/s/ JAN VAN DEN BOSSCHE Jan Van den Bossche	Director	February 24, 2022

Exhibit 4.2

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 130,000,000 shares of common stock, par value $0.0001 per share, and 20,000,000 shares of preferred stock, par value $0.0001 per share.

The following description of our common stock summarizes its material terms and provisions, but it is not complete. For the complete terms of our common stock, please refer to our certificate of incorporation and our bylaws that are incorporated by reference into the Annual Report on Form 10-K of which this exhibit is a part.

Common Stock

As of December 31, 2020, there were 21,168,240 shares of common stock outstanding. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. The holders of common stock are not entitled to cumulative voting rights with respect to the election of directors, and as a consequence, minority stockholders will not be able to elect directors on the basis of their votes alone.

Subject to preferences that may be applicable to any then outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. In the event of a liquidation, dissolution or winding up of us, holders of the common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any then outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. All outstanding shares of common stock are fully paid and non-assessable. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any of our outstanding preferred stock.

Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol “IMUX.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC (“AST”). The transfer agent and registrar’s address is 6201 15th Avenue, Brooklyn, New York 11219.

Dividends

We have not declared any cash dividends on our common stock since inception and we do not anticipate paying any cash dividends on our common stock in the foreseeable future.

Possible Anti-Takeover Effects of Delaware Law and our Charter Documents

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws could make the following transactions more difficult: an acquisition of us by means of a tender offer, an acquisition of us by means of a proxy contest or otherwise, or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interest, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law (the "DGCL"), an anti-takeover statute. In general, Section 203 of the DGCL prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years following the time the person became an interested stockholder, unless the business combination or the acquisition of shares that resulted in a stockholder becoming an interested stockholder is approved in a prescribed manner. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns (or within three years prior to the determination of interested stockholder status did own) 15% or more of a corporation's voting stock. The existence of this provision would be expected to have an anti-takeover effect with respect to transactions not approved in advance by our board of directors, including discouraging attempts that might result in a premium over the market price for the shares of common stock held by our stockholders.

Undesignated Preferred Stock.

The ability of our board of directors, without action by the stockholders, to issue up to 20,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to effect a change in control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Requirements for Advance Notification of Stockholder Nominations and Proposals.

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent.

Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Staggered Board.

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors.

Our amended and restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting.

Our amended and restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. We may use additional shares for a variety of purposes, including future public offerings to raise additional capital, to fund acquisitions and as employee compensation. The existence of authorized but unissued shares of undesignated preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary

obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer, stockholder or stockholder group. The rights of holders of our common stock described above will be subject to, and may be adversely affected by, the rights of any preferred stock that we may designate and issue in the future. The issuance of shares of undesignated preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Director Liability

Our bylaws limit the extent to which our directors are personally liable to us and our stockholders, to the fullest extent permitted by the DGCL. The inclusion of this provision in our bylaws may reduce the likelihood of derivative litigation against directors and may discourage or deter stockholders or management from bringing a lawsuit against directors for breach of their duty of care.

The provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interest.

Exhibit 21.1

Subsidiaries of the Registrant

Set forth below is a list of subsidiaries of the Registrant. All of the subsidiaries listed below are wholly-owned subsidiaries of Immunic, Inc. and are owned directly by Immunic, Inc.

Subsidiary	Jurisdiction of Formation
Immunic AG	Germany

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements on Form S-3 (File No. 333-225230, 333-250083, and 333-255303), Form S-4 (File No. 333-229510), and Form S-8 (File No. 333-233864 and 333-258235) of Immunic, Inc. of our report dated February 24, 2022, relating to the consolidated financial statements of Immunic, Inc., which appears in this annual report on Form 10-K for the year ended December 31, 2021.

/s/ Baker Tilly US, LLP

Minneapolis, Minnesota
February 24, 2022

Exhibit 31.1

CERTIFICATIONS

I, Daniel Vitt, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2021 of Immunic, Inc.;

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 registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer 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 registrant 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 registrant, 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 registrant'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 registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant'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 registrant'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 registrant's internal control over financial reporting.

Date: February 24, 2022

By: /s/ Daniel Vitt
Daniel Vitt
Chief Executive Officer and President
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Glenn Whaley, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2021 of Immunic, Inc.;

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 registrant as of and for the periods presented in this report;

4. The registrant's other certifying officer 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 registrant 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 registrant, 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 registrant'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 registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant'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 registrant'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 registrant's internal control over financial reporting.

Date: February 24, 2022

By: /s/ Glenn Whaley
Glenn Whaley
Principal Financial and Accounting Officer
(Principal Financial and Accounting Officer and Duly Authorized Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Immunic, Inc. (the "Company") for the period ended December 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Daniel Vitt, as Chief Executive Officer and President of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 24, 2022

By: /s/ Daniel Vitt
Daniel Vitt
Chief Executive Officer and President
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Immunic, Inc. (the "Company") for the period ended December 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned,Glenn Whaley as Principal Financial and Accounting Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to my knowledge::

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 24, 2022

By: /s/ Glenn Whaley
Glenn Whaley
Principal Financial and Accounting Officer
(Principal Financial and Accounting Officer and Duly Authorized Officer)