ANNUAL REPORT
2022

www.intracellulartherapies.com

April 28, 2023

Dear Shareholders,

2022 was a successful year for Intra-Cellular Therapies. We have advanced our mission to develop effective, innovative treatments for neuropsychiatric and neurologic disorders with the exceptionally strong commercial launch of CAPLYTA® (lumateperone) in bipolar depression. CAPLYTA is solidly positioned as a pivotal drug for bipolar depression and schizophrenia patients, and its successful uptake is a testament to the strength of our organization. Our commercial performance and our ongoing programs to expand CAPLYTA's indications, together with the quality of our earlier stage pipeline, gives us confidence in a bright future for ITCI.

CAPLYTA is approved for the treatment of schizophrenia and is the first and only treatment approved for bipolar I and bipolar II depression in adults, as monotherapy and as adjunctive therapy with lithium or valproate. During the last year, we received FDA approval and launched two new dosage strengths of CAPLYTA, 10.5 mg and 21 mg. These dosage strengths expand the patient population for CAPLYTA by providing dosage recommendations for patients taking strong or moderate CYP3A4 inhibitors and patients with moderate or severe hepatic impairment.

Demand for CAPLYTA has been very strong with prescriptions tripling in 2022, and we have received overwhelmingly positive feedback from physicians on CAPLYTA's efficacy, tolerability, and ease of use. CAPLYTA is having a positive impact in patients' lives, and we are confident in continued growth.

We continue to study lumateperone in major depressive disorder (MDD) and other mood disorders. We are advancing our registration program evaluating lumateperone as adjunctive treatment in patients with MDD who have partially responded to antidepressants, which includes three Phase 3 studies. Most recently, we reported robust positive data from Study 403 in patients with MDD or bipolar depression with mixed features, adding to the growing body of evidence supporting lumateperone's broad potential in mood disorders. We are particularly pleased with the magnitude and consistency of the results. In this study, lumateperone met the primary and key secondary endpoints with robust treatment effects across all patient populations studied: in the combined population of MDD with mixed features and bipolar depression with mixed features as well as in the individual patient populations of MDD with mixed features and bipolar depression with mixed features.

In addition to CAPLYTA, we continue to invest in our future growth through the advancement of other pipeline programs, which include ITI-1284, our long-acting injectable program for lumateperone, our phosphodiesterase I (PDE1) inhibitors, and ITI-333.

ITI-1284 ODT SL is a deuterated form of lumateperone, formulated as an oral disintegrating tablet for sublingual administration. Having performed earlier stage studies last year, in 2023, we plan to initiate Phase 2 trials of ITI-1284 in patients with agitation in Alzheimer's disease, psychosis in Alzheimer's disease and generalized anxiety disorder.

Additionally, last year we completed a Phase 1 study of lumateperone long-acting injectable formulation for the treatment of schizophrenia. We plan to initiate further Phase 1 studies with several long-acting injectable formulations this year and next year.

In our PDE1 inhibitor program, patient enrollment has commenced in our Phase 2 proof-of-concept study for our lead compound lenrispodun, which is being developed for the treatment of motor symptoms in patients with Parkinson's disease. Changes in cognitive measures and inflammatory biomarkers will also be assessed. We have

an active investigational new drug application for our newest PDE1 inhibitor, ITI-1020, which is being developed as a novel immunotherapy for oncology indications. Clinical conduct has begun in a single ascending dose study in normal healthy volunteers. The potential of a safe and well tolerated small molecule as part of the treatment armamentarium for cancer indications is an exciting prospect and we look forward to continuing to advance our program.

Finally, we are developing ITI-333 for the treatment of opioid use disorder and pain. In Q1 2023, we began clinical conduct in a multiple ascending dose study in healthy volunteers and we have an ongoing neuroimaging study looking at the receptor occupancy.

With our progress in our development programs for lumateperone and our other pipeline assets, we continue to build a solid foundation for ITCI's future growth.

2022 was a year of strong execution at Intra-Cellular Therapies. Our research, clinical and commercial teams' efforts continue to show our commitment to providing new medicines to patients that help them live healthier lives.

We are excited about the prospects of Intra-Cellular Therapies. On behalf of the entire Intra-Cellular Therapies team, we thank you for your continued support.

Sincerely,

Sharon Mates, Ph.D.

Chairman, President, and Chief Executive Officer

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, 2022

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: 001-36274

Intra-Cellular Therapies, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**36-4742850**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

430 East 29th Street
New York, New York 10016
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code (646) 440-9333

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value Per Share	**ITCI**	**The Nasdaq Global Select Market**

Securities registered pursuant to Section 12(g) of the Exchange 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 Section 15(d) of the Exchange 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 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. ☒

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

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

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

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the registrant's most recently completed second fiscal quarter was approximately $5.3 billion.

As of February 27, 2023, the registrant had 95,280,003 shares of common stock outstanding.

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DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated by reference from the Registrant's Proxy Statement for the 2023 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission.

PART I

All brand names or trademarks appearing in this report are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this report is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners. Unless the context requires otherwise, references in this report to the "Company," "we," "us," and "our" refer to Intra-Cellular Therapies, Inc. and its wholly-owned subsidiary, ITI, Inc.

Item 1. BUSINESS

Overview

We are a biopharmaceutical company focused on the discovery, clinical development and commercialization of innovative, small molecule drugs that address underserved medical needs primarily in neuropsychiatric and neurological disorders by targeting intracellular signaling mechanisms within the central nervous system, or CNS. In December 2019, CAPLYTA® (lumateperone) was approved by the U.S. Food and Drug Administration, or FDA, for the treatment of schizophrenia in adults (42mg/day) and we initiated the commercial launch of CAPLYTA in March 2020. In December 2021, CAPLYTA was approved by the FDA for the treatment of bipolar depression in adults (42mg/day). We initiated the commercial launch of CAPLYTA for the treatment of bipolar depression in December 2021. Additionally, in April 2022, the FDA approved two new dosage strengths of CAPLYTA, 10.5 mg and 21 mg capsules, to provide dosage recommendations for patients concomitantly taking strong or moderate CYP3A4 inhibitors, and 21 mg for patients with moderate or severe hepatic impairment (Child-Pugh class B or C). We initiated the commercial launch for these special population doses in August 2022. As used in this report, "CAPLYTA" refers to lumateperone approved by the FDA for the treatment of schizophrenia in adults and for the treatment of bipolar depression in adults, and "lumateperone" refers to, where applicable, CAPLYTA as well as lumateperone for the treatment of indications beyond schizophrenia and bipolar depression. Lumateperone is in Phase 3 clinical development as a novel treatment for major depressive disorder, or MDD.

Our Product

In December 2019, CAPLYTA was approved by the FDA for the treatment of schizophrenia in adults (42mg/day) and we initiated the commercial launch of CAPLYTA in March 2020. In support of our commercialization efforts, we employ a national salesforce consisting of approximately 370 sales representatives. In December 2021, CAPLYTA was approved by the FDA for the treatment of bipolar depression in adults (42mg/day). CAPLYTA is the only FDA-approved treatment for depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults as monotherapy and as adjunctive therapy with lithium or valproate. We initiated the commercial launch of CAPLYTA for the treatment of bipolar depression in December 2021. In addition, the FDA approved new dosage strengths, 10.5mg and 21mg, for special populations of patients, in April 2022. We initiated the commercial launch for these special population doses in August 2022.

The efficacy of CAPLYTA 42 mg in schizophrenia was demonstrated in two placebo-controlled trials, showing a statistically significant separation from placebo on the primary endpoint, the Positive and Negative Syndrome Scale, or PANSS, total score. The most common adverse reactions (>5% and twice the rate of placebo) for the recommended dose of CAPLYTA versus placebo were somnolence/sedation (24% vs. 10%) and dry mouth (6% vs. 2%). In pooled data from short term studies, mean changes from baseline in weight gain, fasting glucose, triglycerides and total cholesterol were similar between CAPLYTA and placebo. The incidence of extrapyramidal symptoms was 6.7% for CAPLYTA and 6.3% for placebo.

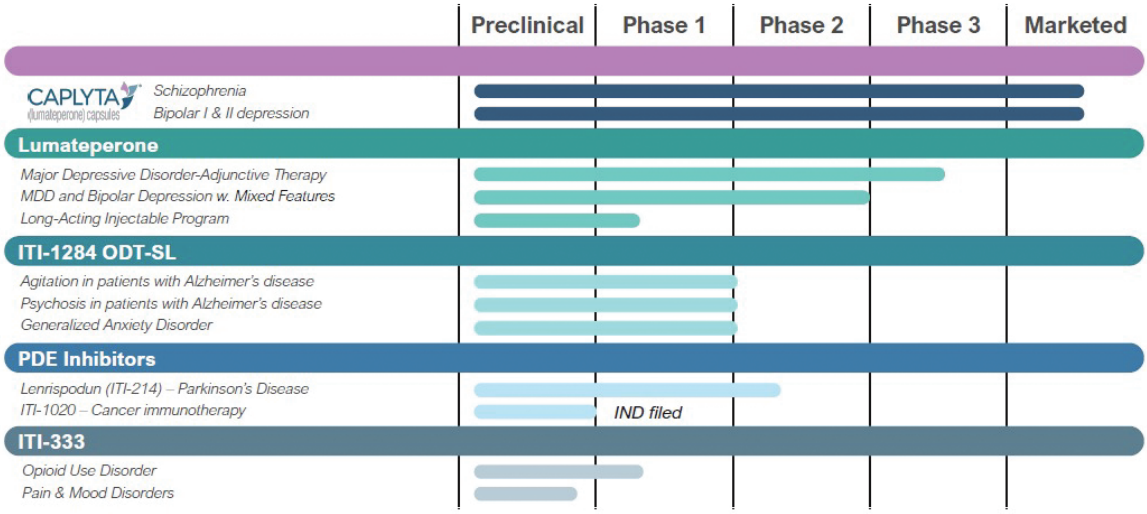
The efficacy of CAPLYTA 42 mg in bipolar depression was demonstrated in two positive Phase 3 placebo-controlled bipolar depression studies, which evaluated the effects of CAPLYTA on depression in adult patients with bipolar I or bipolar II disorder both as monotherapy (Study 404) and as adjunctive therapy with lithium or valproate (Study 402). In these studies, the efficacy of CAPLYTA 42 mg was established by demonstrating

statistically significant improvements over placebo for the change from baseline in the Montgomery-Asberg Depression Rating scale, or MADRS, total score at week 6. CAPLYTA 42 mg also showed a statistically significant improvement in the key secondary endpoint relating to clinical global impression of bipolar disorder in each study. In addition, CAPLYTA demonstrated a favorable tolerability and safety profile consistent with findings in prior clinical studies in schizophrenia. The most common reported adverse reactions (occurring at a rate of 5% or more and at least twice the rate of placebo) were somnolence/sedation, dizziness, nausea, and dry mouth. Mean changes from baseline in weight, fasting glucose, total cholesterol, triglycerides, and LDL cholesterol were similar between CAPLYTA and placebo.

Our Development Programs

Our pipeline includes several product candidates in clinical development and additional product candidates in nonclinical testing. We believe that our product candidates offer innovative therapeutic approaches and may provide advantages relative to current therapies. The following table summarizes our product candidates and programs:

OUR THERAPEUTIC PIPELINE



The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established.

Lumateperone Development Program

The efficacy of lumateperone could be mediated through a combination of antagonist activity at central serotonin 5-HT2A receptors and postsynaptic antagonist activity at central dopamine D2 receptors. In terms of pharmacodynamics, lumateperone has high binding affinity for serotonin 5-HT2A receptors and moderate binding affinity for dopamine D2 receptors, serotonin transporters, dopamine D1 receptors, dopamine D4 receptors and adrenergic alpha 1A and alpha 1B receptors. It lacks biologically relevant interactions with other receptors including muscarinic and histaminergic receptors. As a result, we believe lumateperone may represent a potential treatment across multiple therapeutic indications.

Lumateperone for the treatment of major depressive disorder and other mood disorders

As a potent 5-HT2A receptor antagonist and serotonin reuptake inhibitor, we believe that lumateperone could improve symptoms of depression with fewer side effects than currently marketed antipsychotics and

antidepressants. Dopamine modulation by lumateperone may also reduce irritability and aggression that can accompany many mood disorders. Lumateperone, as a standalone agent, indirectly enhances glutamatergic neurotransmission through both AMPA and NMDA channels in the prefrontal cortex via lumateperone's dopamine D1 receptor activation. By enhancing AMPA neurotransmission, lumateperone also activates key proteins in the mTOR pathway which has shown antidepressant effects. As such, lumateperone may represent a potential treatment for mood disorders including MDD and post-traumatic stress disorder.

Lumateperone is in Phase 3 clinical development as a novel treatment for MDD. Patient enrollment in Study 501 and Study 502, global Phase 3 clinical trials evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of MDD, is ongoing. In addition, in the second quarter of 2023, we expect to initiate a third global Phase 3 trial, Study 505, also evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of MDD. Study 505 is intended to serve as a potential additional registration trial in support of a supplemental New Drug Application, or sNDA, for approval of lumateperone as an adjunctive therapy to antidepressants for the treatment of MDD, if needed. This is a common strategy employed in mood disorder development programs. Subject to the results of Study 501 and Study 502, we expect to file an sNDA with the FDA for approval of lumateperone as an adjunctive therapy to antidepressants for the treatment of MDD in 2024. In the first quarter of 2020, as part of our lumateperone bipolar depression clinical program, we initiated our third monotherapy Phase 3 study, Study 403, evaluating lumateperone as monotherapy in the treatment of major depressive episodes associated with bipolar I or bipolar II disorder. Following the positive results in our adjunctive study that was part of our bipolar depression clinical program, Study 402, we amended Study 403 to evaluate major depressive episodes with mixed features in bipolar disorder in patients with bipolar I or bipolar II disorder and mixed features in patients with MDD. Clinical conduct for Study 403 has been completed, and we expect to report topline results in the first quarter of 2023. Following reporting of topline results, we intend to discuss the results with the FDA to determine whether this study will provide supportive data for a potential future regulatory filing for this indication.

We have also initiated a Phase 3 study evaluating lumateperone for the prevention of relapse in patients with schizophrenia. The study is being conducted in five phases consisting of a screening phase, a 6-week, open-label run-in phase during which all patients will receive 42 mg of lumateperone per day, a 12-week, open-label stabilization phase during which all patients will receive 42 mg of lumateperone per day; a double-blind treatment phase, 26 weeks in duration, during which patients receive either 42 mg of lumateperone per day or placebo (1:1 ratio) and a 2-week safety follow-up phase. This study is being conducted in accordance with our post approval marketing commitment to the FDA in connection with the approval of CAPLYTA for the treatment of schizophrenia as is typical for antipsychotics.

Other Indications for Lumateperone

Within the lumateperone portfolio, we are also developing a long-acting injectable, or LAI, formulation to provide more treatment options to patients suffering from mental illness. We have completed the nonclinical development of an LAI formulation, and we have conducted a Phase 1 single ascending dose study with this formulation. This study evaluated the pharmacokinetics, safety and tolerability of lumateperone LAI in patients with stable symptoms of schizophrenia. We completed this study and it was safe and well tolerated. We are evaluating several additional formulations of the lumateperone LAI with treatment durations of one month and longer. Non-clinical development on these additional formulations is ongoing and expected to be completed in 2023 and we plan to initiate Phase I single ascending dose studies with these formulations in 2023. Given the encouraging tolerability data to date with oral lumateperone, we believe that an LAI option, in particular, may lend itself to being an important formulation choice for certain patients.

We hold exclusive, worldwide commercialization rights to lumateperone and a family of compounds from Bristol-Myers Squibb Company pursuant to an exclusive license.

Other Product Candidates

We are developing ITI-1284-ODT-SL for the treatment of agitation in patients with dementia, the treatment of dementia-related psychosis and the treatment of generalized anxiety disorder. ITI-1284-ODT-SL is a deuterated form of lumateperone, a new molecular entity formulated as an oral disintegrating tablet for sublingual administration. ITI-1284-ODT-SL is formulated as an oral solid dosage form that dissolves almost instantly when placed under the tongue, allowing for ease of use in the elderly and may be particularly beneficial for patients who have difficulty swallowing conventional tablets. Phase 1 single and multiple ascending dose studies in healthy volunteers and healthy elderly volunteers (> than 65 years of age) evaluated the safety, tolerability and pharmacokinetics of ITI-1284-ODT-SL. In these studies, there were no reported serious adverse events in either age group. In the elderly cohort, reported adverse events were infrequent with the most common adverse event being transient dry mouth (mild). Based on these results, we have initiated our program evaluating ITI-1284-ODT-SL for the treatment of agitation in patients with Alzheimer's disease. We are in discussions with the FDA regarding the nonclinical toxicological profile of ITI-1284-ODT-SL. The FDA has informed us that they do not believe the deuterated and undeuterated forms of lumateperone are identical. As a result, the nonclinical data from lumateperone may not be broadly applied to ITI-1284-ODT-SL and we are conducting additional toxicology studies. We expect to commence clinical conduct in a Phase 2 study in agitation in patients with Alzheimer's disease in 2023. Additional studies in psychosis in patients with Alzheimer's disease and generalized anxiety disorder are also planned for 2023. We are continuing with Phase 1 studies with ITI-1284-ODT-SL, including drug-drug interaction studies.

We have another major program that has yielded a portfolio of compounds that selectively inhibit the enzyme phosphodiesterase type 1, or PDE1. PDE1 enzymes are highly active in multiple disease states and our PDE1 inhibitors are designed to reestablish normal function in these disease states. Abnormal PDE1 activity is associated with cellular proliferation and activation of inflammatory cells. Our PDE1 inhibitors ameliorate both of these effects in animal models. We intend to pursue the development of our phosphodiesterase, or PDE, program, for the treatment of aberrant immune system activation in several CNS and non-CNS conditions with a focus on diseases where excessive PDE1 activity has been demonstrated and increased inflammation is an important contributor to disease pathogenesis. Our potential disease targets include immune system regulation, neurodegenerative diseases, cancers and other non-CNS disorders. Lenrispodun (ITI-214) is our lead compound in this program. Following the favorable safety and tolerability results in our Phase 1 program, we initiated our development program for lenrispodun for Parkinson's disease and conducted a Phase 1/2 clinical trial of lenrispodun in patients with Parkinson's disease to evaluate safety and tolerability in this patient population, as well as motor and non-motor exploratory endpoints. In this study, lenrispodun was generally well-tolerated with a favorable safety profile and clinical signs consistent with improvements in motor symptoms and dyskinesias. We have initiated our Phase 2 clinical program with lenrispodun for Parkinson's disease, and expect to commence patient enrollment in the first quarter of 2023. We also have an active Investigational New Drug application to evaluate our newest candidate within the PDE 1 inhibitor program, ITI-1020, as a novel cancer immunotherapy. A Phase 1 program with ITI-1020 in healthy volunteers is anticipated to commence in the first half of 2023.

We also have a development program with our ITI-333 compound as a potential treatment for substance use disorders and pain. There is a pressing need to develop new drugs to treat opioid addiction and safe, effective, non-addictive treatments to manage pain. ITI-333 is a novel compound that uniquely combines activity as an antagonist at serotonin 5-HT2A receptors and a partial agonist at μ-opioid receptors. These combined actions support the potential utility of ITI-333 in the treatment of opioid use disorder and associated comorbidities (e.g., depression, anxiety, sleep disorders) without opioid-like safety and tolerability concerns. We have conducted a Phase 1 single ascending dose study evaluating the safety, tolerability and pharmacokinetics of ITI-333 in healthy volunteers. In this study, ITI-333 achieved plasma exposures at or above those required for efficacy and was generally safe and well-tolerated. We have commenced a neuroimaging study to investigate brain occupancy for receptors that play a role in substance use disorder and also have applicability for pain. The results of this study will support the dose selection for future studies. We commenced a multiple ascending dose study in the first quarter of 2023. We have received a grant from the National Institute on Drug Abuse under the

Helping to End Addiction Long-term Initiative, or NIH HEAL Initiative, that we expect will fund a significant portion of the early stage clinical development costs associated with this program.

Our Drug Discovery Platform and Capabilities

Based on the pioneering efforts of our late co-founder and Nobel laureate, Dr. Paul Greengard, we have developed a detailed understanding of intracellular signaling pathways and intracellular targets. We have used that knowledge to develop several state of the art technology platforms, including one called CNSProfile™. This technology monitors the phosphoprotein changes elicited by major psychotropic drug classes and subclasses, and generates a unique molecular signature for drug compounds. By monitoring how the levels of these phosphoproteins change *in vivo*, we identify intracellular signaling pathways through which several major drug classes operate. Along with what we believe to be state of the art drug discovery efforts, we have used, and may continue to use, this information as a tool to validate our selection of nonclinical candidate molecules.

Given the nature of our research and development and business activities, we do not expect that compliance with federal, state and local environmental laws will result in material costs or have a significant negative effect on our operations.

Disease and Market Overview

Our programs for small molecule therapeutics are designed to address various CNS and other diseases that we believe are underserved or unmet by currently available therapies and that represent large potential commercial market opportunities for us. Background information on the diseases and related commercial markets that may be addressed by our programs is set forth below.

Schizophrenia

Schizophrenia is a disabling and chronic mental illness that is characterized by multiple symptoms during an acute phase of the disorder that can include so-called "positive" symptoms, such as hallucinations, hearing voices, grandiose beliefs and suspiciousness or paranoia. These symptoms can be accompanied by additional, harder to treat symptoms, such as social withdrawal, blunted emotional response and speech deficits, collectively referred to as "negative" symptoms, difficulty concentrating and disorganized thoughts, or cognitive impairment, depression and insomnia. Such residual symptoms often persist even after the acute positive symptoms subside, and contribute substantially to the social and employment disability associated with schizophrenia.

According to the American Psychiatric Association and the National Institute of Mental Health, about 1% of the population (2.4 million adults in the United States) suffers from schizophrenia in any given year. A landmark study funded by the National Institute of Mental Health, the Clinical Antipsychotic Trials of Intervention Effectiveness, also referred to as CATIE, which was published in The New England Journal of Medicine in September 2005, found that 74% of patients taking typical or atypical antipsychotics discontinued treatment within 18 months because of side effects or lack of efficacy.

Bipolar Disorder

Bipolar disorder, sometimes referred to as manic-depressive illness, is characterized by extreme shifts in mood. Individuals with bipolar disorder may experience intense feelings of over-excitement, irritability, impulsivity with grandiose beliefs and racing thoughts, referred to as a manic episode. Symptoms of depression may include feeling tired, hopeless and sad, with difficulty concentrating and thoughts of suicide. Some people experience both types of symptoms in the same "mixed" episode. Severe symptoms of bipolar disorder can be associated with hallucinations or delusions, otherwise referred to as psychosis.

According to the National Institute of Mental Health, an estimated 4.4% of adults in the United States (approximately 11 million adults in the United States) experience bipolar disorder at some time in their lives. Bipolar disorder is often treated with antipsychotic medications alone or in combination with mood stabilizers. The side effects and safety risks associated with antipsychotic drugs in patients with bipolar disorder are similar to those experienced by patients with schizophrenia. Moreover, a large national research program conducted from 1998 to 2005 called the Systematic Treatment Enhancement Program for Bipolar Disorder, or STEP-BD, followed 4,360 patients with bipolar disorder long term and showed that about half of patients who were treated for bipolar disorder, still experienced lingering and recurrent symptoms, indicating a clear need for improved treatments.

Major Depressive Disorder

MDD is a mood disorder that can be associated with symptoms of sadness, hopelessness, helplessness, feelings of guilt, irritability, loss of interest in formerly pleasurable activities, cognitive impairment, disturbed sleep patterns, and suicide ideation or behavior. Different people may experience different symptoms, but everyone with major depression experiences symptoms that are severe enough to interfere with everyday functioning, such as the ability to concentrate at work or school, social interactions, eating and sleeping. Sometimes the depressive episode can be so severe it is accompanied by psychosis (hallucinations and delusions).

According to the National Institute of Mental Health, approximately 8.4% of adults in the United States experience MDD each year. The antidepressant market is primarily composed of selective serotonin reuptake inhibitors such as escitalopram and selective norepinephrine reuptake inhibitors, or SNRIs, such as duloxetine. Antipsychotics such as quetiapine, aripriprazole, Rexulti® and Vraylar® are also used as adjunctive treatments with antidepressant treatment. The National Institute of Mental Health-funded Sequenced Treatment Alternatives to Relieve Depression, or STAR*D, study showed that only one-third of treated patients experience complete remission of depressive symptoms. Nearly two-thirds of patients with depression do not fully recover on an anti-depressant medication.

Behavioral Disturbances in Dementia

The World Health Organization estimates that approximately 55 million people worldwide have dementia, and there are nearly 10 million new cases every year. The Alzheimer's Association estimates more than 6 million Americans are living with Alzheimer's dementia, or AD, in 2022. While the diagnostic criteria for AD and other dementias mostly focus on the related cognitive deficits, it is often the behavioral and psychiatric symptoms that are most troublesome for caregivers and lead to poor quality of life for patients. Several behavioral symptoms are quite prevalent in patients with dementia, including patients with AD. We believe that ITI-1284 may provide a novel therapy for treating the behavioral disturbances accompanying dementia, including AD.

The FDA has not approved any drug to treat the behavioral symptoms of dementia, including AD. We believe there is a large unmet medical need for a safe and effective therapy to treat the behavioral symptoms in patients with dementia, including AD.

Parkinson's Disease

Parkinson's disease is a chronic and progressive neurodegenerative disorder that involves malfunction and death of neurons in a region of the brain that controls movement. This neurodegeneration creates a shortage of an important brain signaling chemical, or neurotransmitter, known as dopamine, thereby rendering patients unable to direct or control their movements in a normal manner. Parkinson's disease is characterized by well-known motor symptoms, including tremors, limb stiffness, slowness of movements, and difficulties with posture and balance, as well as by non-motor symptoms, which include sleep disturbances, mood disorders, cognitive

impairment and psychosis. Parkinson's disease progresses slowly in most people and the severity of symptoms tends to worsen over time.

According to the National Parkinson Foundation, about 1 million people in the United States and more than 10 million people worldwide suffer from this disease. Parkinson's disease is more common in people over 60 years of age, and the prevalence of this disease is expected to increase significantly as the average age of the population increases. Parkinson's disease patients are commonly treated with dopamine replacement therapies, such as levodopa, commonly referred to as L-DOPA, which is metabolized to dopamine, and dopamine agonists, which are molecules that mimic the action of dopamine. Global Data estimated global sales of therapeutics such as L-DOPA, and dopamine agonists used to treat the disease to be approximately $4.3 billion in 2022.

Non-motor symptoms can be particularly distressing and even more troublesome to patients with Parkinson's disease than the primary motor disturbances. Non-motor symptoms substantially contribute to the burden of Parkinson's disease and deeply affect the quality of life of patients and their caregivers. Non-motor symptoms of Parkinson's disease are associated with increased caregiver stress and burden, nursing home placement, and increased morbidity and mortality. Treatment of non-motor symptoms associated with Parkinson's disease poses a challenge to physicians. Current dopamine replacement drugs used to treat the motor symptoms of Parkinson's disease do not help, and sometimes worsen, the non-motor symptoms. We believe there is a large unmet medical need for the treatment of non-motor symptoms associated with Parkinson's disease.

Opioid Use Disorder

The opioid crisis was declared a public health emergency in 2017. According to the 2019 CDC annual surveillance report of drug-related risks and outcomes, opioid misuse is widespread with over 10 million Americans reporting opioid misuse. The rate of drug overdose deaths involving opioids in the United States remains high, with more than 68,000 deaths reported in 2020.

Opioids are a class of drugs that include the illegal drug heroin, synthetic opioids such as fentanyl, and pain relievers available legally by prescription, including oxycodone, hydrocodone, codeine and morphine. Opioids produce high levels of positive reinforcement, increasing the odds that people will continue using them despite negative consequences. Opioid use disorder is a chronic lifelong disorder, with serious potential consequences including disability, relapses, and death. While medications including methadone, buprenorphine and naltrexone are approved to treat opioid use disorder, these medications do not effectively treat psychiatric comorbidities (e.g., mood and anxiety disorders) that may drive opioid use/abuse or dysphoria or the dysphoria and mood disturbances (e.g., depression and anxiety) that often accompany opioid withdrawal and abstinence.

Our Strategy

Our goal is to discover, develop and commercialize novel small molecule therapeutics for the treatment of CNS diseases and other diseases in order to improve the lives of people suffering from such illnesses. Using our key understanding of intracellular signaling, we seek to accomplish our goal, using our in-house expert drug discovery and clinical development teams, in two ways:

- we seek to have the capability to develop first-in-class medications with novel mechanisms that have the potential to treat CNS diseases and other diseases for which there are no previously marketed drugs; and
- we seek to develop drugs that either can differentiate themselves in competitive markets by addressing aspects of CNS diseases and other diseases which are not adequately treated by currently marketed drugs or can be effective with fewer side effects.

The key elements of our strategy are to:

- continue to commercialize CAPLYTA, which has been approved by the FDA for the treatment of schizophrenia and bipolar depression in adults, in the United States;

- complete the development of lumateperone for additional neuropsychiatric indications, such as MDD;
- expand the commercial potential of lumateperone by investigating its usefulness in additional neurological areas;
- continue to advance our other product candidates in clinical development such as lenrispodun, for the treatment of CNS and other disorders; ITI-1284, for the treatment of neuropsychiatric disorders and behavioral disturbances in dementia; and ITI-333, for substance use disorders, pain and psychiatric comorbidities including depression and anxiety; and
- advance the earlier stage product candidates in our pipeline.

Intellectual Property

Our Patent Portfolio

As of February 1, 2023, we owned or controlled approximately 130 patent families filed in the United States and other major markets worldwide, including approximately 125 issued or allowed U.S. patents, 62 pending U.S. patent applications, 527 issued or allowed foreign patents and 343 pending foreign patent applications, directed to novel compounds, formulations, methods of treatment, synthetic methods, and platform technologies.

Lumateperone tosylate is FDA-approved as CAPLYTA® for the treatment of schizophrenia and for the treatment of bipolar depression. We have extensively characterized this compound and related compounds and filed additional patent applications on salt forms, polymorphs, pharmaceutical formulations, new indications, improved methods of manufacture, metabolites, derivatives, and structurally related novel compounds. As of February 1, 2023, our lumateperone program consisted of approximately 36 patent families that we own or control, filed in the United States and other major markets, including 49 issued or allowed U.S. patents, 29 pending U.S. patent applications, 213 issued or allowed foreign patents and 155 pending foreign patent applications. Thirteen patents are currently Orange Book listed in the United States. In addition to patent protection, lumateperone has five years of new chemical entity data exclusivity with the FDA, until December 2024. Patent protection for lumateperone includes:

Summary Description of Patent or Patent Application	United States or Foreign Jurisdiction	Expiration Date
ITI-007 Product Patent (approved drug product—lumateperone tosylate—in any pharmaceutical form)	**Granted:** US (10,464,938*), AU	March 12, 2028 (US: does not include expected 6-month extension in US for pediatric studies)
ITI-007 Crystal Form Patent (approved drug product—lumateperone tosylate—in solid crystalline form)	**Granted:** US (8,648,077*; 9,199,995*; 9,586,960*; RE48,825*), EP (AT, BE, BG, CH, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IT, LT, LU, LV, NL, NO, PL, PT, RO, SE, SI, SK, TR), AU, CA, CN, KR, HK, JP and MX Pending in IL, IN	December 1, 2029 (US; does not include expected 6-month extension for pediatric studies; additional patent term extension possible through 2033**); March 12, 2029 (ex-US)
ITI-007 Dosage and Method of Treatment Patents (including schizophrenia, bipolar depression, sleep disorder indications)	**Granted:** US (8,598,119*; 9,186,258, 9,616,061*, 10,702,522*; 10,117,867*; RE48,839*), AU, CN, JP, KR, MX, EP (allowed) Pending: US (continuation), EP (divisional), IN, KR (divisional), MX (divisional)	December 28, 2029 (US; does not include expected 6-month extension for pediatric studies; additional patent term extension possible through 2033**); May 27, 2029 (ex-US)

Summary Description of Patent or Patent Application	United States or Foreign Jurisdiction	Expiration Date
ITI-007 Residual Symptoms Patent (treatment of negative/residual symptoms of schizophrenia)	**Granted:** US (9,956,227*; 10,960,009*; 11,026,951*), AU, EP, JP, KR, MX, RU Pending: US (continuation), AU (divisional), JP (divisional), EP (divisional), IN, KR (divisional), MX (divisional), CA, BR, IL, CN	December 3, 2034 (US and ex-US; does not include expected US 6-month extension for pediatric studies;)
Patents for Additional Dosage Forms	**Granted:** US (10,695,345*; 11,052,084*) Pending: US (continuation), AU, CA, CN, EP, IN, IL, JP, KR, MX, RU	2037-2039
Patents for Additional Indications (including post-traumatic stress disorder, impulse control disorder, symptoms associated with dementia, acute depression, and acute anxiety)	**Granted:** US (11,053,245; 11,124,514) Granted or pending in US, EP, JP, and other countries	2033-2034

* Orange-Book listed U.S. patents (NB: U.S. 8,598,119 and U.S. 9,586,960 have been requested for delisting as they have been superseded by RE48,839 and RE48,825, respectively)

** We have filed patent term extension applications on two U.S. patents. The U.S. Patent and Trademark Office, or USPTO, has not completed its review of these applications. In the United States, we are permitted to extend the term of one U.S. patent for lumateperone or the use thereof. Accordingly, on completion of the USPTO's review of our patent term extension applications, we must select one of the two patents to which any patent term extension granted will attach. Patent terms may be subject to change not only due to potential patent term extensions but also to any terminal disclaimer that reduces patent term, as well as other factors. Because the U.S. patent laws and related judicial interpretations change, modifications or new interpretations of the laws may impact our patent terms.

Our ITI-1284 program relates to novel lumateperone derivatives for the treatment of behavioral disturbances associated with dementia, and other central nervous system disorders. Six families of patent applications have been filed, which have already resulted in eight U.S. patents and fifteen foreign patents. The ITI-1284 molecule has composition of matter protection to 2037, with possible extensions and additional Orange Book-listable protection to 2042.

Our program on PDE1 inhibitors for cognition, dopamine-mediated and other disorders, cardiovascular disorders, as well as several others, includes patent protection across 55 families, including 31 families for the lead molecule, lenrispodun, as well as a wide range of filings on other proprietary compounds and indications. The lenrispodun lead molecule has composition of matter protection to 2029, with possible extensions and additional Orange Book-listable protection to 2034. Additionally, we expect to have data exclusivity in the European Union (EU) for up to 11 years from commercial launch. We have obtained patent coverage for lenrispodun in the treatment of cardiovascular disorders, including heart failure, that extends to 2034. We are also evaluating potential follow-on compounds for lenrispodun which would have patent protection beyond 2030.

Our ITI-333 program relates to novel compounds for the non-addictive treatment of pain and for the treatment of opiate use disorder. 18 families of patent applications have been filed, including five families which have already resulted in six U.S. patents and three EP grants, as well as thirteen other foreign grants. These patent families will protect the lead compound, as well as many other analogs under development, beyond 2037 (exclusive of any patent term extensions and regulatory exclusivities).

We have also filed patent applications on novel proprietary targets and lead compounds for AD, which would provide compound protection beyond 2028 or beyond 2034, depending on which compound is ultimately selected for development.

License Agreement

The Bristol-Myers Squibb License Agreement

On May 31, 2005, we entered into a worldwide, exclusive License Agreement with Bristol-Myers Squibb Company, or BMS, pursuant to which we hold a license to certain patents and know-how of BMS relating to lumateperone and other specified compounds. The agreement was amended on November 3, 2010. The licensed rights are exclusive, except BMS retains rights in specified compounds in the fields of obesity, diabetes, metabolic syndrome and cardiovascular disease. However, BMS has no right to use, develop or commercialize lumateperone and other specified compounds in any field of use. We have the right to grant sublicenses of the rights conveyed by BMS. We are obliged under the license to use commercially reasonable efforts to develop and commercialize the licensed technology. We are also prohibited from engaging in the clinical development or commercialization of specified competitive compounds.

Under the agreement, we made an upfront payment of $1.0 million to BMS, a milestone payment of $1.25 million in December 2013, and a milestone payment of $1.5 million in December 2014 following the initiation of our first Phase 3 clinical trial for lumateperone for patients with schizophrenia. Upon FDA acceptance of a New Drug Application, or NDA, filing for lumateperone, we were obligated to pay BMS a $2.0 million milestone payment. The FDA accepted our NDA filing for lumateperone for the treatment of schizophrenia in the third quarter of 2018 and, as a result, we paid the milestone payment in the first quarter of 2019. The FDA approved our NDA filing on December 23, 2019 and as a result, we accrued $5.0 million related to that milestone in the fourth quarter of 2019 which was paid in the first quarter of 2020. Remaining potential milestone payments under the agreement with respect to lumateperone total $5.0 million if approvals to market the product are received in certain countries outside the U.S. Under the agreement, we may be obliged to make other milestone payments to BMS, for licensed products other than lumateperone, of up to an aggregate of approximately $14.75 million. We are also obliged to make tiered single digit percentage royalty payments ranging between 5 – 9% on sales of licensed products. We are obliged to pay to BMS a percentage of non-royalty payments made in consideration of any sublicense.

The agreement extends, and royalties are payable, on a country-by-country and product-by-product basis, through the later of ten years after first commercial sale of a licensed product in such country, expiration of the last licensed patent covering a licensed product, its method of manufacture or use, or the expiration of other government grants providing market exclusivity, subject to certain rights of the parties to terminate the agreement on the occurrence of certain events. On termination of the agreement, we may be obliged to convey to BMS rights in developments relating to a licensed compound or licensed product, including regulatory filings, research results and other intellectual property rights.

Manufacturing

We do not own or operate manufacturing facilities for the production of CAPLYTA or any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials inclusive of active pharmaceutical ingredient, or API, and its intermediates, as well as finished product for commercial sales of CAPLYTA and for ournonclinical research and clinical trials, including our ongoing and anticipated trials. We believe that we would be able to contract with other third-party contract manufacturers to obtain active pharmaceutical ingredients, or API, if our existing sources of API were no longer available, but there is no assurance that API would be available from other third-party manufacturers on acceptable terms, on the timeframe that our business would require, or at all.

The Siegfried Supply Agreement

On January 4, 2017, we entered into a supply agreement with Siegfried Evionnaz SA, an affiliate of Siegfried AG, or Siegfried. Following the automatic expiration of the agreement on January 4, 2023, we entered into a new supply agreement with Siegfried effective January 5, 2023, or the Siegfried Agreement. Under the Siegfried Agreement, Siegfried has agreed to manufacture and supply the API for lumateperone in commercial quantities. We agreed to provide Siegfried with a rolling forecast of our anticipated requirements for supply of the API. Under the agreement, our purchase prices for supply of the API from Siegfried are specified prices based on the volume of API produced. The initial term of the Siegfried Agreement is three years until January 5, 2026. The Siegfried Agreement will automatically renew on an evergreen basis for a consecutive one-year period, unless either party notifies the other party of its election to not renew the agreement at least 12 months prior to the end of the initial term or any renewal period then in effect. Either party may terminate the agreement prior to its expiration upon an uncured material breach by the other party, the liquidation or dissolution of the other party, the commencement of insolvency procedures or other bankruptcy-related proceedings that are not dismissed within a certain period of time, the appointment of any receiver, trustee or assignee to take possession of the properties of the other party, the cessation of all or substantially all of the other party's business operations, or a continuing force majeure event affecting the other party. Under the Siegfried Agreement, we have the right to and may purchase the API for lumateperone from other suppliers. As of December 31, 2022, the Company has committed to purchasing production campaigns of API and intermediate product from Siegfried that are expected to be delivered in 2023 and 2024.

The Lonza Manufacturing Services Agreement

On January 10, 2017, we entered into a manufacturing services agreement, as amended on December 19, 2022, or the Lonza Agreement, with Lonza Ltd., or Lonza. Under the Lonza Agreement, Lonza has agreed to manufacture and supply the API for lumateperone, with purchase prices specified based on the volume produced. We agreed to provide Lonza with a written forecast of our estimated quarterly requirements. On December 19, 2022, the Lonza Agreement was amended to, among other items, extend the current term of the agreement until December 31, 2028 and provide for certain minimum annual purchase commitments by the Company for the years 2025 through 2028 for delivery in 2026 through 2029. Either party may terminate the agreement prior to its expiration upon a prior written notice, an uncured material breach by the other party, the insolvency, liquidation, dissolution or bankruptcy of the other party, or a continuing force majeure event affecting the other party, and may be extended by mutual consent. As of December 31, 2022, the Company has committed to purchasing production campaigns of API and intermediate products from Lonza that are expected to be delivered in 2023 and 2024.

Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our manufacturing contractors.

Commercial Operations

We initiated the commercial launch of CAPLYTA for the treatment of schizophrenia in adults in the United States in March 2020. In December 2021 we launched CAPLYTA for the treatment of bipolar depression in adults. In support of our commercialization efforts we employ a national sales force consisting of approximately 370 sales representatives. In the future, we may choose to commercialize CAPLYTA or any other products, in markets outside of the United States, if approved for sale in such markets, by establishing one or more strategic alliances.

Customers

We are currently approved to sell CAPLYTA for the treatment of schizophrenia in adults and for the treatment of bipolar depression in adults in the U.S. CAPLYTA is priced in line with other currently marketed branded antipsychotics indicated for the treatment of schizophrenia and for the treatment of bipolar depression. We distribute CAPLYTA principally through three third-party wholesale drug distributors whose concentration are each between 28% and 39% of total sales.

Competition

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the United States and abroad. We compete, or will compete, with existing and new products being developed by our competitors. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions that our research and development programs target.

Even if we are successful in commercializing CAPLYTA and developing and obtaining approval of our product candidates, we would compete with a variety of established drugs in the areas of our targeted CNS therapeutic indications. CAPLYTA for the treatment of schizophrenia and for the treatment of bipolar depression competes with, among other branded products, Fanapt®, marketed by Vanda Pharmaceuticals, Lybalvi®, marketed by Alkermes, Rexulti®, marketed by Otsuka Pharmaceutical, and Vraylar®, marketed by AbbVie. In addition, CAPLYTA competes and our product candidates, if approved, would compete with, among other generic antipsychotic products, aripiprazole, clozapine, haloperidol, lurasidone, olanzapine, paliperidone, quetiapine/XR and risperidone.

In addition, the companies described above and other competitors may have a variety of drugs in development or be awaiting FDA approval that could reach the market and become established before our approved product is established in the market or before we are able to sell our product candidates, if approved. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Many of our competitors are using technologies or methods different or similar to ours to identify and validate drug targets and to discover novel small molecule drugs. Many of our competitors and their collaborators have significantly greater experience than we do in the following:

- identifying and validating targets;
- screening compounds against targets;
- nonclinical studies and clinical trials of potential pharmaceutical products; and
- obtaining FDA and other regulatory clearances.

In addition, many of our competitors and their collaborators have substantially greater advantages in the following areas:

- capital resources;
- research and development resources;
- manufacturing capabilities; and
- sales and marketing.

Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved by the FDA or are in advanced development. We face competition from other companies, academic institutions, governmental agencies and other public and private research organizations for collaborative arrangements with pharmaceutical and biotechnology companies,

in recruiting and retaining highly qualified commercial, scientific and management personnel and for licenses to additional technologies. Our competitors, either alone or with their collaborators, may succeed in developing technologies or drugs that are more effective, safer, and more affordable or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. Developments by others may render our product candidates or our technologies obsolete. Our failure to compete effectively could have a material adverse effect on our business.

Government Regulation

United States—FDA Process

The research, development, testing, manufacture, labeling, promotion, advertising, import and export, distribution and marketing, among other things, prescription of drug products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, clinical holds, warning letters, fines, civil penalties, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

Drug Approval Process. None of our drug product candidates may be marketed in the United States until the drug has received FDA approval. Such approval can take many years to obtain and may be rejected by the FDA at a number of steps. The steps required before a drug may be marketed in the United States generally include the following:

- completion of extensive nonclinical laboratory tests, potentially animal studies, and formulation studies in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an Investigational New Drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each proposed indication;
- submission to the FDA of an NDA after completion of all clinical trials;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the API and finished drug product are produced and tested to assess compliance with current Good Manufacturing Practices, or cGMPs;
- satisfactory completion of FDA inspections of clinical trial sites to assure that data supporting the safety and effectiveness of the product candidate has been generated in compliance with Good Clinical Practices; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Nonclinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The Consolidated Appropriations Act for 2023, signed into law on December 29, 2022, (P.L. 117-328) amended the FDCA to specify that nonclinical testing for drugs may, but is not required to, include *in vivo* animal testing. According to the amended language, a sponsor may fulfill nonclinical testing requirements by completing various *in vitro* assays (e.g., cell-based assays, organ chips, or microphysiological systems), *in silico* studies (i.e., computer modeling), other human or non-human biology-based tests (e.g., bioprinting), or *in vivo* animal tests. The conduct of the nonclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the nonclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA,

unless before that time the FDA raises concerns or questions about the conduct of the trial, such as whether human research subjects will be exposed to an unreasonable health risk. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. The FDA, the trial's sponsor or an Institutional Review Board, or IRB, overseeing the trial also may place a study on hold at any time during its execution.

Clinical trials involve administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be provided to the FDA as part of a separate submission to the IND. Further, an IRB, for each site proposing to conduct the clinical trial, must review and approve the study protocol and informed consent information for study subjects for any clinical trial before it commences at that center, and the IRB must monitor the study until it is completed. There are also requirements governing reporting of on-going clinical trials and clinical trial results to public registries. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The ClinicalTrials.gov registration and reporting final rule became effective in 2017, and the government has begun enforcing those requirements against non-compliant clinical trial sponsors. Study subjects must provide informed consent before being enrolled to participate in a clinical trial.

Clinical trials necessary for product approval typically are conducted in three sequential phases, but the phases may overlap.

- Phase 1 usually involves the initial introduction of the investigational drug into a limited population, typically healthy humans, to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness.
- Phase 2 usually involves trials in a limited patient population to (i) evaluate dosage tolerance and appropriate dosage; (ii) identify possible adverse effects and safety risks; and (iii) evaluate preliminarily the efficacy of the drug for specific targeted indications. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3 trials, commonly referred to as pivotal studies, are undertaken in an expanded patient population at multiple, geographically dispersed clinical trial centers to further evaluate clinical efficacy and test further for safety by using the drug in its final form.

The FDA may approve an NDA for a product candidate, but require that the sponsor conduct additional clinical trials to further assess the drug after NDA approval under a post-approval commitment. Post-approval trials are typically referred to as Phase 4 clinical trials.

Congress also recently amended the FDCA, as part of the Consolidated Appropriations Act for 2023, in order to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must include the sponsor's diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Sponsors must submit a diversity action plan to the FDA by the time the sponsor submits the relevant clinical trial protocol to the agency for review. The FDA may grant a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect Phase 3 trial planning and timing or what specific information FDA will expect in such plans, but if the FDA objects to a sponsor's diversity action plan, it may delay trial initiation.

During the development of a new drug, sponsors are given an opportunity to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach an agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug. A sponsor may request a Special Protocol Assessment, or SPA, to reach an agreement with the FDA that the protocol design, clinical endpoints, and statistical analyses are acceptable to support regulatory approval of the product candidate with respect to effectiveness in the indication studied. If such an agreement is reached, it will be documented and made part of the administrative record, and it will be binding on the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining the safety or effectiveness of the product after clinical studies begin, or if the sponsor fails to follow the protocol that was agreed upon with the FDA. There is no guarantee that a study will ultimately be adequate to support an approval even if the study is subject to an SPA.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Assuming successful completion of the required clinical testing, the results of nonclinical studies and of clinical studies, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. An NDA must be accompanied by a significant user fee, and the sponsor of an approved NDA is also subject to an annual program fee. These fees are typically adjusted annually, but exemptions and waivers may be available under certain circumstances. The NDA is subject to a sixty-day acceptance period, and if sufficiently complete to permit substantive review, will be filed by the FDA at the end of that period. For NDAs that are assigned a standard review designation, the FDA's goal is to complete its review ten months from the date the FDA files the NDA and, for NDA determined by the agency to be eligible for priority review, six months from the date the FDA files the NDA. These goals can be extended by the FDA through requests for additional information from the sponsor.

The testing and approval process requires substantial time, effort and financial resources. The FDA will review the NDA to determine, among other things, whether product candidate is safe and effective for its intended use. FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. The FDA may also refer the application to the appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee, but it typically follows such recommendations.

Before approving an NDA, the FDA inspects the facility or the facilities at which the drug and/or its active pharmaceutical ingredient is manufactured and will not approve the product unless the manufacturing is in compliance with cGMPs. On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, it may issue an approval letter or a Complete Response Letter. The approval letter authorizes commercial marketing of the drug for specific indications. As a condition of NDA approval, the FDA may require post-marketing testing and surveillance to monitor the drug's safety or efficacy, or impose other conditions, as discussed further below. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its current form. A Complete Response Letter outlines the deficiencies in the submission and may

require additional clinical data and/or additional clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may choose to either resubmit the NDA addressing all of the deficiencies identified in the letter or withdraw the application. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials is not always conclusive and the FDA may interpret data differently than we or our collaborators interpret data. Alternatively, the FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy, or REMS, to mitigate risks of the drug, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. Once the FDA approves a drug, the FDA may withdraw product approval if on-going regulatory requirements are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing, including Phase 4 clinical trials, and surveillance programs to monitor the safety of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs or other information.

Post-Approval Requirements. After a drug has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical trials. If post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. In addition, certain changes to an approved product, such as adding new indications, making certain manufacturing changes, or making certain additional labeling claims, are subject to further FDA review and approval. Before a company can market products for additional indications, it must obtain additional approvals from the FDA, typically through the submission and approval of a supplemental NDA. Obtaining approval for a new indication generally requires that additional clinical trials be conducted. A company cannot be sure that any additional approval for new indications for any product candidate will be approved on a timely basis, or at all.

In addition, holders of an approved NDA are required to (i) report certain adverse reactions to the FDA and maintain pharmacovigilance programs to proactively look for these adverse events; (ii) comply with certain requirements concerning advertising and promotional labeling for their products; and (iii) continue to have quality control and manufacturing procedures conform to cGMPs after approval. The FDA periodically inspects the sponsor's records related to safety reporting and the approved drug's manufacturing facilities, which includes assessment of on-going compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. We intend to continue to use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in new restrictions on a product, manufacturer or holder of an approved NDA, including recall of the product from the market, imposition of a REMS program, or withdrawal of approval of the NDA for that drug, among other potential consequences.

Moreover, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or the PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription drug product samples and impose requirements to ensure accountability in distribution. Most recently, the Drug Supply Chain Security Act, or DSCSA, was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a ten-year period that is expected to culminate in November 2023. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Patent Term Restoration and Marketing Exclusivity. Depending upon the timing, duration and specifics of FDA approval of the use of our drugs, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the extension must be requested prior to expiration of the patent. Also, the approval must be the first permitted commercial marketing or use of the active ingredient under the relevant provision of law. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. We have applied for, and in the future we intend to apply for, restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Data and market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the data and information associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct, or obtain a right of reference to all of the nonclinical studies and clinical trials necessary to demonstrate safety and effectiveness. The FDCA also provides seven years of market exclusivity for a drug designated for a rare disease or condition (e.g., a disease or condition that affects less than 200,000 people in the United States) that begins to run after the drug's marketing approval for that condition. The exclusivity prohibits the approval of the same drug for the same disease or condition unless there is a showing of clinical superiority or other exceptions are triggered.

Foreign Regulation

In addition to regulations in the United States, we may become subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials and approval of foreign countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Pricing and Reimbursement

In the United States and internationally, sales of any approved products, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability of adequate coverage and reimbursement

from third-party payors, such as state and federal governments, managed care providers and private insurance plans. Private insurers, such as health maintenance organizations and managed care providers, have implemented cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that govern the drugs and biologics that will be offered and the out-of-pocket obligations of member patients for such products. We may need to conduct pharmacoeconomic studies to demonstrate the cost-effectiveness of our products for formulary coverage and reimbursement. Even with such studies, our products may be considered less safe, less effective or less cost-effective than existing products, and third-party payors may not provide coverage and reimbursement for our product candidates, in whole or in part.

In addition, particularly in the United States and increasingly in other countries, we are required to provide discounts and pay rebates to state and federal governments and agencies in connection with purchases of our products that are reimbursed by such entities. It is possible that future legislation in the United States and other jurisdictions could be enacted to potentially impact reimbursement rates for the products we are developing and may develop in the future and could further impact the levels of discounts and rebates paid to federal and state government entities. Any legislation that impacts these areas could impact, in a significant way, our ability to generate revenues from sales of any approved product that we bring to market. Most recently, on August 16, 2022, President Biden signed into the law the Inflation Reduction Act of 2022, or the IRA. Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Starting in 2023, a manufacturer of drugs or biological products covered by Medicare Parts B or D must pay a rebate to the federal government if their drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting for payment year 2026, the Centers for Medicare & Medicaid Services (CMS) will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities but their impact on the pharmaceutical industry in the United States remains uncertain. In addition to the IRA's drug price negotiation provisions, President Biden's Executive Order 14087, issued in October 2022, called for CMS to prepare and submit a report to the White House on potential payment and delivery modes that would complement to IRA, lower drug costs, and promote access to innovative drugs. As of mid-January 2023, the report had not been released but it is expected to further inform the current Administration's priorities and activities in this area.

Political, economic and regulatory influences are subjecting the health care industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the health care system in ways that could significantly affect our future business. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, or collectively, the ACA, enacted in March 2010, substantially changed the way health care is financed by both governmental and private insurers. Certain legislative changes to and regulatory changes under the ACA have occurred over the past few years and further legislative changes to and regulatory changes under the ACA remain possible. We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that may be charged for any of our product candidates, if approved. Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers (PBMs) and other members of the health care and pharmaceutical supply chain, an important decision that appears to be leading towards further and more aggressive efforts by states in this area. The Federal Trade Commission in mid-2022 also launched sweeping investigations into the practices of the PBM industry

that could lead to additional federal legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. Significant efforts to change the PBM industry as it currently exists in the U.S. may affect the entire pharmaceutical supply chain and the business of other stakeholders, including pharmaceutical companies like us.

Sales and Marketing

The FDA, in conjunction with the U.S. Federal Trade Commission, or FTC, regulates all advertising and promotion activities for products under FDA's jurisdiction prior to and after approval, including standards and regulations for direct-to-consumer advertising, dissemination of off-label information, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA. There are also continuing annual user fee requirements that are now assessed as program fees for certain NDA-approved drugs.

Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patient. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses.

Our commercial marketing of CAPLYTA and related business activities could become subject to scrutiny and enforcement under one or more federal or state health care fraud and abuse laws and regulations. These fraud and abuse laws, and other applicable health care laws include:

- The federal Anti-Kickback Law, which prohibits, among other things, knowingly or willingly offering, paying, soliciting or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward the purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any goods or services for which payment may be made, in whole or in part, by federal health care programs such as Medicare and Medicaid;
- The federal civil False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds or knowingly making, using or causing to be made or used, a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government, and which provides for civil whistleblower or qui tam actions against individuals or entities alleged to have submitted a false claim;
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, or knowingly and willfully making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- The federal Physician Payment Sunshine Act, which requires manufacturers of FDA-approved drugs (among others) covered by Medicare or Medicaid to report to CMS, on an annual basis,

information related to payments and other transfers of value to physicians, teaching hospitals, and certain advanced non-physician health care practitioners and physician ownership and investment interests, with such data then being made publicly available on a website maintained by CMS called Open Payments; and

- Analogous state and foreign laws and regulations, including state anti-kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, apply regardless of the payer, as well as other state laws that require pharmaceutical companies to report expenses related to the marketing and promotion of pharmaceutical products, prohibit certain gifts or payments to health care providers in the state, and/or require pharmaceutical companies to implement compliance programs or marketing codes of conduct.

State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. We also are subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our business.

Violations of fraud and abuse laws, or other health care laws may be punishable by significant criminal and/or civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal health care programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties also may be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called "responsible corporate officer" doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing. Given the penalties that may be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government was to allege or convict us or our executive officers, employees or consultants of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions under some of the fraud and abuse laws described above. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and extensive enforcement of them by law enforcement authorities. Further, federal and state laws that require manufacturers to make reports on pricing and marketing information could subject us to penalty provisions.

Human Capital

As of February 1, 2023, we employed 561 employees all of whom were full-time. We consider our relations with our employees to be good. To successfully commercialize CAPLYTA and develop our drug candidates, we must be able to attract and retain highly skilled personnel. We anticipate hiring a number of additional employees during 2023. We continually evaluate the business need and opportunity and balance in-house expertise and capacity with outsourced expertise and capacity. Currently, we outsource substantial clinical trial work to clinical research organizations and drug manufacturing to contract manufacturers.

Compensation and Benefits

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. Pharmaceutical companies both large and small compete for a limited number of qualified applicants to fill specialized positions. To attract qualified applicants, we offer a total rewards package consisting of base salary and cash target bonus, a comprehensive benefit package and equity compensation for every employee. Bonus opportunity and equity compensation increase as a percentage of total compensation based on level of responsibility. Actual bonus payout is based on performance.

Diversity, Equity and Inclusion

Much of our success is rooted in the diversity of our teams and our commitment to inclusion. We value diversity at all levels. We believe that our business benefits from the different perspectives a diverse workforce brings, and we pride ourselves on having a strong, inclusive and positive culture based on our shared mission and values.

At all times we strive to distinguish ourselves as a respected biopharmaceutical company that is differentiated by top talent and innovative research to develop products that address underserved medical needs.

Communication is critical in our ability to continuously enhance our company culture and create a more inclusive environment. The implementation of an announcement board allowed us to share what is important and impactful to us as a business. It also allows for us to host events that affect our employees on both a personal and professional level.

Health, Wellness and Safety

We believe that the safety and health of our employees and their families is essential to our business. Our culture is driven by a desire to do what is right, and we strive to support the well-being of our employees. We prioritize the safety and well-being of our employees as they face both mental and physical challenges related to the COVID-19 pandemic. Our employees have demonstrated great resilience during the pandemic, and we continue to provide resources to support their well-being. Beginning in March 2020, we have supported our employees and government efforts to curb the COVID-19 pandemic through a multi-faceted communication, infrastructure, and behavior modification and enforcement effort that includes:

- establishing clear and regular COVID-19 policies, safety protocols, and updates to all employees;
- strongly encouraging all office-based employees to work from home; and
- implementing protocols to address actual and suspected COVID-19 cases and potential exposure.

Our financial, medical, and mental health benefits that were already in place prior to the COVID-19 pandemic were designed to help employees through crisis, and we further expanded our offerings to create appropriate “work from home” conditions for success and wellness, including purchasing additional IT equipment and office supplies and increasing communications related to our mental health benefits. In particular, we offered sessions on mindfulness to further support the mental health of our employees.

Environmental, Social and Governance

Our commitment to integrating sustainability across our organization begins with our Board of Directors, or the Board. The Nominating and Governance Committee of the Board has oversight of strategy and risk management related to Environmental, Social and Governance, or ESG. Applying Nasdaq’s listing standards for independence, four of our five directors are independent.

All employees are responsible for upholding our core values, including to communicate, collaborate, innovate and be respectful, as well as for adhering to our Code of Ethics and Business Conduct, including our policies on bribery, corruption, conflicts of interest and our whistleblower program. We encourage employees to come to us with observations and complaints, ensuring we understand the severity and frequency of an event in order to escalate and assess accordingly. Our Chief Compliance Officer strives to ensure accountability, objectivity, and compliance with our Code of Ethics and Business Conduct. If a complaint is financial in nature, the Audit Committee Chair is notified concurrently, which triggers an investigation, action and report.

We are committed to protecting the environment and attempt to mitigate any negative impact of our operations. We monitor resource use, improve efficiency, and at the same time, reduce our emissions and waste.

In order to reduce the overall impact of our product on the environment, we have taken steps to enhance the sustainability of our manufacturing processes for our drug substances.

We are systematically addressing the environmental impacts of the buildings we rent as we make improvements, including adding energy control systems and other energy efficiency measures. Waste in our own operation is minimized by our commitment to reduce both single-use plastics and operating paper-free, primarily in a digital environment. We have safety protocols in place for handling biohazardous waste in our labs, and we use third-party vendors for biohazardous waste and chemical disposal.

Corporate Information

We were originally incorporated in the State of Delaware in August 2012 under the name "Oneida Resources Corp." Oneida Resources Corp. was a "shell" company registered under the Securities Exchange Act of 1934, as amended, or the Exchange Act, with no specific business plan or purpose until it began operating the business of Intra-Cellular Therapies, Inc. (now re-named ITI, Inc., or ITI) through a reverse merger transaction on August 29, 2013, or the Merger. ITI was incorporated in Delaware in May 2001 to focus primarily on the development of novel drugs for the treatment of neuropsychiatric and neurologic diseases and other disorders of the central nervous system. Effective upon the Merger, a wholly owned subsidiary of the Company merged with and into ITI. ITI continues as the operating subsidiary of the Company. As used herein, the words the "Company," "we," "us," and "our" refer to Intra-Cellular Therapies, Inc. and its wholly owned subsidiary, ITI, Inc.

Our corporate headquarters and laboratory are located at 430 East 29th Street, New York, New York 10016, and our telephone number is (646) 440-9333. We also have an office in Towson, Maryland. We maintain a website at www.intracellulartherapies.com, to which we regularly post copies of our press releases as well as additional information about us. We make available free of charge through the Investors section of our web site 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 as soon as reasonably practicable after such material is electronically filed with or furnished to the Securities and Exchange Commission. The Securities and Exchange Commission maintains an internet site (http://www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the Securities and Exchange Commission. We include our web site address in this Annual Report on Form 10-K only as an inactive textual reference. Information contained in our website does not constitute a part of this report or our other filings with the SEC.

Item 1A. RISK FACTORS

Except for the historical information contained herein, this report contains forward-looking statements that involve risks and uncertainties. These statements include projections about our finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed in the following section, as well as those discussed in Part II, Item 7 titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this report.

You should consider carefully the following risk factors, together with all of the other information included or incorporated by reference in this report. If any of the following risks, either alone or taken together, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common stock could decline, and stockholders may lose all or part of their investment.

Summary of Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in this section below, that represent challenges that we face in connection with the successful implementation of our strategy. The occurrence of one or more of the events or circumstances described in more detail in the risk factors below, alone or in combination with other events or circumstances, may have an adverse effect on our business, cash flows, financial condition and results of operations. Such risks include, but are not limited to:

- In order to execute our business plan and achieve profitability, we need to effectively expand the commercialization of CAPLYTA, which received FDA approval in December 2019 for the treatment of schizophrenia in adults and in December 2021 for the treatment of bipolar depression in adults.
- If we do not obtain regulatory approval of lumateperone for other indications in the United States, or for any indication in foreign jurisdictions, we will not be able to market lumateperone for other indications or in other jurisdictions, which will limit our commercial revenues.
- If the sales and marketing capabilities we have established or our third-party relationships for the commercialization of lumateperone are not effective, lumateperone may not be successfully commercialized.
- We have generated limited revenue from product sales and there is no guarantee that our revenue from the sale of CAPLYTA will result in us achieving profitability.
- There is no guarantee that our planned clinical trials for lumateperone will be successful.
- We expect our net losses to continue and are unable to predict the extent of future losses or when we will become profitable, if ever.
- We may require additional funding, which may not be available to us on acceptable terms, or at all, and, if not so available, may require us to delay, limit, reduce or cease our operations.
- Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations.
- Delays, suspensions and terminations in our clinical trials or the need to conduct additional clinical or nonclinical studies could result in increased costs to us, delay our ability to generate product revenues and therefore may have a material adverse effect on our business, results of operations and future growth prospects.

- Even though the FDA has granted approval of CAPLYTA for the treatment of schizophrenia and bipolar depression, the terms of the approval may limit its commercial potential. Additionally, CAPLYTA is still subject to ongoing regulatory requirements.
- Safety issues with our product candidates or approved product, or with product candidates or approved products of third parties that are similar to our product candidates, could give rise to delays in the regulatory approval process, restrictions on labeling or product withdrawal after approval.
- Preliminary and interim data from our clinical studies that we may announce or publish from time to time may change as more patient data become available.
- We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing our product candidates.
- Even if we successfully complete the clinical trials of one or more of our product candidates, the product candidates may fail for other reasons.
- We are subject to ongoing regulatory obligations and restrictions with regard to CAPLYTA and, following regulatory approval of any of our product candidates, we will be subject to ongoing regulatory obligations and restrictions with regard to such product candidates, which may result in significant expense and limit our ability to commercialize lumateperone and our other potential products.
- CAPLYTA and our product candidates, if approved, may not gain acceptance among physicians, patients, or the medical community, thereby limiting our potential to generate revenues, which will undermine our future growth prospects.
- We rely on third-party manufacturers to manufacture and supply lumateperone and our other product candidates for us. If one of our suppliers or manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts to find new suppliers or manufacturers. We may also face significant delays in our clinical trials, regulatory approvals and product introductions and commercialization.
- We will need to continue to manage our organization and we may encounter difficulties with our staffing and any future transitions, which could adversely affect our results of operations.
- Our ability to compete may be undermined if we do not adequately protect our proprietary rights.
- Our ability to generate product revenues will be diminished if lumateperone or any of our other potential products does not receive and maintain coverage from payors or sells for inadequate prices, or if patients are unable to obtain adequate levels of reimbursement.
- The COVID-19 pandemic could continue to have a material impact on our business, financial condition and results of operations, including our commercial operations and sales, clinical trials and nonclinical studies.
- Many of our competitors have greater resources and capital than us, putting us at a competitive disadvantage. If our competitors develop and market products that are more effective than lumateperone or our other product candidates, they may reduce or eliminate our commercial opportunity.
- Numerous factors could result in substantial volatility in the trading price of our stock.
- The price of our common stock could be subject to volatility related or unrelated to our operations.

Risks Related to Our Business

In order to execute our business plan and achieve profitability, we need to effectively expand the commercialization of CAPLYTA, which received FDA approval in December 2019 for the treatment of schizophrenia in adults and in December 2021 for the treatment of bipolar depression in adults.

CAPLYTA is our only drug that has been approved for sale and it has been approved only for the treatment of schizophrenia in adults and bipolar depression in adults in the United States only. We are focusing a significant portion of our activities and resources on CAPLYTA, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize CAPLYTA for the treatment of schizophrenia in adults and for the treatment of bipolar depression in adults in the United States.

Successful commercialization of CAPLYTA is subject to many risks. We have never, as an organization, launched or commercialized any other product, and there is no guarantee that we will be able to successfully commercialize CAPLYTA for its approved indications. There are numerous examples of failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us. We expect that continued commercial success of CAPLYTA for the treatment of schizophrenia and bipolar depression will depend on many factors, including the following:

- the efficacy, cost, approved use, and side-effect profile of CAPLYTA regimens relative to competitive treatment regimens for the treatment of schizophrenia and bipolar depression;
- the effectiveness of our commercial strategy for the marketing of CAPLYTA, including our pricing strategy and the effectiveness of our efforts to obtain adequate third-party reimbursements;
- maintaining and successfully monitoring commercial manufacturing arrangements for CAPLYTA with third-party manufacturers to ensure they meet our standards and those of regulatory authorities, including the FDA, which extensively regulate and monitor pharmaceutical manufacturing facilities;
- our ability to meet the demand for commercial supplies of CAPLYTA;
- the acceptance of CAPLYTA by patients, the medical community and third-party payors; and
- the effect of recent or potential health care legislation in the United States.

While we believe that CAPLYTA for the treatment of schizophrenia and bipolar depression has a commercially competitive profile, we cannot accurately predict the amount of revenue that will be generated from the sale of CAPLYTA. If we do not effectively commercialize CAPLYTA, we will not be able to execute our business plan and may not be able to achieve profitability. If our revenues, market share and/or other indicators of market acceptance of CAPLYTA do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

If we do not obtain regulatory approval of lumateperone for other indications in the United States, or for any indication in foreign jurisdictions, we will not be able to market lumateperone for other indications or in other jurisdictions, which will limit our commercial revenues.

While CAPLYTA has been approved by the FDA for the treatment of schizophrenia and bipolar depression in adults, lumateperone has not been approved by the FDA for any other indications, and it has not been approved in any other jurisdiction for these indications or for any other indication. In order to market lumateperone for other indications or in other jurisdictions, we must obtain regulatory approval for each of those indications and in each of the applicable jurisdictions, and we may never be able to obtain such approval. Approval of CAPLYTA by the FDA for the treatment of schizophrenia and bipolar depression does not ensure that foreign jurisdictions will also approve CAPLYTA for those indications, nor does it ensure that lumateperone will be approved by the FDA for additional indications or populations. Lumateperone is in Phase 3 clinical

development as an adjunctive therapy for the treatment of MDD. There is no guarantee that any ongoing or future studies of lumateperone in other indications will be successful, or that the FDA or any regulatory authority in foreign jurisdictions will approve lumateperone for any of those indications. The research, testing, manufacturing, labeling, approval, sale, import, export, marketing, and distribution of pharmaceutical product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, whose regulations differ from country to country. We will be required to comply with different regulations and policies of the jurisdictions where we seek approval for our product candidates, and we have not yet identified all of the requirements that we will need to satisfy to submit lumateperone for approval for other indications or in other jurisdictions. This will require additional time, expertise and expense, including the potential need to conduct additional studies or development work for other jurisdictions beyond the work that we have conducted to support our NDA submission in schizophrenia or our sNDA submissions in bipolar depression. In addition, strategic considerations need to be taken into account when determining whether and when to submit lumateperone for approval in other jurisdictions. If we do not receive marketing approval for lumateperone for any other indication or from any regulatory agency outside of the United States, we will never be able to commercialize lumateperone for any other indication in the United States or for any indication in any other jurisdiction. Even if we do receive additional regulatory approvals, we may not be successful in commercializing those opportunities.

If the results or timing of regulatory filings, the regulatory process, regulatory developments, clinical trials or nonclinical studies, or other activities, actions or decisions related to lumateperone do not meet our or others' expectations, the market price of our common stock could decline significantly.

If the sales and marketing capabilities we have established or our third-party relationships for the commercialization of lumateperone are not effective, lumateperone may not be successfully commercialized.

Prior to the commercial launch of CAPLYTA in March 2020, we had no experience as a company in marketing drugs or with respect to pricing and obtaining adequate third-party reimbursement for drugs. We continue to build our commercial organization and capabilities in the United States in order to market CAPLYTA for the treatment of schizophrenia and bipolar depression. We will need to successfully complete the expansion of our capabilities and/or enter into arrangements with third parties to sell and market CAPLYTA for the treatment of schizophrenia and bipolar depression and, if approved, to sell and market our other product candidates. If our sales and marketing capabilities or our third-party relationships for the commercialization of our products are not effective, our business could be materially harmed.

We have generated limited revenue from product sales and there is no guarantee that our revenue from the sale of CAPLYTA will result in us achieving profitability.

Our ability to generate revenue from product sales and achieve profitability depends on our ability to successfully commercialize CAPLYTA for the treatment of schizophrenia and bipolar depression in adults in the United States as well as our ability to complete the development of and obtain regulatory approvals necessary to commercialize lumateperone in other indications or to manufacture and market our other product candidates. We have a limited operating history on which to evaluate our business and prospects. To date, we have generated limited product revenues from CAPLYTA and we cannot guarantee that CAPLYTA will be successfully commercialized or that any of our product candidates currently in development will ever become marketable products.

We must demonstrate that our product candidates satisfy rigorous standards of safety and efficacy for their intended uses before the FDA and other regulatory authorities in the European Union and elsewhere will approve them for commercialization. Significant additional research, nonclinical testing and clinical testing is required before we can submit applications to the FDA or other regulatory authorities for approval of our drug candidates. In addition, to compete effectively, our drugs must be easy to administer, cost-effective and economical to manufacture on a commercial scale. We may not achieve any of these objectives.

Lumateperone is in Phase 3 clinical development as a novel treatment for MDD. Patient enrollment in Study 501 and Study 502, global Phase 3 clinical trials evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of MDD, is ongoing. In addition, in the second quarter of 2023, we expect to initiate a third global Phase 3 trial, Study 505, also evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of MDD. Study 505 is intended to serve as a potential additional registration trial in support of an sNDA, for approval of lumateperone as an adjunctive therapy to antidepressants for the treatment of MDD, if needed. This is a common strategy employed in mood disorder development programs. Subject to the results of Study 501 and Study 502, we expect to file an sNDA with the FDA for approval of lumateperone as an adjunctive therapy to antidepressants for the treatment of MDD in 2024.In the first quarter of 2020, as part of our lumateperone bipolar depression clinical program, we initiated our third monotherapy Phase 3 study, Study 403, evaluating lumateperone as monotherapy in the treatment of major depressive episodes associated with bipolar I or bipolar II disorder. Following the positive results in our adjunctive study that was part of our bipolar depression clinical program, Study 402, we amended Study 403 to evaluate major depressive episodes with mixed features in bipolar disorder in patients with bipolar I or bipolar II disorder and mixed features in patients with MDD. Clinical conduct in Study 403 has been completed, and we expect to report topline results in the first quarter of 2023. Following reporting of topline results, we intend to discuss the results with the FDA to determine whether this study will provide supportive data for a potential future regulatory filing for this indication.

In addition, we intend to pursue the development of our PDE program, including lenrispodun for the treatment of several CNS and non-CNS conditions, including cardiovascular disease. Following the favorable safety and tolerability results in our Phase 1 program, we initiated our development program for lenrispodun for Parkinson's disease. In the fourth quarter of 2018, we announced that the Phase 1/2 clinical trial of lenrispodun has been completed and topline results demonstrated lenrispodun was generally well-tolerated with a favorable safety profile and clinical signs consistent with improvements in motor symptoms and dyskinesias. We have initiated our Phase 2 clinical program with lenrispodun for Parkinson's disease and expect to commence patient enrollment in the first quarter of 2023.

We cannot be certain that the clinical development of these or any other drug candidates in nonclinical testing or clinical development will be successful, that we will receive the regulatory approvals required to commercialize them or that any of our other research and drug discovery programs will yield a drug candidate suitable for investigation through clinical trials.

There is no guarantee that our planned clinical trials for lumateperone will be successful.

The historical rate of failures for product candidates in clinical development and late-stage clinical trials is high. We are conducting and plan to conduct further clinical trials in lumateperone in indications beyond schizophrenia and bipolar depression, and there is no guarantee that we will have the same level of success in these trials as we have had in certain of our previous clinical trials, or be successful at all.

In addition, although we believe that lumateperone and follow-on compounds may also have clinical utility in indications other than schizophrenia and bipolar depression, such as behavioral disturbances in dementia, intermittent explosive disorder, non-motor disorders associated with Parkinson's disease, obsessive compulsive disorder and anxiety disorders and post-traumatic stress disorder, we have never tested lumateperone in Phase 3 clinical trials in the patient populations for these other indications, except for our ITI-007-201 Phase 3 trial in patients with a clinical diagnosis of probable AD and clinically significant symptoms of agitation, which we determined to discontinue following our independent data monitoring committee's, or DMC's, recommendation that the study should be stopped for futility.

If we do not successfully complete clinical development and obtain approval of lumateperone in indications beyond schizophrenia and bipolar depression, we will be unable to market, sell and generate revenue from lumateperone in any of these other indications. Even though we have successfully completed certain clinical

trials for CAPLYTA in patients with schizophrenia and bipolar depression, those results are not necessarily predictive of results of future trials that may be needed before we may submit an NDA to the FDA for any indication beyond schizophrenia and bipolar depression. Of the vast number of drugs in development, only a small percentage result in the submission of an NDA to the FDA, and even fewer result in the NDA ultimately being approved by the FDA for commercialization.

We expect our net losses to continue and are unable to predict the extent of future losses or when we will become profitable, if ever.

We have experienced significant net losses since inception. As of December 31, 2022, we had an accumulated deficit of approximately $1.5 billion. We expect to continue to incur net losses as we advance our programs and incur significant clinical development costs. To date, we have received limited revenues from the commercialization of CAPLYTA. Prior to our commercial launch of CAPLYTA in March 2020, substantially all of our revenues were from our license and collaboration agreement with Takeda and our agreements with various U.S. governmental agencies and other parties, including our research and development grants. To obtain revenues from lumateperone, we must successfully commercialize lumateperone in its approved indications. To obtain revenues from our product candidates, we must succeed, either alone or with others, in developing, obtaining regulatory approval for, and manufacturing and marketing drugs with significant market potential. We may never succeed in these activities, and may never generate revenues that are significant enough to achieve profitability.

We may require additional funding, which may not be available to us on acceptable terms, or at all, and, if not so available, may require us to delay, limit, reduce or cease our operations.

We have consumed substantial amounts of capital since our inception. Our cash, cash equivalents, investment securities and restricted cash totaled $593.7 million at December 31, 2022. With our cash, cash equivalents and investment securities, we intend to fund our drug development programs and our working capital needs in connection with the commercialization of CAPLYTA. Accordingly, we may require additional capital to continue our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds we will require to complete research and development and commercialize our products under development.

Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the amount of product sales from lumateperone;
- the costs of maintaining and expanding our sales and marketing capabilities for lumateperone;
- the costs of preparing applications for regulatory approvals for lumateperone in additional indications beyond schizophrenia and bipolar depression, and potentially in jurisdictions other than the United States, and for other product candidates, as well as the costs required to support review of such applications;
- the costs of manufacturing and distributing lumateperone for commercial use in the United States;
- our ability to obtain regulatory approval for, and subsequently generate product sales from, lumateperone in additional indications beyond schizophrenia and bipolar depression or in jurisdictions other than the United States;
- the progress in, and the costs of, our nonclinical studies and clinical trials and other research and development programs;
- the scope, prioritization and number of our research and development programs;
- our ability to enter into new, and to maintain any existing, collaboration and license agreements;

- the ability of any future collaborators and us to reach the milestones, and other events or developments, triggering payments under any future collaboration agreements or to otherwise make payments under such agreements;
- the extent to which any future collaborators are obligated to reimburse us for clinical trial costs under any future collaboration agreements;
- the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;
- the costs of maintaining or securing manufacturing and supply arrangements for clinical or commercial production of lumateperone or our other product candidates;
- the costs of preparing applications for regulatory approvals for our product candidates;
- the costs of preparing for and establishing, or contracting for, sales and marketing capabilities if we obtain regulatory approvals for our product candidates;
- the costs involved in maintaining and expanding the accounting and data management systems to support commercial operations; and
- the costs associated with litigation, including the costs incurred in defending against any product liability claims that may be brought against us related to lumateperone or our other product candidates.

Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through our existing cash, cash equivalents and investment securities, strategic collaborations, private or public sales of our securities, debt financings, grant funding, or by licensing all or a portion of our products, product candidates or technology. Turmoil and volatility in the financial markets have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. This, coupled with other factors, may limit our access to additional financing. This could have a material adverse effect on our ability to access sufficient funding. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. If we do obtain additional funding through equity offerings, the ownership of our existing stockholders and purchasers of shares of our common stock in any such offering will be diluted, and the terms of any financing may adversely affect the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline. If funds are not available, we will be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. We also could be required to seek funds through arrangements with collaboration partners or otherwise that may require us to relinquish rights to some of our technologies, products or product candidates or otherwise agree to terms unfavorable to us.

Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations.

Our management has significant flexibility in applying our cash resources and could use these resources for corporate purposes that do not increase our market value, or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which could adversely affect our future growth prospects.

Delays, suspensions and terminations in our clinical trials or the need to conduct additional clinicals or nonclinical studies could result in increased costs to us, delay our ability to generate product revenues and therefore may have a material adverse effect on our business, results of operations and future growth prospects.

The commencement of clinical trials can be delayed for a variety of reasons, including delays in: demonstrating sufficient safety and pharmacological activity to justify seeking to commence a clinical trial;

reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites; manufacturing sufficient quantities of a product candidate; obtaining clearance from the FDA to commence clinical trials pursuant to an IND; obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site; and patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

Once a clinical trial has begun, it may be delayed, suspended or terminated due to a number of factors, including: ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results; failure to conduct clinical trials in accordance with regulatory requirements; lower than anticipated screening or retention rates of patients in clinical trials; serious adverse events or side effects experienced by participants; and insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials.

Many of these factors may also ultimately lead to denial of regulatory approval of a current or potential product candidate. If we experience delays, suspensions or terminations in a clinical trial or are required to conduct additional clinical trials or nonclinical studies, our costs will increase, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed.

Even though the FDA has granted approval of CAPLYTA for the treatment of schizophrenia and bipolar depression, the terms of the approval may limit its commercial potential. Additionally, CAPLYTA is still subject to ongoing regulatory requirements.

Even though the FDA has granted approval of CAPLYTA, the scope and terms of the approval may limit our ability to commercialize CAPLYTA and, therefore, our ability to generate substantial sales revenues. The FDA has approved CAPLYTA only for the treatment of schizophrenia and bipolar depression in adults. The label for CAPLYTA also contains a "boxed" warning that elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death and that CAPLYTA is not approved for the treatment of patients with dementia-related psychosis.

The manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for CAPLYTA also continue to be subject to extensive and ongoing regulatory requirements. These requirements include, but are not limited to, submissions of safety and other post-marketing information and reports and manufacturing establishment registration. We will also have to continue to comply with current good manufacturing processes, good clinical practices, international council for harmonization guidelines and good laboratory practices, which are regulations and guidelines enforced by the FDA for all of our nonclinical and clinical development and for any clinical trials that we conduct post-approval.

Discovery of any issues post-approval, including any safety concerns, such as unexpected side effects or drug-drug interaction problems, adverse events of unanticipated severity or frequency, or concerns over misuse or abuse of the product, problems with the facilities where the product is manufactured, packaged or distributed, or failure to comply with regulatory requirements, may result in, among other things, restrictions on CAPLYTA or on us, including:

- withdrawal of approval, addition of warnings or narrowing of the approved indication in the product label;
- requirement of a Risk Evaluation and Mitigation Strategy, or REMS, program to mitigate the risk of off-label use in populations where the FDA may believe that the potential risks of use may outweigh its benefits;
- voluntary or FDA-requested recalls;
- warning letters;

- suspension of any ongoing clinical studies;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us,;
- restrictions on operations, including restrictions on the marketing or manufacturing of the product or the imposition of costly new manufacturing requirements; or
- seizure or detention, or refusal to permit the import or export of products.

If any of these actions were to occur, we may have to delay or discontinue the commercialization of CAPLYTA, limit our sales and marketing efforts, conduct further post-approval studies, and/or delay, discontinue or change any other ongoing or planned clinical studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues.

Safety issues with our product candidates or approved product, or with product candidates or approved products of third parties that are similar to our product candidates, could give rise to delays in the regulatory approval process, restrictions on labeling or product withdrawal after approval.

Problems with product candidates or approved products marketed by third parties that utilize the same therapeutic target or that belong to the same therapeutic class as our product candidates or approved product could adversely affect the development and regulatory approval of our product candidates or commercialization or our approved product. In 2012, the FDA released draft guidance recommending that prospective suicidality assessments be performed in clinical trials of any drug being developed for a psychiatric indication. Our development programs are focused on psychiatric indications. Our PDE program is a novel target and may have unexpected safety effects that do not appear until late in clinical development or after commercial approval. As we continue the development and clinical trials of our product candidates and continue to commercialize our approved product, there can be no assurance that our product candidates or approved product will not experience significant safety issues.

Discovery of previously unknown class effect problems may prevent or delay clinical development and commercial approval of product candidates or result in restrictions on permissible uses after their approval, including withdrawal of the medicine from the market. Many drugs acting on the CNS include boxed warnings and precautions related to suicidal behavior or ideation, driving impairment, somnolence/sedation and dizziness, discontinuation, weight gain, non-insulin dependent (type II) diabetes, cardiovascular side effects, sleep disturbances, and motor disturbances. The label for CAPLYTA contains a “boxed” warning that elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death and that CAPLYTA is not approved for the treatment of patients with dementia-related psychosis. If we or others later identify undesirable side effects caused by the mechanisms of action or classes of our products or product candidates or any specific products or product candidates:

- we may be required to conduct additional clinical trials or implement a REMS program prior to or following approval;
- regulatory authorities may not approve our product candidates or, as a condition of approval, may require specific warnings and contraindications;
- regulatory authorities may withdraw their approval of the product and require us to take our drug off the market;
- we may have limitations on how we promote our drugs;
- sales of products may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase our commercialization costs and expenses, which, in turn, could delay or prevent us from generating significant revenues from its sale.

Finally, if the FDA determines that a drug may present a risk of substance abuse, it can recommend to the Drug Enforcement Administration, or DEA, that the drug be scheduled under the Controlled Substances Act, or the CSA. Controlled substances are subject to a high degree of regulation under the CSA, which establishes, among other things, certain registration, manufacturing quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA that are separate and apart from FDA's regulatory requirements. The DEA classifies controlled substances into five schedules. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use by the FDA may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse. Any regulatory decision that one of our product candidates should be controlled under the CSA would create additional operational, financial, and commercialization burdens for such a product, which could affect our business and cash flows.

If we seek to enter into strategic alliances for our drug candidates, but fail to enter into and maintain successful strategic alliances, we may have to reduce or delay our drug candidate development or increase our expenditures.

An important element of a biotechnology company's strategy for developing, manufacturing and commercializing its drug candidates may be to enter into strategic alliances with pharmaceutical companies or other industry participants to advance its programs and enable it to maintain its financial and operational capacity. We may face significant competition in seeking appropriate alliances. If we seek such alliances, we may not be able to negotiate alliances on acceptable terms, if at all. In addition, these alliances may be unsuccessful. On October 31, 2014, we entered into the Termination Agreement with Takeda, which terminated the Takeda License Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. If we seek such alliances and then fail to create and maintain suitable alliances, we may have to limit the size or scope of, or delay, one or more of our drug development or research programs. If we elect to fund drug development or research programs on our own, we will have to increase our expenditures and will need to obtain additional funding, which may be unavailable or available only on unfavorable terms.

To the extent we are able to enter into collaborative arrangements or strategic alliances, we will be exposed to risks related to those collaborations and alliances.

Biotechnology companies at our stage of development sometimes become dependent upon collaborative arrangements or strategic alliances to complete the development and commercialization of drug candidates, particularly after the Phase 2 stage of clinical testing. If we elect to enter into collaborative arrangements or strategic alliances, these arrangements may place the development of our drug candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

Dependence on collaborative arrangements or strategic alliances would subject us to a number of risks, including the risk that:

- we may not be able to control the amount and timing of resources that our collaborators may devote to the drug candidates;
- our collaborators may experience financial difficulties;
- we may be required to relinquish important rights, such as marketing and distribution rights;

- business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement;
- a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and
- collaborative arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

Preliminary and interim data from our clinical trials that we may announce or publish from time to time may change as more patient data become available.

From time to time, we may announce or publish preliminary or interim data from our clinical trials. Preliminary and interim data of a clinical trial are not necessarily predictive of final data. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. As a result, preliminary and interim data should be viewed with caution until the final data are available. Material adverse changes in the final data compared to the interim data could affect our planned clinical path for our product candidates, including increasing costs of and/or causing delays in such development, and could significantly harm our business prospects.

We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing our product candidates.

Although we design and manage our current nonclinical studies and clinical trials, we do not currently have the ability to conduct clinical trials for our product candidates on our own. In addition to our collaborators, we rely on contract research organizations, medical institutions, clinical investigators, and contract laboratories to perform data collection and analysis and other aspects of our clinical trials. In addition, we also rely on third parties to assist with our nonclinical studies, including studies regarding biological activity, safety, absorption, metabolism, and excretion of product candidates.

Our nonclinical activities or clinical trials may be delayed, suspended, or terminated if: the quality or accuracy of the data obtained by the third parties on whom we rely is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or if for other reasons, these third parties do not successfully carry out their contractual duties or fail to meet regulatory obligations or expected deadlines, or these third parties need to be replaced.

If the third parties on whom we rely fail to perform, our development costs may increase, our ability to obtain regulatory approval, and consequently, to commercialize our product candidates may be delayed or prevented altogether. We currently use several contract research organizations to perform services for our nonclinical studies and clinical trials. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or incurring additional expenses.

Further, we are currently conducting clinical trials for our product candidates in many countries, including the United States, Europe, and Asia and may expand to other geographies. Timely enrollment of, completion of and reporting on our clinical trials is dependent upon these global clinical trial sites which are, or in the future may be, adversely affected by political instability or conflict. Political instability and conflict in areas in the world where we have clinical operations, may delay our trials and negatively affect our business and operations in those regions.

Our employees, independent contractors, principal investigators, contract research organizations, consultants or vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, contract research organizations, consultants or vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA; manufacturing standards; federal and state health care fraud and abuse laws and regulations; or laws that require the true, complete and accurate reporting of financial information or data. In addition, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations 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 commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our nonclinical studies or clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

It is not always possible to identify and deter misconduct by our employees and other third parties, 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 or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal health care programs, contractual damages, reputational harm, diminished potential profits and future earnings, and curtailment of our operations, any of which could adversely affect our business, financial condition, results of operations or prospects.

Even if we successfully complete the clinical trials of one or more of our product candidates, the product candidates may fail for other reasons.

Even if we successfully complete the clinical trials for one or more of our product candidates, the product candidates may fail for other reasons, including the possibility that the product candidates will:

- fail to receive the regulatory approvals required to market them as drugs;
- be subject to proprietary rights held by others requiring the negotiation of a license agreement prior to marketing;
- be difficult or expensive to manufacture on a commercial scale;
- have adverse side effects that make their use less desirable; or
- fail to compete with product candidates or other treatments commercialized by our competitors.

If we are unable to receive the required regulatory approvals, secure our intellectual property rights, minimize the incidence of any adverse side effects or fail to compete with our competitors' products, our business, financial condition, cash flows and results of operations could be materially and adversely affected.

We are subject to ongoing regulatory obligations and restrictions with regard to CAPLYTA and, following regulatory approval of any of our product candidates, we will be subject to ongoing regulatory obligations and restrictions with regard to such product candidates, which may result in significant expense and limit our ability to commercialize lumateperone and our other potential products.

With regard to CAPLYTA and our product candidates, if any, approved by the FDA, or by another regulatory authority, we are held to extensive regulatory requirements over product manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping. Regulatory approvals may also be subject to significant limitations on the indicated uses or marketing of the product candidates. Potentially costly follow-up or post-marketing clinical studies may be required as a condition of approval to further substantiate safety or efficacy, or to investigate specific issues of interest to the regulatory authority.

Previously unknown problems with the product candidate, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

In addition, the law or regulatory policies governing pharmaceuticals may change. New statutory requirements or additional regulations may be enacted that could prevent or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or elsewhere. If we are not able to maintain regulatory compliance, we might not be permitted to market our drugs and our business could suffer.

CAPLYTA and our product candidates, if approved, may not gain acceptance among physicians, patients, or the medical community, thereby limiting our potential to generate revenues, which will undermine our future growth prospects.

The degree of market acceptance by physicians, health care professionals and third-party payors of CAPLYTA, and any product candidate for which we obtain regulatory approval, and our profitability and growth will depend on a number of factors, including:

- our ability to provide acceptable evidence of safety and efficacy;
- the scope of the approved indication(s) for the product;
- the inclusion of any warnings or contraindications in the product label;
- pricing and cost effectiveness, which may be subject to regulatory control;
- our ability to obtain sufficient third-party insurance coverage or reimbursement;
- effectiveness of our or our collaborators' sales and marketing strategy;
- relative convenience and ease of administration;
- patient adherence to treatment;
- prevalence and severity of any adverse side effects; and
- availability of alternative treatments.

If any product that we develop does not provide a treatment regimen that is at least as beneficial as the current standard of care or otherwise does not provide some additional patient benefit over the current standard of care, that product will not achieve market acceptance and we will not generate sufficient revenues to achieve profitability.

The failure to attract and retain skilled personnel and key relationships could impair our drug development and commercialization efforts.

We are highly dependent on our senior management and key clinical development, sales and marketing, scientific and technical personnel. Competition for these types of personnel is intense. The loss of the services of

any member of our senior management, clinical development, sales and marketing, scientific or technical staff may significantly delay or prevent the achievement of drug development, commercialization and other business objectives and could have a material adverse effect on our business, operating results and financial condition. We also rely on consultants and advisors to assist us in formulating our strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us. We intend to expand and develop new drug candidates, and may need additional funding to grow our business. We will need to hire additional employees in order to continue our research and clinical trials and to market our drugs when approved. This strategy may require us to recruit additional executive management and clinical development, regulatory, scientific, technical and sales and marketing personnel. There is currently intense competition for skilled executives and employees with relevant clinical development, regulatory, scientific, technical and sales and marketing expertise, and this competition is likely to continue. The inability to attract and retain sufficient clinical development, scientific, technical, sales and marketing, and managerial personnel, due to intense competition and our limited resources, would limit or delay our product development and commercialization efforts, which would adversely affect the development of our product candidates and commercialization of CAPLYTA and our product candidates, if approved, and growth of our business.

We may not be able to continue or fully exploit our partnerships with outside scientific and clinical advisors, which could impair the progress of our clinical trials and our research and development efforts.

We work with scientific and clinical advisors at academic and other institutions who are experts in the field of CNS disorders. They advise us with respect to our clinical trials. These advisors are not our employees and may have other commitments that would limit their future availability to us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services, which may impair our reputation in the industry and delay the development or commercialization of our approved product or product candidates.

We rely on third-party manufacturers to manufacture and supply lumateperone and our other product candidates for us. If one of our suppliers or manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts to find new suppliers or manufacturers. We may also face significant delays in our clinical trials, regulatory approvals and product introductions and commercialization.

We have no manufacturing facilities and have limited experience in the manufacturing of drugs or in designing drug-manufacturing processes. We have contracted with third-party manufacturers to produce, in collaboration with us, our product candidates, including lumateperone, for clinical trials and to produce lumateperone for commercial sales. For example, in January 2017, we entered into a supply agreement with Siegfried and entered into a new supply agreement with Siegfried in January 2023, under which Siegfried has agreed to manufacture and supply the API for lumateperone in commercial quantities. Each month, we will provide Siegfried with a rolling forecast of our anticipated requirements for supply of the API. Under the Siegfried Agreement, we have the right to and may purchase the API for lumateperone from other suppliers. In addition, in January 2017, we entered into a manufacturing services agreement with Lonza, as amended in December 2022, under which Lonza has agreed to manufacture and supply the API for lumateperone commercial quantities, with purchase prices determined in each project plan. We agreed to provide Lonza with a written forecast of our estimated quarterly requirements. While we believe that there are alternative sources available to manufacture our product candidates, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty but, if they were to occur, they could cause a delay in our development and commercialization efforts. If our existing or planned third-party manufacturing arrangements are terminated or if the sources of supply from such arrangements are inadequate and we must seek supply agreements from alternative sources, we may be unable to enter into such agreements or do so on commercially reasonable terms, which could delay a product launch or subject our commercialization efforts to significant supply risk.

Manufacturers of our product candidates are obliged to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs. The manufacture of pharmaceutical products in compliance with the cGMPs requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product or product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced cGMP requirements, other federal and state regulatory requirements and foreign regulations. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our ability to provide product for commercial sale or product candidates in our clinical trials would be jeopardized. Any delay or interruption in the supply of commercial quantities of approved product could have a material adverse impact on our revenue from product sales and any delay or interruption in the supply of clinical trial materials could delay the completion of our clinical trials, increase the costs associated with maintaining our clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at significant additional expense or terminate the clinical trials completely.

In addition, the facilities used by our contract manufacturers or other third-party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections conducted following our request for regulatory approval for our product candidates from the FDA. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. We have little control over our manufacturers' compliance with these regulations and standards. A failure of any of our current or future contract manufacturers to establish and follow cGMPs or to document their adherence to such practices may lead to significant delays in obtaining regulatory approval of product candidates or the ultimate launch of products, if approved, into the market. Failure by our current or future third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant marketing approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions, and criminal prosecutions. If the safety of any product supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical studies, regulatory submissions, approvals or commercialization of our product candidates or approved product, entail higher costs or impair our reputation.

We will need to continue to manage our organization and we may encounter difficulties with our staffing and any future transitions, which could adversely affect our results of operations.

We will need to manage our operations and facilities effectively in order to advance our drug development programs (including lumateperone, ITI-1284, lenrispodun and ITI-333), facilitate any future collaborations, and pursue other development activities. It is possible that our infrastructure may be inadequate to support our future efforts and growth. In particular, we will need to further develop information technology systems and internal sales, marketing, and distribution capabilities for any drug that we may successfully develop, including additional indications for lumateperone. We may not successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals.

Our ability to generate product revenues will be diminished if lumateperone or any of our other potential products does not receive and maintain coverage from payors or sells for inadequate prices, or if patients are unable to obtain adequate levels of reimbursement.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and

reimbursement from governmental health care programs, such as Medicare and Medicaid, and commercial payors are critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Even if we obtain coverage for lumateperone or other potential products, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use lumateperone or other product candidates, if approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of those products.

In addition, the market for lumateperone or any product candidate for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available, even if not approved for the indication for which lumateperone is approved.

Third-party payors, whether foreign or domestic, governmental or commercial, are developing increasingly sophisticated methods of controlling health care costs.

The current environment is putting pressure on companies to price products below what they may feel is appropriate. Selling lumateperone at less than an optimized price could impact our revenues and overall success as a company. We do not know if the price we have selected, or may select in the future, for lumateperone is or will be the optimized price. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products such as lumateperone may differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our drug products such as lumateperone to each payor separately, with no assurance that coverage will be obtained. If we are unable to obtain and maintain coverage of, and adequate payment levels for, our products from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize any approved products and thereby adversely impact our profitability, results of operations, financial condition, and future success.

Health care legislation may make it more difficult to receive revenues from CAPLYTA or future products.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals in recent years to change the health care system in ways that could impact our ability to sell our products profitably. For example, on August 16, 2022, President Biden signed into the law the Inflation Reduction Act of 2022, or the IRA. Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Starting in 2023, a manufacturer of drugs or biological products covered by Medicare Parts B or D must pay a rebate to the federal government if their drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting for payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities but their impact on the pharmaceutical industry in the United States remains uncertain. Further legislative changes to health care and pharmaceutical laws in the U.S. remain possible. We expect that health care reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and in

additional downward pressure on the price that may be charged for lumateperone or any of our other product candidates, if approved. 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 health care reforms may prevent us from being able to generate revenue, attain profitability, or commercialize CAPLYTA or any other products for which we receive regulatory approval.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with any products we may market, which could negatively impact our profitability.

We currently have very limited experience as a company in marketing and distributing pharmaceutical products and rely on third-party distributors to distribute CAPLYTA. If we are unable to effectively commercialize CAPLYTA, we may not be able to generate adequate product revenues.

CAPLYTA, which was approved by the FDA in December 2019 for the treatment of schizophrenia in adults in the United States and in December 2021 for the treatment of bipolar depression in adults in the United States, is our only drug that has been approved for sale by any regulatory body. We initiated the commercial launch of CAPLYTA in March 2020. As such, as an organization, this was the first time we have launched or commercialized any pharmaceutical product. In order to continue to successfully market CAPLYTA, we must continue to develop our sales, marketing, managerial, compliance, and related capabilities or make arrangements with third parties to perform these services. If we are unable to maintain and develop adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to continue to appropriately commercialize and generate revenue from sales of CAPLYTA and may not become profitable.

We are employing our own internal sales force to commercialize CAPLYTA for the treatment of schizophrenia and bipolar depression as part of our commercialization strategy in the United States. We are competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. These efforts will continue to be expensive and time-consuming, and we cannot be certain that we will be able to successfully maintain and further develop our sales force.

Additionally, our strategy in the United States includes distributing CAPLYTA through third-party distributors. While we have entered into, or will attempt to enter into, agreements with these distributors to distribute CAPLYTA in the United States, they may not perform as agreed or they may terminate their agreements with us. Also, we may need to enter into agreements with additional distributors, and there is no guarantee that we will be able to do so on commercially reasonable terms or at all. If we are unable to maintain and, if needed, expand, our network of distributors, we would be exposed to substantial distribution risk.

In the event we are unable to effectively develop and maintain our commercial team, including our U.S. sales force, or maintain and, if needed, expand, our network of distributors, our ability to effectively commercialize CAPLYTA and generate product revenues would be limited.

The FDA has granted marketing approval of CAPLYTA for the treatment of schizophrenia and bipolar depression in adults, and we could face liability if a regulatory authority determines that we are promoting CAPLYTA for any "off-label" uses.

A company may not promote "off-label" uses for its drug products. An off-label use is the use of a product for an indication or patient population that is not described in the product's FDA-approved label in the United States or for uses in other jurisdictions that differ from those approved by the applicable regulatory agencies. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from pharmaceutical companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. A company that is found to have promoted off-label use of its product may be subject to significant liability, including civil and criminal sanctions. We intend to comply with the requirements and restrictions of the FDA and other regulatory agencies with respect to our promotion of CAPLYTA, and any other products we may market, but we cannot be sure that the FDA or other regulatory agencies will agree that we have not violated their restrictions. As a result, we may become subject to criminal and civil liability should an agency determine that such violations occurred. In addition, our management's attention could be diverted to handle any such alleged violations. A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice, or DOJ, and various U.S. Attorneys' Offices, the Health and Human Services Office of Inspector General, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the civil False Claims Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. If the FDA, DOJ, or any other governmental agency initiates an enforcement action against us, or if we are the subject of a qui tam suit under the False Claims Act and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects, and reputation.

There are possible limitations on our use of net operating losses.

As of December 31, 2022, we had net operating loss carryforwards, or NOLs, of approximately $663.2 million, which are available to reduce any future federal and state taxable income, of which $131.1 million will begin to expire at various dates through 2037 and $532.1 million do not expire. The use of our NOLs may be restricted due to changes in our ownership, including as a result of our public offerings.

Under Section 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, changes in our ownership (as defined by the foregoing sections of the Code) may limit the amount of NOLs and tax credit carryforwards that could be utilized annually in the future to offset taxable income.

For the years ended December 31, 2022, 2021 and 2020, we performed a Section 382 ownership analysis and determined that no ownership change occurred (within the meaning of Section 382 of the Code) as a result of our public offerings in 2020 and 2022. Our previous ownership analysis through December 31, 2015 reflected an ownership change occurred as a result of our 2015 public offerings.

Changes in tax laws could adversely affect our business and financial condition.

On March 27, 2020, the United States enacted The Coronavirus Aid, Relief and Economic Security (CARES) Act which includes several significant business tax provisions, of which the immediate relevance to the

Company is the acceleration of refunds of previously generated corporate AMT credits. The CARES Act also adds an employee retention credit to encourage employers to maintain headcounts even if employees cannot report to work because of issues related to the coronavirus, a temporary provision allowing companies to defer remitting to the government the employee share of some payroll taxes, among other things. The Company reviewed the provisions and there was not a material tax impact on its financial statements for the years ended December 31, 2022, 2021 and 2020. We did reclassify its deferred tax asset related to the AMT tax credit carryforward of $0.3 million to a current tax receivable in the first quarter of 2020 upon the filing of its tax return for year ended December 31, 2019 and received the refund in July 2020.

On August 9, 2022, the United States enacted the CHIPS and Science Act which provides an investment tax credit for 25% of qualified investments primarily used for manufacturing of semiconductors and related equipment in the U.S. On August 16, 2022, the United States enacted the Inflation Reduction Act ("IRA") which includes a provision for a 15% corporate alternative minimum tax on companies with average annual adjusted financial statement income over $1 billion effective for tax years ending after December 31, 2022. In addition to other provisions included such as stock buy-back and prescription drug pricing, we reviewed the provisions and there was not a material tax impact on its financial statements for the year ended December 31, 2022.

On December 31, 2022, ITI Limited, our wholly-owned Bermuda subsidiary, was merged into Intra-Cellular Therapies, Inc., a Delaware corporation. The intellectual property rights were transferred to the Delaware corporation as a result of this merger. ITI Limited is solvent as the fair market value of the intellectual property exceeds the liabilities of the entity. This merger and the subsequent liquidation of the Bermuda subsidiary does not have any impact from a U.S. or Bermuda income tax perspective.

We continue to examine the impact this tax reform legislation may have on our business and depending on possible foreign operations, among other things, the impact of this tax reform is uncertain and could be adverse. This report does not discuss any such tax legislation or the manner in which it might affect holders of our common stock. We urge our stockholders to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our common stock.

Security breaches, loss of data and other disruptions could compromise sensitive information related to our business, prevent us from accessing critical information or expose us to liability, which could adversely affect our business and our reputation.

We are increasingly dependent upon technology systems and data to operate our business. The COVID-19 pandemic has caused us to modify our business practices in ways that heighten this dependence, including changing the requirement that most of our office-based employees in the U.S. and our other key markets work from the office. As a result, we are increasingly dependent upon our technology systems to operate our business and our ability to effectively manage our business depends on the security, reliability and adequacy of our technology systems and data, which includes use of cloud technologies. Breakdowns, invasions, corruptions, destructions and/or breaches of our technology systems, including our cloud technologies, and/or unauthorized access to our data and information could subject us to liability, negatively impact our business operations, and/or require replacement of technology and/or ransom payments. Our technology systems, including our cloud technologies, continue to increase in multitude and complexity, increasing our vulnerability when breakdowns, malicious intrusions, and random attacks occur. Data privacy or security breaches also pose a risk that sensitive data, including intellectual property, trade secrets or personal information belonging to us, patients, customers or other business partners, may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity, and are becoming increasingly difficult to detect, when they impact vendors, customers or companies, including vendors, suppliers and other companies in our supply chain. They are often carried out by motivated, well-resourced, skilled and persistent actors, including nation states, organized crime groups, "hacktivists" and employees or contractors acting with careless or malicious intent. Cyber-attacks include deployment of harmful malware and key loggers, ransomware, a denial-of-service attack, a malicious website, the use of social engineering and other means to affect the confidentiality, integrity and

availability of our technology systems and data. Cyber-attacks also include manufacturing, hardware or software supply chain attacks, which could cause a delay in the manufacturing of products or products produced for contract manufacturing or lead to a data privacy or security breach. Our key business partners face similar risks and any security breach of their systems could adversely affect our security posture. In addition, our increased use of cloud technologies heightens these and other operational risks, and any failure by cloud or other technology service providers to adequately safeguard their systems and prevent cyber-attacks could disrupt our operations and result in misappropriation, corruption or loss of confidential or trade secret information. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, there can be no assurance that we will promptly detect any such disruption or security breach, if at all. 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, we could incur liability and the commercialization of our approved product and the further development of our product candidates could be delayed or otherwise adversely impacted.

While we continue to build and improve our systems and infrastructure, including our business continuity plans, there can be no assurance that our efforts will prevent disruptions or breaches in our systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, operational or reputational harm to us, loss of competitive advantage or loss of consumer confidence. Our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks, and other related breaches.

Our business is subject to complex and evolving U.S. and foreign laws and regulations, information security policies and contractual obligations relating to privacy and data protection, including the use, processing, and cross-border transfer of personal information. These laws and regulations are subject to change. The actual or perceived failure by us, or vendors to comply could harm our reputation, and subject us to significant fines and liability.

A growing body of increasingly stringent domestic and foreign laws and regulations governs the collection, use, disclosure, transfer and other processing of personal data. Privacy laws in the United States are becoming increasingly complex and changing rapidly. California was the first U.S. state to enact a comprehensive privacy law, California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020. The CCPA requires covered companies to provide new disclosures to California residents and honor their requests to access, delete and opt-out of certain sharing of their personal data. The CCPA provides for civil penalties for violations and statutory damages for certain data breaches. Since the enactment of the CCPA, new privacy and data security laws have been enacted in Virginia, Colorado, Connecticut, and Utah, reflecting a trend toward more stringent privacy legislation in the United States. The CCPA has also been substantially amended by a voter-approved ballot initiative called the California Privacy Rights Act, or CPRA. The CPRA went into full effect on January 1, 2023, and, among other things, creates a new administrative agency to implement and enforce California's privacy laws. While certain clinical trial activities are exempt from some state privacy law requirements, other personal information that we handle may be subject to these various laws, which may increase our compliance costs, exposure to regulatory enforcement action and other liabilities.

In addition to U.S. privacy laws, we may also be subject to privacy regulations elsewhere in the world, including the European Union's General Data Protection Regulation, or GDPR. The GDPR imposes stringent requirements for controllers and processors of personal data, including, for example, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention of information, increased requirements pertaining to special categories of data, such as health data, and additional obligations when we contract with third-party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Economic Area to the United States and other countries, and a recent decision of the European Union's highest court has made complying with those rules more challenging. In addition, the GDPR provides that

European Union member states may adopt further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

The GDPR applies extraterritorially, and we may be subject to the GDPR because of our data processing activities that involve the personal data of individuals residing in the European Union. Failure to comply with the requirements of the GDPR and the applicable national data protection laws of the European Union member states may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, bans on processing personal data and other administrative penalties. GDPR regulations may impose additional responsibility and liability in relation to the personal data that we process and we may be required to put in place additional mechanisms to ensure compliance with the new data protection rules.

In addition, the GDPR includes restrictions on cross-border data transfers. A recent decision by the Court of Justice of the European Union (the "Schrems II" ruling), however, has invalidated the EU-U.S. Privacy Shield Framework, which was one of the primary mechanisms used by U.S. companies to import personal information from Europe, and raised questions about whether the European Commission's Standard Contractual Clauses, or SCCs, one of the primary alternatives to the Privacy Shield, can lawfully be used for personal information transfers from Europe to the United States or most other countries. Similarly, the Swiss Federal Data Protection and Information Commissioner recently opined that the Swiss-U.S. Privacy Shield is inadequate for transfers of data from Switzerland to the United States. The United Kingdom (UK), whose data protection laws are similar to those of the European Union, may similarly determine that the EU-U.S. Privacy Shield is not a valid mechanism for lawfully transferring personal information from the UK to the United States. The European Commission recently proposed updates to the SCCs, and additional regulatory guidance has been released that seeks to impose additional obligations on companies seeking to rely on the SCCs. Given that, at present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the SCCs, any transfers by us or our vendors of personal data from Europe may not comply with European data protection law, which may increase our exposure to the GDPR's heightened sanctions for violations of its cross-border data transfer restrictions and may prohibit our transfer of EU personal data outside of the EU (including clinical trial data), and may adversely impact our operations, product development and ability to provide our products.

If we are unable to implement safeguards necessary to ensure that our transfers of personal data from and within Europe are lawful, we will face increased exposure to regulatory actions, substantial fines and bans on processing personal data from Europe. In addition, we may be required to increase our data processing capabilities in Europe at significant expense. Inability to import personal data from Europe may also restrict our clinical trials activities in the EU and limit our ability to collaborate with contract research organizations, service providers, contractors and other companies subject to European data protection laws. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of operating our business.

The GDPR, CCPA and many other laws and regulations relating to privacy and data protection are still being tested in courts, and they are subject to new and differing interpretations by courts and regulatory officials. We are working to comply with the privacy and data protection laws and regulations that apply to us, and we anticipate needing to devote significant additional resources to complying with these laws and regulations. It is possible that the GDPR, CCPA or other laws and regulations relating to privacy and data protection may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with our current policies and practices. Compliance with the various and rapidly-changing privacy laws is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases,

impact our ability to operate in certain jurisdictions. Data protection laws and data protection worldwide is, and is likely to remain, uncertain for the foreseeable future. While we strive to comply with applicable data protection laws, external and internal privacy and security policies, and contractual data protection obligations to the extent possible, we may at times fail to do so, or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our personnel, collaborators, partners or vendors do not comply with applicable data protection laws, external and internal privacy and security policies, and contractual data protection obligations. Actual or perceived failure to comply with U.S. and international data protection laws could result in government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individual's privacy rights, even if we are found not liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

We are also subject to the terms of our external and internal privacy and security policies, representations, certifications, publications and frameworks, and contractual obligations to third parties related to privacy, information security and processing. Failure or a perceived failure to comply with these policies, or if these policies are, in whole or part, found or perceived to be inaccurate, incomplete, deceptive, unfair, or misrepresentative of our actual practices, could result in reputational harm; result in litigation; cause a material adverse impact to business operations or financial results; and otherwise result in other material harm to our business.

Our actual or perceived failure to adequately comply with applicable laws and regulations relating to privacy and data protection, or to protect personal data and other data we process or maintain, could result in regulatory fines and bans on processing personal information, investigations and enforcement actions, penalties and other liabilities, claims for damages by affected individuals, and damage to our reputation, any of which could materially affect our business, financial condition, results of operations and growth prospects.

The COVID-19 pandemic could continue to have a material impact on our business, financial condition and results of operations, including our commercial operations and sales, clinical trials and nonclinical studies.

In December 2019, a novel strain of coronavirus, SARS-CoV-2, which causes coronavirus disease 2019, or COVID-19, surfaced in Wuhan, China. Since then, SARS-CoV-2 and COVID-19 have spread to countries worldwide, including the United States. The COVID-19 pandemic continues to evolve, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. As a result of the COVID-19 pandemic, we may continue to experience disruptions, which could severely impact our business, including our ability to successfully commercialize our only commercial product, CAPLYTA, in the United States, and could negatively impact our sales of CAPLYTA. Our commercial organization, sales force and medical organization have had, and, depending on the severity and duration of the pandemic, may continue to have significantly reduced personal interactions with physicians and customers and may need to continue to conduct many promotional activities virtually, and we may elect to cease in-person interactions with physicians and customers entirely for some period of time in the interest of employee and community safety. In addition, the pandemic may continue to impact the willingness of patients to visit their healthcare provider. Business interruptions from the current or future pandemics may also adversely impact the third parties we rely on to sufficiently manufacture CAPLYTA and to produce our product candidates in quantities we require, which may impair the commercialization and our research and development activities.

We conduct clinical trials for our product candidates in many countries and regions, including the United States, Europe and Asia, and may expand to other geographies. Timely enrollment of, completion of and reporting on our clinical trials is dependent upon these global clinical trial sites which are, or in the future may be, adversely affected by the COVID-19 pandemic or other pandemics. Some factors from the COVID-19 pandemic that have or may adversely affect the timing and conduct of our clinical trials and adversely impact our

business generally, include but are not limited to, delays or difficulties in clinical site initiation, patient enrollment, diversion of healthcare resources away from clinical trials to pandemic concerns, limitations on travel, regulatory delays and supply chain disruptions.

The COVID-19 pandemic continues to evolve, and the severity and duration of the pandemic remain uncertain. The extent to which the pandemic impacts our business, including our commercial results, clinical trials, and nonclinical studies will depend on future developments, which are highly uncertain.

Risks Related to Our Intellectual Property

Our ability to compete may be undermined if we do not adequately protect our proprietary rights.

Our commercial success depends on obtaining and maintaining proprietary rights to our products and product candidates and technologies and their uses, as well as successfully defending these rights against third-party challenges. We will only be able to protect our products and product candidates, proprietary technologies, and their uses from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. We have patent rights under issued patents in many cases covering our lumateperone, lenrispodun, ITI-1284 and ITI-333 development programs. Nonetheless, the issued patents and patent applications covering our primary technology programs remain subject to uncertainty and continuous monitoring and action by us due to a number of factors, including:

- we may not have been the first to make the inventions covered by our pending patent applications or issued patents;
- we may not have been the first to file patent applications for our products, product candidates or the technologies we rely upon;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our pending patent applications may not result in issued patents;
- we may not seek or obtain patent protection in all countries that will eventually provide a significant business opportunity;
- any patents issued to us or our collaborators may not provide a basis for commercially viable products, may not provide us with any competitive advantages or may be challenged by third parties;
- our proprietary technologies may not be patentable;
- others may design around our patent claims to produce competitive products which fall outside of the scope of our patents;
- others may identify prior art which could invalidate our patents; and
- changes to patent laws may limit the exclusivity rights of patent holders.

Even if we have or obtain patents covering our products, product candidates or technologies, we may still be barred from making, using and selling our products, product candidates or technologies because of the patent rights of others. Others have or may have filed, and in the future are likely to file, patent applications covering compounds, assays, genes, gene products and therapeutic products that are similar or identical to ours. There are many issued U.S. and foreign patents relating to genes, nucleic acids, polypeptides, chemical compounds or therapeutic products, and some of these may encompass reagents utilized in the identification of candidate drug

compounds or compounds that we desire to commercialize. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the area of CNS disorders and the other fields in which we are developing product candidates. These could materially affect our ability to develop our product candidates or sell our products. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, that may later result in issued patents that our products, product candidates or technologies may infringe. These patent applications may have priority over patent applications filed by us.

We regularly conduct searches to identify patents or patent applications that may prevent us from obtaining patent protection for our proprietary compounds or that could limit the rights we have claimed in our patents and patent applications. Disputes may arise regarding the ownership or inventorship of our inventions. It is difficult to determine how such disputes would be resolved. Others may challenge the validity, enforceability, scope and term of our patents. Additionally, any patent term extensions that we seek may not be granted on a timely basis, if at all. If our patents are found to be invalid, we will lose the ability to exclude others from making, using or selling the inventions claimed in our patents.

Some of our academic institutional licensors, research collaborators and scientific advisors have rights to publish data and information to which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information will be impaired. Additionally, any employee whose employment with us terminates, whether voluntarily by the employee or by us in connection with restructurings or otherwise, may seek future employment with our competitors. Although each of our employees is required to sign a confidentiality agreement with us at the time of hire, we cannot guarantee that the confidential nature of our proprietary information will be maintained in the course of such future employment. In addition, technology that we may license-in may become important to some aspects of our business. We generally will not control the patent prosecution, maintenance or enforcement of in-licensed technology.

Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.

Because we operate in the highly technical field of drug discovery and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. We enter into confidentiality and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties any confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. The failure to obtain or maintain trade secret protection could adversely affect our competitive position.

A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business.

There is significant litigation in our industry regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our products, product candidates, technologies or activities infringe the intellectual property rights of others. If our drug development or commercialization activities are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. We may need to resort to litigation to enforce a patent

issued to us, protect our trade secrets or determine the scope and validity of third-party proprietary rights. From time to time, we may hire scientific personnel formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of their prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We also may not be able to afford the costs of litigation.

The patent applications of pharmaceutical and biotechnology companies involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. The standards of the U.S. Patent and Trademark Office, or USPTO, are uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings in the USPTO (and foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office), which proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. Similarly, opposition or invalidity proceedings could result in loss of rights or reduction in the scope of one or more claims of a patent in foreign jurisdictions. In addition, such interference, reexamination and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

In addition, changes in or different interpretations of patent laws in the United States and foreign countries may permit others to use our discoveries or to develop and commercialize our technology, products and product candidates without providing any compensation to us or may limit the number of patents or claims we can obtain. In particular, there have been proposals to shorten the exclusivity periods available under U.S. patent law that, if adopted, could substantially harm our business. Our approved product and the product candidates that we are developing are protected by intellectual property rights, including patents and patent applications. For our approved product and any of our product candidates that become a marketable product, if any, we will rely on our exclusivity under patents to sell the compound and recoup our investments in the research and development of the compound. If the exclusivity period for patents is shortened, then our ability to generate revenues without competition will be reduced and our business could be materially adversely impacted. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans and, in these countries, patent protection may not be available at all to protect our products or product candidates. In addition, U.S. patent laws may change, which could prevent or limit us from filing patent applications or patent claims to protect our products, product candidates and/or technologies or limit the exclusivity periods that are available to patent holders. For example, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law in 2011 and includes a number of significant changes to U.S. patent law. These include changes to transition from a “first-to-invent” system to a “first-to-file” system and to the way issued patents are challenged. These changes may favor larger and more established companies that have more resources to devote to patent application filing and prosecution. The USPTO has been in the process of implementing regulations and procedures to administer the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act may affect our ability to obtain, enforce or defend our patents. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will ultimately have on the cost of prosecuting our patent applications, our ability to obtain patents based on our discoveries and our ability to enforce or defend our issued patents.

If we fail to obtain and maintain patent protection and trade secret protection of our products, product candidates, proprietary technologies and their uses, we could lose our competitive advantage and competition we face would increase, reducing our potential revenues and adversely affecting our ability to attain or maintain profitability.

We may not be able to protect our intellectual property and proprietary rights throughout the world, which could negatively impact our business.

Filing, prosecuting and defending patents relating to our products, product candidates and technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as U.S. laws. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors or other third parties 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 or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant difficulties in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology, which could make it difficult, costly or impossible for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary 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, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us or any of our future licensors. We may not prevail in any lawsuits or other adversarial proceedings 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 and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Further, many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Risks Related to Our Industry

We are subject to stringent regulation in connection with the marketing of CAPLYTA and any other products derived from our product candidates, which could delay the development and commercialization of our products.

The pharmaceutical industry is subject to stringent regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Neither we nor our collaborators can market a pharmaceutical product in the United States until we or they have completed rigorous nonclinical testing and clinical trials and an extensive regulatory clearance process implemented by the FDA. Satisfaction of regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product, and requires substantial resources. Even if regulatory approval is obtained, it may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, and/or marketing of such products, and requirements for post-approval studies, including additional research and development and clinical trials. For example, the label for CAPLYTA contains a “boxed” warning that elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death and that CAPLYTA is not approved for the treatment of patients with dementia-related psychosis. These limitations may reduce the size of the market

for the product or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues and continue our business.

Outside the United States, the ability to market a product is contingent upon receiving approval from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing, and reimbursement vary widely from country to country. Only after the appropriate regulatory authority is satisfied that adequate evidence of safety, quality, and efficacy has been presented will it grant a marketing authorization. Approval by the FDA does not automatically lead to the approval by regulatory authorities outside the United States and, similarly, approval by regulatory authorities outside the United States will not automatically lead to FDA approval.

Many of our competitors have greater resources and capital than us, putting us at a competitive disadvantage. If our competitors develop and market products that are more effective than lumateperone or our other product candidates, they may reduce or eliminate our commercial opportunity.

Competition in the pharmaceutical and biotechnology industries is intense and increasing. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the United States and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our drug development programs.

For example, CAPLYTA for the treatment of schizophrenia and for the treatment of bipolar depression competes with, among other branded products, Fanapt®, marketed by Vanda Pharmaceuticals, Lybalvi®, marketed by Alkermes, Rexulti®, marketed by Otsuka Pharmaceutical, and Vraylar®, marketed by AbbVie. In addition, CAPLYTA competes and our product candidates, if approved, would compete with, among other generic antipsychotic products, aripiprazole, clozapine, haloperidol, lurasidone, olanzapine, paliperidone, quetiapine/XR and risperidone.

Many of our competitors and their collaborators have significantly greater experience than we do in the following:

- identifying and validating targets;
- screening compounds against targets;
- nonclinical studies and clinical trials of potential pharmaceutical products;
- obtaining FDA and other regulatory approvals; and
- commercializing pharmaceutical products.

In addition, many of our competitors and their collaborators have substantially greater capital and research and development resources, manufacturing, sales and marketing capabilities, and production facilities. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate drug targets and to discover novel small molecule drugs. Our competitors, either alone or with their collaborators, may succeed in developing drugs that are more effective, safer, more affordable, or more easily administered than ours, have fewer side effects than ours, and may achieve patent protection or commercialize drugs sooner than us. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Our failure to compete effectively could have a material adverse effect on our business.

Any claims relating to improper handling, storage, or disposal of biological, hazardous, and radioactive materials used in our business could be costly and delay our research and development efforts.

Our research and development activities involve the controlled use of potentially harmful hazardous materials, including volatile solvents, biological materials such as blood from patients that have the potential to transmit disease, chemicals that cause cancer, and various radioactive compounds. Our operations also produce hazardous waste products. We face the risk of contamination or injury from the use, storage, handling or disposal of these materials. We are subject to federal, state and local laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. The cost of compliance with these laws and regulations could be significant, and current or future environmental regulations may impair our research, development, or production efforts. If one of our employees were accidentally injured from the use, storage, handling, or disposal of these materials, the medical costs related to their treatment would be covered by our workers' compensation insurance policy. However, we do not carry specific biological or hazardous waste insurance coverage and our general liability insurance policy specifically excludes coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be subject to criminal sanctions or fines or be held liable for damages, our operating licenses could be revoked, and we could be required to suspend or modify our operations and our research and development efforts.

We are subject, directly and indirectly, to federal, state and foreign healthcare and data protection laws and regulations, including healthcare fraud and abuse laws, false claims laws, physician payment transparency laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Our operations are directly, and indirectly through our customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our clinical research, sales, marketing, grants, charitable donations, and education programs and constrain the business or financial arrangements with healthcare providers, physicians, charitable foundations, and other parties that have the ability to directly or indirectly influence the prescribing, ordering, marketing, or distribution of our products for which we obtain marketing approval. In addition, we and any potential future collaborators, partners or service providers are subject to data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business. Finally, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, 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 U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or *qui tam* actions, and civil monetary penalties laws, which impose criminal and civil penalties on individuals or entities for, among other things, knowingly presenting, or causing to be presented to the U.S. federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- HIPAA, and its implementing regulations, and as amended again by the Final HIPAA Omnibus Rule, Modifications to the HIPAA Privacy, Security, Enforcement and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules, published in January 2013, which imposes criminal and civil liability for, among other things, 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) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- We are not directly subject to HIPAA, however, we could be subject to penalties, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a HIPAA-covered health care provider or research institution that has not complied with HIPAA's requirements for disclosing such information. Furthermore, the number of government investigations related to data security incidents and privacy violations continue to increase and government investigations typically require significant resources and generate negative publicity, which could harm our business and our reputation;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act", which was enacted as part of the ACA and its implementing regulations and requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS information related to certain payments and other transfers of value made to physicians (as defined to include doctors of medicine, dentists, optometrists, podiatrists and chiropractors under such law), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members, which was expanded beginning in 2022, to require applicable manufacturers to report such information regarding its relationships with physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year;
- analogous state and local laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities and/or the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of personal information and 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; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers, and data protection under the GDPR; we anticipate that over time we may expand our business operations to include additional operations in the EU and with such expansion, we would be subject to increased governmental regulation in the EU

countries in which we might operate, including the GDPR. In addition, our failure to comply with GDPR and privacy laws of EU Member States or the United Kingdom may result in regulators prohibiting our processing of the personal information of EU data subjects, which could impact our operations and ability to develop our products and provide our services, including interrupting or ending EU clinical trials.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, additional reporting requirements and/or oversight, and the curtailment or restructuring of our operations. Moreover, while we do not bill third-party payors directly and our customers make the ultimate decision on how to submit claims, from time-to-time, for CAPLYTA, and any other product candidates that may be approved, we may provide reimbursement guidance to patients and healthcare providers. If a government authority were to conclude that we provided improper advice and/or encouraged the submission of a false claim for reimbursement, we could face action against us by government authorities. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of CAPLYTA, or any other product candidates that may be approved, outside of the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of lumateperone or any other product for which we obtain regulatory approval, or development or commercialization of our product candidates.

We face an inherent risk of product liability as a result of commercial sales of lumateperone in the United States and the clinical testing of our product candidates, and will face an even greater risk following commercial launch of lumateperone in additional jurisdictions, if approved, or if we engage in the clinical testing of new product candidates or commercialize any additional products.

For example, we may be sued if lumateperone or any other product we develop allegedly causes injury or is found to be otherwise unsuitable for administration in humans. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection laws. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products or product candidates that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;

- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize our products or product candidates; and
- a decline in our stock price.

Although we currently have product liability insurance that covers our clinical trials and the commercialization of CAPLYTA for the treatment of schizophrenia and bipolar depression, we may need to increase and expand this coverage, including if lumateperone is approved for the treatment of indications beyond schizophrenia and bipolar depression or if other product candidates are approved for commercial sale. This insurance may be prohibitively expensive or may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products that we or our collaborators develop. If we determine that it is prudent to increase our product liability coverage, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. Our liability could exceed our total assets if we do not prevail in a lawsuit from any injury caused by our drug products. Product liability claims could have a material adverse effect on our business and results of operations.

Our business is affected by macroeconomic conditions.

Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates and overall economic conditions and uncertainties, including those resulting from the current and future conditions in the global financial markets. For instance, if inflation or other factors were to significantly increase our business costs, it may not be feasible to pass price increases on to our customers due to the process by which healthcare providers are reimbursed for our product by the government. Interest rates, the liquidity of the credit markets and the volatility of the capital markets has and could continue to also affect the value of our investments and our ability to liquidate our investments in order to fund our operations. We purchase or enter into a variety of financial instruments and transactions, including high-grade corporate bonds and commercial paper. If any of the issuers or counter parties to these instruments were to default on their obligations, it could materially reduce the value of the transaction and adversely affect our cash flows. Interest rates and the ability to access credit markets could also adversely affect the ability of our customers and distributors to purchase, pay for and effectively distribute our products. Similarly, these macroeconomic factors could affect the ability of our suppliers and manufacturers to supply or manufacture our product.

Risks Related to Owning Our Common Stock

Numerous factors could result in substantial volatility in the trading price of our stock.

During the year ended December 31, 2022, the price per share of our common stock on the Nasdaq Global Select Market has ranged from a high of $66.00 to a low of $38.51. We have several stockholders who hold substantial blocks of our stock. Sales of large numbers of shares by any of our large stockholders could adversely affect our trading price. If stockholders holding shares of our common stock sell, indicate an intention to sell, or if it is perceived that they will sell, substantial amounts of their common stock in the public market, the trading price of our common stock could decline.

In addition, the trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

- the success of our commercialization of CAPLYTA in the United States for the treatment of schizophrenia and bipolar depression;
- timing and announcement of regulatory developments, submissions and approvals or preliminary, interim or final results of clinical trials;
- actual or anticipated quarterly variation in our results of operations or the results of our competitors;
- announcements of medical innovations or new products or product candidates by our competitors;
- issuance of new or changed securities analysts' reports or recommendations for our stock;
- developments or disputes concerning our intellectual property or other proprietary rights;
- commencement of, or our involvement in, litigation;
- market conditions in the biopharmaceutical industry;
- any future sales of our common stock or other securities in connection with raising additional capital or otherwise;
- any major change to the composition of our board of directors or management; and
- general economic conditions and slow or negative growth of our markets.

The stock market in general, and market prices for the securities of biotechnology companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance. In several recent situations where the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a securities class action lawsuit against us, such as the purported class action lawsuits brought against us and certain of our executive officers in May 2017, consolidated in July 2017 and voluntarily dismissed in November 2017, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

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

We may need to satisfy our future cash needs through public or private sales of our equity securities, sales of debt securities, the incurrence of debt from commercial lenders, strategic collaborations, licensing a portion or all of our products, product candidates and technology and, to a lesser extent, grant funding, although there can be no assurances such financing can be obtained. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or grant licenses on terms that are not favorable to us.

The price of our common stock could be subject to volatility related or unrelated to our operations.

The market price of our common stock could fluctuate substantially due to a variety of factors, including market perception of our ability to meet our growth projections and expectations, quarterly operating results of

other companies in the same industry, trading volume in our common stock, changes in general conditions in the economy and the financial markets or other developments affecting our business and the business of others in our industry. In addition, the stock market itself is subject to extreme price and volume fluctuations. This volatility has had a significant effect on the market price of securities issued by many companies for reasons related and unrelated to their operating performance and could have the same effect on our common stock.

We incur substantial costs and demands upon management as a result of complying with the laws and regulations affecting public companies, which could harm our operating results.

As a public company, we have incurred and will incur significant legal, accounting and other expenses, including costs associated with public company reporting requirements. We also have incurred and will incur costs associated with current corporate governance requirements, including requirements under Section 404 and other provisions of the Sarbanes-Oxley Act, as well as rules implemented by the SEC or the Nasdaq Global Select Market or any other stock exchange or inter-dealer quotations system on which our common stock may be listed in the future. The expenses incurred by public companies for reporting and corporate governance purposes have increased dramatically in recent years.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.

We are required to comply with Section 404 of the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to maintain effective internal control over financial reporting. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting. In addition, we are required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be re-evaluated frequently. We currently outsource the internal audit function. We have hired and may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge to establish an internal audit function. If we fail to maintain the effectiveness of our internal controls or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, this could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would require additional financial and management resources. In addition, if our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Our ability to successfully implement our business plan and comply with Section 404 requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and to obtain an unqualified report on internal controls from our independent registered public accounting firm as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our common stock, and could adversely affect our ability to access the capital markets.

If securities or industry analysts do not publish, or cease publishing, research or reports about us, our business or our market, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock is and will be influenced by whether industry or securities analysts publish or continue to publish research and reports about us, our business, our market or our competitors and, to the extent analysts do publish such reports, what they publish in those reports. We may not continue to have or to obtain analyst coverage in the future. Any analysts that do cover us may make adverse recommendations regarding our stock, adversely change their recommendations from time to time, and/or provide more favorable relative recommendations about our competitors. If any analyst who covers us or may cover us in the future were to cease coverage of us or fail to regularly publish reports on us, or if analysts fail to cover us or publish reports about us at all, we could lose, or never gain, visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions of the Delaware law, our restated certificate of incorporation and our restated bylaws may delay or prevent a takeover which may not be in the best interests of our stockholders.

The provisions of Delaware law and our restated certificate of incorporation and restated bylaws could discourage or make it more difficult to accomplish a proxy contest or other change in our management or the acquisition of control by a holder of a substantial amount of our voting stock. 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 interests or in our best interests. These provisions are intended to enhance the likelihood of continuity and stability in the composition of our board of directors and in the policies formulated by the board of directors and to discourage certain types of transactions that may involve an actual or threatened change of our control. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy fights. Such provisions also may have the effect of preventing changes in our management.

We do not anticipate paying cash dividends in the foreseeable future.

We currently intend to retain any future earnings for funding growth. We do not anticipate paying any cash dividends in the foreseeable future. As a result, you should not rely on an investment in our securities if you require dividend income. Capital appreciation, if any, of our shares may be your sole source of gain for the foreseeable future. Moreover, you may not be able to re-sell your shares at or above the price you paid for them.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This report includes forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Words such as, but not limited to, "believe," "expect," "anticipate," "estimate," "intend," "may," "plan," "potential," "predict," "project," "targets," "likely," "will," "would," "could," "should," "continue," and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this report, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. The description of our Business set forth in Item 1, the Risk Factors set forth in this Item 1A and our Management's Discussion and Analysis of Financial Condition and Results of Operations set forth in Item 7 as well as other sections in this report, discuss some of the factors that could contribute to these differences. These forward-looking statements include, among other things, statements about:

- the accuracy of our estimates regarding expenses, revenues, uses of cash, cash equivalents and investment securities, capital requirements and the need for additional financing;
- our expectations regarding our commercialization of CAPLYTA;
- the duration and severity of the COVID-19 pandemic and its continued impact on our business;
- the supply and availability of and demand for our product;
- the initiation, cost, timing, progress and results of our development activities, nonclinical studies and clinical trials;
- the timing of and our ability to obtain and maintain regulatory approval, or submit an application for regulatory approval, of lumateperone and our other existing product candidates, any product candidates that we may develop, and any related restrictions, limitations, and/or warnings in the label of any approved product candidates;
- our plans to research, develop and commercialize lumateperone and our other current and future product candidates;
- the election by any collaborator to pursue research, development and commercialization activities;
- our ability to obtain future reimbursement and/or milestone payments from our collaborators;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to successfully commercialize lumateperone and our other product candidates;
- the size and growth of the markets for lumateperone and our other product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of any current or future products;
- the success of competing drugs that are or become available;
- regulatory developments in the United States and other countries;
- the performance of our third-party suppliers and manufacturers and our ability to obtain alternative sources of raw materials;

- our ability to obtain additional financing;
- our use of the proceeds from our securities offerings;
- any restrictions on our ability to use our net operating loss carryforwards;
- our exposure to investment risk, interest rate risk, inflation risk and capital market risk; and
- our ability to attract and retain key scientific, management or sales and marketing personnel.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important cautionary statements in this report, particularly in the Risk Factors set forth in Item 1A of this Annual Report on Form 10-K, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this report and the documents that we reference in this report and have filed as exhibits to this report completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this report are made as of the date of this report, and we do not assume, and specifically disclaim, any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

Our headquarters are located at 430 East 29th Street, New York, New York 10016, where we occupy approximately 32,287 square feet of useable office and laboratory space. The term of the lease, as amended, expires in March 2029. We also lease a small amount of office space in Towson, Maryland.

Item 3. LEGAL PROCEEDINGS

On July 8, 2022, a purported shareholder derivative complaint was filed in the Supreme Court for the State of New York against the directors serving on the Company's board of directors and the Company as a nominal defendant alleging breach of fiduciary duty and unjust enrichment alleging that compensation awarded to the director defendants for service on the board of directors was excessive. We believe that the complaint is without merit. At present, we are unable to estimate potential losses, if any, related to the lawsuit.

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 traded on the Nasdaq Global Select Market under the symbol "ITCI."

Stockholders

As of February 27, 2023, we had 95,280,003 outstanding shares of common stock and no outstanding shares of preferred stock. As of February 27, 2023, there were approximately 78 holders of record of our outstanding shares of common stock.

Unregistered Sales of Securities

Not applicable.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. [RESERVED]

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion of the financial condition and results of our operations should be read in conjunction with the financial statements and the notes to those statements appearing elsewhere in this Annual Report on Form 10-K. This section of this Annual Report on Form 10-K generally discusses the fiscal years ended December 31, 2022 and 2021 items and year to year comparisons between the fiscal years ended December 31, 2022 and 2021. The discussion around results of operations for the fiscal year ended December 31, 2020 and a comparison of our results for the fiscal years ended December 31, 2021 and 2020 is included in Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations, of our Annual Report on Form 10-K for fiscal year ended December 31, 2021, filed with the SEC on March 1, 2022. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should read the Risk Factors set forth in Item 1A of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the discovery, clinical development and commercialization of innovative, small molecule drugs that address underserved medical needs primarily in neuropsychiatric and neurological disorders by targeting intracellular signaling mechanisms within the central nervous system, or CNS. In December 2019, CAPLYTA® (lumateperone) was approved by the U.S. Food and Drug Administration, or FDA, for the treatment of schizophrenia in adults (42mg/day) and we initiated the commercial launch of CAPLYTA in March 2020. In December 2021, CAPLYTA was approved by the FDA for the treatment of bipolar depression in adults (42mg/day). We initiated the commercial launch of CAPLYTA for the treatment of bipolar depression in December 2021. Additionally, in April 2022, the FDA approved two new dosage strengths of CAPLYTA, 10.5 mg and 21 mg capsules, to provide dosage recommendations for patients concomitantly taking strong or moderate CYP3A4 inhibitors, and 21 mg for patients with moderate or severe hepatic impairment (Child-Pugh class B or C). We initiated the commercial launch of these special population doses in August 2022. As used in this report, "CAPLYTA" refers to lumateperone approved by the FDA for the treatment of schizophrenia in adults and for the treatment of bipolar depression in adults, and "lumateperone" refers to, where applicable, CAPLYTA as well as lumateperone for the treatment of indications beyond schizophrenia and bipolar depression.

Lumateperone is in Phase 3 clinical development as a novel treatment for MDD. Patient enrollment in Study 501 and Study 502, global Phase 3 clinical trials evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of MDD, is ongoing. In addition, in the second quarter of 2023, we expect to initiate a third global Phase 3 trial, Study 505, also evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of MDD. Study 505 is intended to serve as a potential additional registration trial in support of a supplemental New Drug Application, or sNDA, for approval of lumateperone as an adjunctive therapy to antidepressants for the treatment of MDD, if needed. This is a common strategy employed in mood disorder development programs. Subject to the results of Study 501 and Study 502, we expect to file an sNDA with the FDA for approval of lumateperone as an adjunctive therapy to antidepressants for the treatment of MDD in 2024. In the first quarter of 2020, as part of our lumateperone bipolar depression clinical program, we initiated our third monotherapy Phase 3 study, Study 403, evaluating lumateperone as monotherapy in the treatment of major depressive episodes associated with bipolar I or bipolar II disorder. Following the positive results in our adjunctive study that was part of our bipolar depression clinical program, Study 402, we amended Study 403 to evaluate major depressive episodes with mixed features in bipolar disorder in patients with bipolar I or bipolar II disorder and mixed features in patients with MDD. Clinical conduct for Study 403 has been completed, and we expect to report topline results in the first quarter of 2023. Following reporting of topline

results, we intend to discuss the results with the FDA to determine whether this study will provide supportive data for a potential future regulatory filing for this indication.

We have also initiated a Phase 3 study evaluating lumateperone for the prevention of relapse in patients with schizophrenia. The study is being conducted in five phases consisting of a screening phase, a 6-week, open-label run-in phase during which all patients will receive 42 mg of lumateperone per day, a 12-week, open-label stabilization phase during which all patients will receive 42 mg of lumateperone per day; a double-blind treatment phase, 26 weeks in duration, during which patients receive either 42 mg of lumateperone per day or placebo (1:1 ratio) and a 2-week safety follow-up phase. This study is being conducted in accordance with our post approval marketing commitment to the FDA in connection with the approval of CAPLYTA for the treatment of schizophrenia as is typical for antipsychotics.

Within the lumateperone portfolio, we are also developing a long-acting injectable, or LAI, formulation to provide more treatment options to patients suffering from mental illness. We have completed the nonclinical development of an LAI formulation, and we have conducted a Phase 1 single ascending dose study with this formulation. This study evaluated the pharmacokinetics, safety and tolerability of lumateperone LAI in patients with stable symptoms of schizophrenia. We completed this study and it was safe and well tolerated. We are evaluating several additional formulations of the lumateperone LAI with treatment durations of one month and longer. Non-clinical development on these additional formulations is ongoing and expected to be completed in 2023 and we plan to initiate Phase I single ascending dose studies with these formulations in 2023. Given the encouraging tolerability data to date with oral lumateperone, we believe that an LAI option, in particular, may lend itself to being an important formulation choice for certain patients.

We are developing ITI-1284-ODT-SL for the treatment of agitation in patients with dementia, the treatment of dementia-related psychosis and the treatment of certain depressive disorders in the elderly. ITI-1284-ODT-SL is a deuterated form of lumateperone, a new molecular entity formulated as an oral disintegrating tablet for sublingual administration. ITI-1284-ODT-SL is formulated as an oral solid dosage form that dissolves almost instantly when placed under the tongue, allowing for ease of use in the elderly and may be particularly beneficial for patients who have difficulty swallowing conventional tablets. Phase 1 single and multiple ascending dose studies in healthy volunteers and healthy elderly volunteers (> than 65 years of age) evaluated the safety, tolerability and pharmacokinetics of ITI-1284-ODT-SL. In these studies, there were no reported serious adverse events in either age group. In the elderly cohort, reported adverse events were infrequent with the most common adverse event being transient dry mouth (mild). Based on these results, we have initiated our program evaluating ITI-1284-ODT-SL for the treatment of agitation in patients with Alzheimer's disease. We are in discussions with the FDA regarding the nonclinical toxicological profile of ITI-1284-ODT-SL. The FDA has informed us that they do not believe the deuterated and undeuterated forms of lumateperone are identical. As a result, the nonclinical data from lumateperone may not be broadly applied to ITI-1284-ODT-SL and we are conducting additional toxicology studies. We expect to commence clinical conduct in a Phase 2 study in agitation in patients with Alzheimer's disease in 2023. Additional studies in psychosis in patients with Alzheimer's disease and generalized anxiety disorder are also planned for 2023. We are continuing with Phase 1 studies with ITI-1284-ODT-SL, including drug-drug interaction studies.

We have another major program that has yielded a portfolio of compounds that selectively inhibit the enzyme phosphodiesterase type 1, or PDE1. PDE1 enzymes are highly active in multiple disease states and our PDE1 inhibitors are designed to reestablish normal function in these disease states. Abnormal PDE1 activity is associated with cellular proliferation and activation of inflammatory cells. Our PDE1 inhibitors ameliorate both of these effects in animal models. We intend to pursue the development of our phosphodiesterase, or PDE, program, for the treatment of aberrant immune system activation in several CNS and non-CNS conditions with a focus on diseases where excessive PDE1 activity has been demonstrated and increased inflammation is an important contributor to disease pathogenesis. Our potential disease targets include immune system regulation, neurodegenerative diseases, cancers and other non-CNS disorders. Lenrispodun (ITI-214) is our lead compound in this program. Following the favorable safety and tolerability results in our Phase 1 program, we initiated our

development program for lenrispodun for Parkinson's disease and conducted a Phase 1/2 clinical trial of lenrispodun in patients with Parkinson's disease to evaluate safety and tolerability in this patient population, as well as motor and non-motor exploratory endpoints. In this study, lenrispodun was generally well-tolerated with a favorable safety profile and clinical signs consistent with improvements in motor symptoms and dyskinesias. We have initiated our Phase 2 clinical program with lenrispodun for Parkinson's disease, and expect to commence patient enrollment in the first quarter of 2023. We also have an active Investigational New Drug application to evaluate our newest candidate within the PDE 1 inhibitor program, ITI-1020, as a novel cancer immunotherapy. A Phase 1 program with ITI-1020 in healthy volunteers is anticipated to commence in the first half of 2023.

We also have a development program with our ITI-333 compound as a potential treatment for substance use disorders, pain and psychiatric comorbidities including depression and anxiety. There is a pressing need to develop new drugs to treat opioid addiction and safe, effective, non-addictive treatments to manage pain. ITI-333 is a novel compound that uniquely combines activity as an antagonist at serotonin 5-HT2A receptors and a partial agonist at μ-opioid receptors. These combined actions support the potential utility of ITI-333 in the treatment of opioid use disorder and associated comorbidities (e.g., depression, anxiety, sleep disorders) without opioid-like safety and tolerability concerns. We have conducted a Phase 1 single ascending dose study evaluating the safety, tolerability and pharmacokinetics of ITI-333 in healthy volunteers. In this study, ITI-333 achieved plasma exposures at or above those required for efficacy and was generally safe and well-tolerated. We have commenced a neuroimaging study to investigate brain occupancy for receptors that play a role in substance use disorder and also have applicability for pain. The results of this study will support the dose selection for future studies. We commenced a multiple ascending dose study in the first quarter of 2023. We have received a grant from the National Institute on Drug Abuse under the Helping to End Addiction Long-term Initiative, or NIH HEAL Initiative, that we expect will fund a significant portion of the early stage clinical development costs associated with this program.

We have assembled a management team with significant industry experience to lead the commercialization of our product and the discovery, development and potential commercialization of our product candidates. We complement our management team with a group of scientific and clinical advisors that includes recognized experts in the fields of schizophrenia, bipolar depression and other CNS disorders.

COVID-19

In December 2019, a novel strain of coronavirus, SARS-CoV-2, which causes coronavirus disease 2019, or COVID-19, surfaced in Wuhan, China. Since then, SARS-CoV-2 and COVID-19 have spread to countries worldwide, including the United States. The COVID-19 pandemic continues to evolve, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. As a result of the COVID-19 pandemic, we may continue to experience disruptions, which could severely impact our business, including our ability to successfully commercialize our only commercial product, CAPLYTA, in the United States, and could negatively impact our sales of CAPLYTA. Our commercial organization, sales force and medical organization have had, and, depending on the severity and duration of the pandemic, may continue to have significantly reduced personal interactions with physicians and customers and may need to continue to conduct many promotional activities virtually, and we may elect to cease in-person interactions with physicians and customers entirely for some period of time in the interest of employee and community safety. In addition, the pandemic may continue to impact the willingness of patients to visit their healthcare provider. Business interruptions from the current or future pandemics may also adversely impact the third parties we rely on to sufficiently manufacture CAPLYTA and to produce our product candidates in quantities we require, which may impair the commercialization and our research and development activities.

We conduct clinical trials for our product candidates in many countries and regions, including the United States, Europe and Asia, and may expand to other geographies. Timely enrollment of, completion of and reporting on our clinical trials is dependent upon these global clinical trial sites which are, or in the future may

be, adversely affected by the COVID-19 pandemic or other pandemics. Some factors from the COVID-19 pandemic that have or may adversely affect the timing and conduct of our clinical trials and adversely impact our business generally, include but are not limited to, delays or difficulties in clinical site initiation, patient enrollment, diversion of healthcare resources away from clinical trials to pandemic concerns, limitations on travel, regulatory delays and supply chain disruptions.

The COVID-19 pandemic continues to evolve, and the severity and duration of the pandemic remain uncertain. The extent to which the pandemic impacts our business, including our commercial results, clinical trials, and nonclinical studies will depend on future developments, which are highly uncertain.

Results of Operations

The following discussion summarizes the key factors our management believes are necessary for an understanding of our financial statements.

Revenues

Net revenues from product sales consist of sales of CAPLYTA, which was approved by the FDA for the treatment of schizophrenia in adults in December 2019 and for the treatment of bipolar depression in adults in December 2021. In addition, in April 2022, the FDA approved two new dosage strengths of CAPLYTA for certain patients. We initiated the commercial launch of CAPLYTA in March 2020. During the years ended December 31, 2022 and 2021, net sales increased from approximately $81.7 million for the year ended December 31, 2021 to approximately $249.1 million for the year ended December 31, 2022.

Expenses

The process of researching, developing and commercializing drugs for human use is lengthy, unpredictable and subject to many risks. We are unable, with certainty, to estimate either the costs or the timelines in which those costs will be incurred. The costs associated with the commercialization of CAPLYTA are substantial and will be incurred prior to our generating sufficient revenue to offset these costs. Costs for the clinical development of lumateperone-related projects, including for the treatment of MDD, consumes and, together with our required post marketing studies and other anticipated clinical development programs, will continue to consume a large portion of our current, as well as projected, resources. We intend to pursue other disease indications that lumateperone may address, but there are significant costs associated with pursuing FDA approval for those indications, which would include the cost of additional clinical trials.

Our PDE, ITI-1284 and ITI-333 development programs are currently in clinical development. Our other programs are still in the nonclinical stages and will require extensive funding not only to complete nonclinical testing, but also to commence and complete clinical trials. Expenditures that we incur on these programs will be subject to availability of funding in addition to the funding required for the advancement of lumateperone. Any failure or delay in the advancement of lumateperone could require us to re-allocate resources from our other programs to the advancement of lumateperone, which could have a material adverse impact on the advancement of these other programs and on our results of operations.

Our operating expenses are comprised of (i) costs of product sales, (ii) selling expenses, (iii) general and administrative expenses, and (iv) research and development expenses.

Costs of product sales are comprised of:

- royalty payments on product sales;
- direct costs of formulating, manufacturing and packaging drug product; and

- overhead costs consisting of labor, share-based compensation, shipping, outside inventory management and other miscellaneous operating costs.

Selling expenses are incurred in three major categories:

- salaries and related benefit costs of a dedicated sales force;
- sales operation costs; and
- marketing and promotion expenses.

General and administrative expenses are incurred in three major categories:

- salaries and related benefit costs;
- patent, legal, and professional costs; and
- office and facilities overhead.

Research and development costs are comprised of:

- fees paid to external parties who provide us with contract services, such as nonclinical testing, manufacturing and related testing, clinical trial activities and license milestone payments; and
- internal recurring costs, such as costs relating to labor and fringe benefits, materials, supplies, facilities and maintenance.

Product sold through December 31, 2022 consisted of API and drug product that was previously charged to research and development expense prior to FDA approval of CAPLYTA and other direct, indirect, and overhead costs required to make final product for sale. Because the Company's policy does not allow for the capitalization of pre-approval product, the cost of drug product sold is lower than it would have been and has a positive impact on our cost of product sales for the years ended December 31, 2022, 2021 and 2020. We expect to continue to have this favorable impact on cost of product sales and related product gross margins until the cost of our sales of CAPLYTA include drug product that is manufactured entirely after the FDA approval. We expect that this will be the case for the near term and, as a result, our cost of product sales will be less than we anticipate it will be in future periods.

We expect that research and development expenses will increase considerably as we proceed with our clinical trials, including increased manufacturing of drug product for clinical trials and nonclinical development activities. We also expect that our selling, general and administrative costs will increase from prior periods primarily due to costs associated with promotional activities to support the commercial sales of CAPLYTA as well as costs associated with building and maintaining infrastructure, which will include hiring additional personnel and increasing technological capabilities. We granted significant share-based awards in 2022, 2021 and 2020. We expect to continue to grant share-based awards in the future due to our growing employee base, which will increase our share-based compensation expense in future periods.

The following table sets forth our revenues, operating expenses, interest income, net and income tax expense for the years ended December 31, 2022, 2021 and 2020 (in thousands):

	For the Year Ended December 31,		
	2022	2021	2020
Revenues			
Product sales, net	**$ 249,132**	$ 81,708	$ 22,531
Grant revenue	**1,182**	2,095	282
Total revenues, net	**250,314**	83,803	22,813
Expenses			
Cost of product sales	**20,443**	8,035	1,895
Selling, general and administrative	**358,782**	272,611	186,364
Research and development	**134,715**	88,845	65,782
Total costs & expenses	**513,940**	369,491	254,041
Loss from operations	**(263,626)**	(285,688)	(231,228)
Interest income, net	**7,376**	1,568	4,235
Income tax expense	**(6)**	(6)	(13)
Net loss	**$(256,256)**	$(284,126)	$(227,006)

Comparison of Years Ended December 31, 2022 and December 31, 2021

Product Sales, Net

Net product sales were approximately $249.1 million for the year ended December 31, 2022 and $81.7 million for the year ended December 31, 2021. Net product revenue in 2021 was comprised of sales of CAPLYTA for the treatment of schizophrenia, while net product revenue in 2022 was comprised of sales of CAPLYTA for the treatment of schizophrenia and bipolar depression.

Cost of Product Sales

Cost of product sales was approximately $20.4 million and $8.0 million for the years ended December 31, 2022 and 2021, respectively. Cost of product sales consisted primarily of product royalty fees, overhead and direct costs. Drug product costs, including certain direct, indirect, and overhead costs, for product sales through December 31, 2022 were previously charged to research and development expense prior to FDA approval in December 2019 and are not a component of cost of product sales. This minimal cost drug product had a positive impact on our cost of product sales and related product gross margins for the years ended December 31, 2022 and 2021.

We will continue to have a lower cost of product sales that excludes the cost of the drug product that was incurred prior to FDA approval until our sales of CAPLYTA include drug product that is entirely manufactured after the FDA approval. We expect that this will be the case for the near-term and, as a result, our cost of product sales will be less than we anticipate it will be in future periods.

Selling, General and Administrative Expenses

Selling, general and administrative costs for the year ended December 31, 2022 were $358.8 million as compared to $272.6 million in the year ended December 31, 2021, which represents an increase of 32%.

Selling costs were $277.8 million for the year ended December 31, 2022 as compared to $203.5 million in the year ended December 31, 2021, or an increase of 37%. This increase is primarily due to increases of marketing and advertising expenses of approximately $45.6 million, sales related labor costs of approximately

$21.9 million, and approximately $6.8 million in travel, lease expense and other costs. Salaries, bonuses and related benefit costs for our sales and marketing functions for the years ended December 31, 2022 and 2021 constituted approximately 34% and 35%, respectively, of our selling costs.

General and administrative expenses for the year ended December 31, 2022 were $81.0 million as compared to $69.1 million for the year ended December 31 2021, an increase of 17%. This increase is due to increases in share-based compensation expense of approximately $3.0 million, IT related services of approximately $2.8 million, labor related expense of approximately $2.2 million, and the remainder for insurance, lease expense, regulatory fees and other administrative expenses. Salaries, bonuses and related benefit costs for our general and administrative functions for the years ended December 31, 2022 and 2021 constituted approximately 55% and 57%, respectively, of our general and administrative costs.

We expect selling, general and administrative costs to increase in 2023 as compared to the year ended December 31, 2022 due to our recent sales force expansion and increased marketing, promotional and advertising costs.

Research and Development Expenses

The following tables set forth our research and development expenses for the years ended December 31, 2022 and 2021 (in thousands):

	2022	2021
External costs	$ 88,803	$53,166
Internal costs	45,912	35,679
Total Research and development expenses	$134,715	$88,845
Lumateperone project costs	$ 70,416	$51,187
Non-lumateperone project costs	38,210	18,675
Share-based compensation	15,828	9,832
Overhead and other costs	10,261	9,151
Total Research and development expenses	$134,715	$88,845

Research and development expenses increased to $134.7 million for the year ended December 31, 2022 as compared to $88.8 million for the year ended December 31, 2021, representing an increase of approximately 52%. This increase is due primarily to increases of approximately $19.3 million for lumateperone costs, approximately $19.5 million for non-lumateperone costs, including the ITI-1284, ITI-214, and ITI-333 programs, among others, approximately $6.0 million for share-based compensation expense and approximately $1.1 million on overhead and other expenses. External costs increased by approximately $35.6 million due primarily to outsourced clinical expenses, outsourced laboratory testing of our lumateperone and other program expenses, and outsourced development-based manufacturing activities. Internal costs increased by approximately $10.2 million for the year due primarily to labor related costs and share-based compensation.

As the development of lumateperone and non-lumateperone programs progresses, we anticipate research and development costs will increase significantly due primarily to nonclinical testing and conducting ongoing and planned clinical trials during the next several years. We are also required to complete nonclinical testing to obtain FDA approval and manufacture materials needed for clinical trial use, which includes nonclinical testing of the drug product, and manufacturing of drug product in anticipation of possible additional FDA approvals of lumateperone for indications beyond schizophrenia and bipolar depression.

As of December 31, 2022, we employed 75 full-time personnel in our research and development group as compared to 67 full-time personnel in our research and development group at December 31, 2021. The increase is due primarily to additional personnel for our clinical development team as we continue our ongoing programs.

We expect to hire additional staff as we increase our development efforts and grow our business in the upcoming years.

The research and development process necessary to develop a pharmaceutical product for commercialization is subject to extensive regulation by numerous governmental authorities in the United States and other countries. This process typically takes years to complete and requires the expenditure of substantial resources. The steps required before a drug may be marketed in the United States generally include the following:

- completion of extensive nonclinical laboratory tests, animal studies, and formulation studies in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an Investigational New Drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each proposed indication;
- submission to the FDA of a New Drug Application, or NDA, after completion of all clinical trials;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient, or API, and finished drug product are produced and tested to assess compliance with current Good Manufacturing Practices, or cGMPs;
- satisfactory completion of FDA inspections of clinical trial sites to assure that data supporting the safety and effectiveness of product candidates has been generated in compliance with Good Clinical Practices; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

The successful development of our product candidates and the approval process requires substantial time, effort and financial resources, and is uncertain and subject to a number of risks. We cannot be certain that any of our product candidates will prove to be safe and effective, will meet all of the applicable regulatory requirements needed to receive and maintain marketing approval, or will be granted marketing approval on a timely basis, if at all. Data from nonclinical studies and clinical trials are susceptible to varying interpretations that could delay, limit or prevent regulatory approval or could result in label warnings related to or recalls of approved products. We, the FDA, or other regulatory authorities may suspend clinical trials at any time if we or they believe that the subjects participating in such trials are being exposed to unacceptable risks or if such regulatory agencies find deficiencies in the conduct of the trials or other problems with our product candidates. Other risks associated with our product candidates are described in the section titled "Risk Factors" in this Annual Report on Form 10-K.

Liquidity and Capital Resources

From inception through December 31, 2022, we have financed the Company primarily through public and private offerings of our common stock and other securities, and to a far lesser extent, through proceeds from grants from government agencies and foundations. In 2022, we collected approximately $259.5 million from product sales, which we believe will increase going forward. We do not believe that grant revenue will be a significant source of funding in the future.

As of December 31, 2022, we had a total of approximately $593.7 million in cash and cash equivalents, available-for-sale investment securities and restricted cash, and approximately $83.2 million of short-term liabilities consisting entirely of liabilities from operations. In the year ended December 31, 2022, we used approximately $495 million in cash for operating costs. During this period, we collected $259.5 million from

product sales, $6.4 million of interest income, and we paid approximately $44.1 million related to our customer program liabilities, which resulted in $271.0 million of net cash used for operations and equipment. The use of cash was primarily for selling and marketing costs in connection with our commercialization of CAPLYTA, conducting clinical trials and nonclinical testing, funding recurring operating expenses, and product manufacturing.

Based on our current operating plans, we expect that our existing cash, cash equivalents, marketable securities, and product sales will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months from the filing date of this Annual Report. During that time, we expect that our expenses will increase, primarily due to the continued commercialization of CAPLYTA for the treatment of schizophrenia and bipolar depression; the development of lumateperone in our late-stage clinical programs; the development of our other product candidates, including ITI-1284, ITI-214, and ITI-333; and infrastructure expansion and general operations.

We seek to balance the level of cash, cash equivalents and investments on hand with our projected needs and to allow us to withstand periods of uncertainty relative to the availability of funding on favorable terms. Subject to our ability to generate significant revenues from operations, we may need to satisfy our future cash needs through public or private sales of our equity securities, sales of debt securities, incurrence of debt from commercial lenders, strategic collaborations, licensing a portion or all of our product candidates and technology and, to a lesser extent, grant funding.

We cannot be sure that future funding will be available to us when we need it on terms that are acceptable to us, or at all. We sell securities and incur debt when the terms of such transactions are deemed favorable to us and as necessary to fund our current and projected cash needs. The amount of funding we raise through sales of our common stock or other securities depends on many factors, including, but not limited to, the magnitude of sales of CAPLYTA, the status and progress of our product development programs, projected cash needs, availability of funding from other sources, our stock price and the status of the capital markets. Due to the volatile nature of the financial markets, equity and debt financing may be difficult to obtain. Additionally, the uncertain market conditions and continued effects of COVID-19 may limit our ability to access any financing. In addition, any unfavorable results in the commercialization of CAPLYTA and unfavorable development or delay in the progress of our lumateperone program could have a material adverse impact on our ability to raise additional capital.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

If adequate funds are not available to us on a timely basis, we may be required to: (1) delay, limit, reduce or terminate nonclinical studies, clinical trials or other clinical development activities for one or more of our product candidates, including our lead product candidate lumateperone, and our other product candidates; (2) delay, limit, reduce or terminate our discovery research or nonclinical development activities; (3) enter into licenses or other arrangements with third parties on terms that may be unfavorable to us or sell, license or relinquish rights to develop or commercialize our product candidates, technologies or intellectual property at an earlier stage of development and on less favorable terms than we would otherwise agree; or (4) limit or reduce commercialization efforts related to CAPLYTA.

Our cash is maintained in checking accounts, money market accounts, money market mutual funds, U.S. government agency securities, certificates of deposit, commercial paper, corporate notes and corporate bonds at major financial institutions. Due to the recent history of low interest rates available for these instruments, we have been earning limited interest income. During the year ended December 31, 2022, however, interest rates have risen which is increasing interest income. This increase in interest rates has, however, resulted in approximately $4.2 million of unrealized losses on investments during the year ended December 31, 2022. Due to the short-term nature of these investments and our intention to hold these investments to maturity, we do not expect to recognize these losses. Even with the rise or further potential rise in interest rates, we do not expect interest income to be a significant source of funding. In addition, our investment portfolio historically has not been adversely impacted by problems in the credit markets, but there can be no assurance that our investment portfolio will not be adversely affected in the future.

Our cash requirements in the short and long term consist of operational, manufacturing, and capital expenditures, a portion of which contain contractual or other obligations. We plan to fund our cash requirements with our current financial resources together with our anticipated receipts from product sales. We manage future cash requirements relative to our long-term business plans. Our primary uses of cash and operating expenses relate to administering clinical trials, manufacturing and marketing our products, paying employees and consultants, and providing technology and facility infrastructure to support our operations.

We have two kinds of long-term contractual commitments—operating leases and purchase obligations. In 2014, we entered into a lease of 16,753 square feet of useable laboratory and office space located at 430 East 29th Street, New York, New York 10016. In September 2018, we amended the lease to obtain an additional 15,534 square feet of office space beginning October 1, 2018 and to extend the term of the lease for previously acquired space. The lease, as amended, has a term of 14.3 years ending in May 2029. Refer to Note 7—*Leases* to our consolidated financial statements for further details.

In addition to operating leases, we enter into certain other long-term commitments for goods and services that are outstanding for periods greater than one year. We recently amended our significant manufacturing service agreements with Siegfried Evionnaz SA and Lonza Ltd, committing to certain minimum annual purchase commitments which we anticipate payments for within the years 2025 through 2029. We also enter into short-term agreements with various vendors and suppliers of goods and services in the normal course of operations through purchase orders. Such short-term agreements are generally outstanding for periods less than a year and are settled by cash payments upon delivery of goods and services. The nature of the work being conducted under these agreements is such that, in most cases, the services may be stopped on short notice without penalty. In such event, we would not be liable for the full amount of the agreement.

Critical Accounting Policies and Estimates

The discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires management to make estimates and assumptions that affect reported amounts of assets and liabilities as of the date of the balance sheet and reported amounts of revenues and expenses for the periods presented. Judgments must also be made about the disclosure of contingent liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management makes estimates and exercises judgment in research and development, including clinical trial accruals. Actual results may differ from those estimates and under different assumptions or conditions.

We believe that the following critical accounting policy affects management's more significant judgments and estimates used in the preparation of our financial statements:

Research and Development, Including Clinical Trial Expenses

We recognize our research and development expenses as the services are incurred. Research and development costs primarily consist of salaries and related expenses for personnel and resources and the costs of clinical trials. Other research and development expenses include nonclinical analytical testing, manufacturing of drug product for use in clinical and nonclinical trials, outside services, providers, materials and consulting fees.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to us by our vendors, among other factors with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

As part of the process of preparing our financial statements, we are required to estimate expenses resulting from the obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. Our objective is to reflect the appropriate clinical trial expenses in our financial statements by matching those expenses with the period in which services are performed and efforts are expended. We account for these expenses according to the progress of the clinical trial as measured by subject progression and the timing of various aspects of the trial. We determine accrual estimates through financial models taking into account various clinical information provided by vendors and discussion with applicable personnel and external service providers as to the progress or state of consummation of trials, or the services completed. During the course of a clinical trial, we adjust our clinical expense recognition if actual results differ from our estimates. We make estimates of our accrued expenses as of each balance sheet date based on the facts and circumstances known to us at that time. Our clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations, clinical sites and other third-party vendors. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low for any particular period.

Revenue Recognition

In accordance with ASC Topic 606, we recognize revenue when the customer obtains control of a promised good or service, in an amount that reflects the consideration that we expect to receive in exchange for the good or service.

To determine revenue recognition for arrangements that we determine are within the scope of ASC Topic 606, we perform the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to arrangements that meet the definition of a contract under ASC Topic 606, including when it is probable that we will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC Topic 606, we assess the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the

respective performance obligation when (or as) the performance obligation is satisfied. For additional discussion of accounting for product sales, see *Product Sales, net* (below).

To date, our only source of product sales has been from sales of CAPLYTA in the United States, which we began shipping to customers in March 2020.

Product Sales, net

We sell CAPLYTA to a limited number of customers which include a number of national and select regional distributors. These customers subsequently resell our products to specialty pharmacy providers, as well as other retail pharmacies and certain medical centers or hospitals. In addition to distribution agreements with customers, we enter into arrangements with health care providers and payers that provide for government mandated and/or privately negotiated rebates, chargebacks, and discounts with respect to the purchase of our products. We recognize revenue on product sales when the customer obtains control of our product, which occurs at a point in time (upon delivery). Product revenues are recorded net of applicable reserves for variable consideration, including rebates, discounts and allowances, among others. If taxes should be collected from customers relating to product sales and remitted to governmental authorities, they will be excluded from revenue.

Reserves for Variable Consideration

Revenues are calculated based on the wholesale acquisition cost that we charge to distributors for CAPLYTA less variable consideration for which reserves are established. Components of variable consideration may include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payer rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between us and our customers, payers, and other indirect customers relating to sales of our product.

These reserves are based on the amounts earned, or to be claimed on the related sales, include our best estimates that take into consideration a range of possible outcomes which are considered more likely in accordance with the expected value method in ASC Topic 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, and forecasted customer buying and payment patterns. Our estimates utilizing payer mix are based on CAPLYTA's actual channel mix in 2022. The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Our analyses also contemplated application of the constraint in accordance with the guidance, under which it determined it was probable that a significant reversal of revenue would not occur in a future period for the estimates detailed below as of December 31, 2022 and 2021, therefore, the transaction price was not reduced further during the years ended December 31, 2022 and 2021. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product sales and earnings in the period such variances become known.

Government Rebates—We are subject to discount obligations under state Medicaid and Medicare programs. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Chargebacks, discounts, fees, and returns are recorded as reductions of trade receivables, net on the consolidated balance sheets. Government and other rebates are recorded as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

Recently Issued Accounting Pronouncements

We review new accounting standards to determine the expected financial impact, if any, that the adoption of each such standard will have. Based on our assessment, all new accounting pronouncements were determined to be either not applicable or are expected to have minimal impact on our consolidated financial statements or related disclosures.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity. As of December 31, 2022, we had cash, cash equivalents, marketable securities and restricted cash of approximately $593.7 million, consisting of cash deposited in a highly rated financial institution in the United States and in a short-term U.S. Treasury money market fund, as well as high-grade corporate bonds and commercial paper. The primary objective of our investment activities is to preserve our capital for the purpose of funding operations and we do not enter into investments for trading or speculative purposes. We believe that we do not have material exposure to high-risk investments such as mortgage-backed securities, auction rate securities or other special investment vehicles within our money-market fund investments. We believe that we do not have any material exposure to changes in fair value as a result of changes in interest rates, although the recent increase in interest rates has resulted in our unrealized loss on investments, net, as of December 31, 2022 of approximately $4.2 million and an unrealized gain on investments, net, in 2021 totaling approximately $0.9 million. We plan on holding those investments to maturity and should interest rates rise, there would be no recognition of impairment required. Declines in interest rates, however, would reduce future investment income.

Inflation Risk. Inflation generally may affect us by increasing our cost of labor, clinical trial costs, and other outsourced activities. To date, inflation has not had a material impact on our business, but if the global inflationary trends continue, we expect appreciable increases in clinical trial, selling, labor, and other operating costs. If our costs were to become subject to significant inflationary pressures, we may not be able to fully offset such higher costs through price increases of our product. Our inability or failure to do so could adversely affect our business, financial condition and results of operations.

Capital Market Risk. Although we receive product revenues from commercial sales of CAPLYTA, we continue to depend on funds raised through other sources. One possible source of funding is through further equity offerings. Our ability to raise funds in this manner depends upon capital market forces affecting our stock price.

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INTRA-CELLULAR THERAPIES, INC.

Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

Item 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were effective at the reasonable assurance level to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, as a process designed by, or under the supervision of, the Company's principal executive and principal financial officers and effected by the Company's board of directors, management and other personnel 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. The Company's internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. 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.

The Company's management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2022. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013).

Based on our assessment, management believes that, as of December 31, 2022, the Company's internal control over financial reporting is effective based on those criteria**.**

Our independent registered public accounting firm has issued an audit report on the effectiveness of our internal control over financial reporting. This report appears further below in this Item 9A.

Changes in Internal Controls

There were no changes in our internal control over financial reporting during the fourth quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Intra-Cellular Therapies, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Intra-Cellular Therapies, Inc. and subsidiary (the Company's) internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting at December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"), and our report dated March 1, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Inherent Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP
Baltimore, MD
March 1, 2023

Item 9B. OTHER INFORMATION

Not applicable.

Item 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management and Corporate Governance," "Delinquent Section 16(a) Reports," and "Code of Ethics and Business Conduct" in the Company's Proxy Statement for the 2023 Annual Meeting of Stockholders.

Item 11. EXECUTIVE COMPENSATION

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Executive Officer and Director Compensation," "Compensation Discussion and Analysis," "Management and Corporate Governance—Compensation Committee Interlocks and Insider Participation," "Compensation Committee Report" and "Risks Related to Compensation Practices and Policies" in the Company's Proxy Statement for the 2023 Annual Meeting of Stockholders. The section titled "Pay Versus Performance" in the Company's 2023 Proxy Statement is not incorporated by reference herein.

Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" in the Company's Proxy Statement for the 2023 Annual Meeting of Stockholders.

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Certain Relationships and Related Person Transactions" and "Management and Corporate Governance" in the Company's Proxy Statement for the 2023 Annual Meeting of Stockholders.

Item 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Ratification of Appointment of Independent Registered Public Accounting Firm" in the Company's Proxy Statement for the 2023 Annual Meeting of Stockholders.

PART IV

Item 15. **EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

Item 15(a). **The following documents are filed as part of this annual report on Form 10-K:**

Item 15(a)(1) and (2) See "Index to Financial Statements and Financial Statement Schedules" at Item 8 to this Annual Report on Form 10-K. Other financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.

Item 15(a)(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
2.1		Agreement and Plan of Merger, dated as of August 23, 2013, by and among the Registrant, ITI, Inc. and Intra-Cellular Therapies, Inc.		8-K (Exhibit 2.1)	8/29/2013	000-54896
2.2		Agreement and Plan of Merger, dated as of August 29, 2013, by and between the Registrant and Intra-Cellular Therapies, Inc., relating to the name change of the Registrant.		8-K (Exhibit 2.2)	9/5/2013	000-54896
3.1		Restated Certificate of Incorporation of the Registrant, as amended.		10-Q (Exhibit 3.1)	8/9/2021	001-36274
3.2		Certificate of Merger relating to the Merger of ITI, Inc. with and into Intra-Cellular Therapies, Inc., filed with the Secretary of State of the State of Delaware on August 29, 2013.		8-K (Exhibit 3.3)	9/5/2013	000-54896
3.3		Certificate of Ownership and Merger relating to the Merger of Intra-Cellular Therapies, Inc. with and into the Registrant, filed with the Secretary of State of the State of Delaware on August 29, 2013, relating to the name change of the Registrant.		8-K (Exhibit 3.4)	9/5/2013	000-54896
3.4		Restated Bylaws of the Registrant.		8-K (Exhibit 3.5)	9/5/2013	000-54896
4.1		Form of common stock certificate.		8-K (Exhibit 4.1)	9/5/2013	000-54896
4.2		Description of securities.		10-K (Exhibit 4.2)	3/1/2022	001-36274
10.1	.1	License Agreement dated as of May 31, 2005 by and between Bristol-Meyers Squibb Company and Intra-Cellular Therapies, Inc.**		8-K (Exhibit 10.1)	8/9/2022	001-36274

Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
	.2	Amendment No. 1 to License Agreement dated as of November 3, 2010 by and between Bristol-Meyers Squibb Company and Intra-Cellular Therapies, Inc.		8-K (Exhibit 10.1.2)	9/5/2013	000-54896
10.2		Supply Agreement dated as of January 5, 2023 by and between Siegfried AG and the Registrant.**	X			
10.3	.1	Master Services Agreement, effective as of January 10, 2017, by and between ITI Limited and Lonza Ltd.**		10-Q (Exhibit 10.1)	11/9/2020	001-36274
	.2	Amendment No. 1 to Master Services Agreement dated as of December 19, 2022 by and between ITI Limited and Lonza Ltd.	X			
10.4		Employment Agreement effective as of February 26, 2008 by and between Sharon Mates, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.3)	9/5/2013	000-54896
10.5	.1	Employment Agreement effective as of August 3, 2015 by and between Michael I. Halstead and Intra-Cellular Therapies, Inc.*		10-Q (Exhibit 10.1)	11/5/2015	001-36274
	.2	Amendment No. 1 to Employment Agreement dated as of November 9, 2016 by and between Michael I. Halstead and Intra-Cellular Therapies, Inc.*		10-Q (Exhibit 10.1)	11/9/2016	001-36274
10.6		Employment Agreement effective as of February 26, 2008 by and between Lawrence J. Hineline and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.4)	9/5/2013	001-36274
10.7		Employment Agreement effective as of October 15, 2018 by and between Mark Neumann and Intra-Cellular Therapies, Inc.		10-K (Exhibit 10.9)	2/27/2019	001-36274
10.8		Employment Agreement effective as of September 12, 2018 by and between Suresh Durgam, M.D. and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.8)	3/1/2022	001-36274
10.9		Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of September 1, 2003 by and between Sharon Mates, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.8)	9/5/2013	000-54896
10.10		Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of July 29, 2014 by and between Michael Halstead and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.11)	3/12/2015	001-36274

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.11	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of December 1, 2003 by and between Lawrence J. Hineline and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.9)	9/5/2013	000-54896
10.12	Employee Proprietary Information, Inventions, Inventions, and Non-Competition Agreement effective as of December 10, 2018 by and between Mark Neumann and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.16)	2/27/2019	001-36274
10.13	Employee Proprietary Information, Inventions, Inventions, and Non-Competition Agreement effective as of September 12, 2018 by and between Suresh Durgam, M.D. and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.13)	3/1/2022	001-36274
10.14	Form of Indemnification Agreement by and between the Company and its directors and executive officers.*		8-K (Exhibit 10.13)	9/5/2013	000-54896
10.15	2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.14)	9/5/2013	000-54896
10.16	Form of Stock Option Agreement under the 2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.15)	9/5/2013	000-54896
10.17	Amended and Restated 2013 Equity Incentive Plan.*		8-K (Exhibit 10.1)	6/18/2015	001-36274
10.18	Form of Stock Option Agreement under the 2013 Equity Incentive Plan.*		10-K (Exhibit 10.19)	3/25/2014	001-36274
10.19	Amended and Restated 2018 Equity Incentive Plan.*		8-K (Exhibit 10.1)	5/28/2020	001-36274
10.20	Form of Stock Option Agreement under the 2018 Equity Incentive Plan.*		8-K (Exhibit 10.2)	6/21/2018	001-36274
10.21	Form of Director Stock Option Agreement under the 2018 Equity Incentive Plan.*		8-K (Exhibit 10.3)	6/21/2018	001-36274
10.22	Form of Restricted Stock Unit Agreement under the 2018 Equity Incentive Plan.*		8-K (Exhibit 10.4)	6/21/2018	001-36274
10.23	Form of Director Restricted Stock Unit Agreement under the 2018 Equity Incentive Plan.*		8-K (Exhibit 10.5)	6/21/2018	001-36274
10.24	Form of Stock Option Agreement under the Amended and Restated 2018 Equity Incentive Plan.*		10-Q (Exhibit 10.2)	8/10/2020	001-36274

Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.25		Form of Director Stock Option Agreement under the Amended and Restated 2018 Equity Incentive Plan.*		10-Q (Exhibit 10.3)	8/10/2020	001-36274
10.26		Form of Restricted Stock Unit Agreement under the Amended and Restated 2018 Equity Incentive Plan.*		10-Q (Exhibit 10.4)	8/10/2020	001-36274
10.27		Form of Director Restricted Stock Unit Agreement under the Amended and Restated 2018 Equity Incentive Plan.*		10-Q (Exhibit 10.5)	8/10/2020	001-36274
10.28		Non-Employee Director Compensation Policy, as amended.*		10-Q (Exhibit 10.1)	5/10/2022	001-36274
10.29		Redemption Agreement dated as of August 29, 2013 by and between the Registrant and NLBDIT 2010 Services, LLC.		8-K (Exhibit 10.17)	9/5/2013	000-54896
10.30		Indemnity Agreement dated as of August 29, 2013 by and among the Registrant, Intra-Cellular Therapies, Inc. and Samir N. Masri.		8-K (Exhibit 10.18)	9/5/2013	000-54896
10.31		Registration Rights Agreement dated as of August 29, 2013 by and among Intra-Cellular Therapies, Inc., the stockholders named therein and the Registrant.		8-K (Exhibit 10.19)	9/5/2013	000-54896
10.32		Intra-Cellular Therapies, Inc. 2019 Inducement Award Plan.*		10-K (Exhibit 10.32)	3/2/2020	001-36274
10.33		Form of Restricted Stock Unit Agreement under the 2019 Inducement Award Plan.*		10-K (Exhibit 10.33)	3/2/2020	001-36274
10.34		Form of Stock Option Agreement under the 2019 Inducement Award Plan.*		10-K (Exhibit 10.34)	3/2/2020	001-36274
21.1		Subsidiaries.	X	10-K (Exhibit 21.1)		
23.1		Consent of Ernst & Young LLP.	X			
31.1		Certification of the Chief Executive Officer.	X			
31.2		Certification of the Chief Financial Officer.	X			
32.1		Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101	.INS	Inline XBRL Instance Document—the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.	X			

Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
	.SCH	Inline XBRL Taxonomy Extension Schema Document.	X			
	.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.	X			
	.DEF	Inline XBRL Taxonomy Extension Definition.	X			
	.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.	X			
	.PRE	Inline XBRL Taxonomy Presentation Linkbase Document.	X			
104		Cover Page Interactive Date File (formatted as Inline XBRL and contained in Exhibit 101).	X			

* Management contract or compensatory plan or arrangement.

** Certain confidential portions of this Exhibit were omitted by means of marking such portions with brackets ("[***]") because the identified confidential portions (i) are not material and (ii) are the type of information that the Company treats as private or confidential.

Item 16. FORM 10-K SUMMARY

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

INTRA-CELLULAR THERAPIES, INC.

Date: March 1, 2023

By: /s/ Sharon Mates, Ph.D.
Sharon Mates, Ph.D.
Chairman, President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
By: /s/ Sharon Mates, Ph.D. Sharon Mates, Ph.D.	Chairman, President and Chief Executive Officer (principal executive officer)	March 1, 2023
By: /s/ Lawrence J. Hineline Lawrence J. Hineline	Senior Vice President of Finance and Chief Financial Officer (principal financial officer and principal accounting officer)	March 1, 2023
By: /s/ Joel S. Marcus Joel S. Marcus	Director	March 1, 2023
By: /s/ Rory B. Riggs Rory B. Riggs	Director	March 1, 2023
By: /s/ E. Rene Salas E. Rene Salas	Director	March 1, 2023
By: /s/ Robert L. Van Nostrand Robert L. Van Nostrand	Director	March 1, 2023

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Intra-Cellular Therapies, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Intra-Cellular Therapies, Inc. and its subsidiary (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2022, 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 at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 1, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the 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 financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

Responsibilities of Management for the Financial Statements

Management is responsible for the preparation and fair presentation of the financial statements in accordance with accounting principles generally accepted in the United States of America, and for the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of financial statements that are free of material misstatement, whether due to fraud or error.

In preparing the financial statements, management is required to evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern for one year after the date that the financial statements are available to be issued.

Critical Audit Matter

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 our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Clinical trial expenses

Description of the Matter	As described in Note 2 to the consolidated financial statements, at each consolidated balance sheet date, the Company recognizes research and development expenses, which include clinical trials, as the services are incurred. When recording the estimate of clinical trial costs incurred, the Company is required to evaluate the progress toward completion of contractually agreed upon tasks using subject enrollment, clinical site activations and other information provided to the Company by vendors. Since billings under the contracts with third parties may not coincide with costs incurred to date, the Company must apply significant judgment to determine the estimated expense and related balance sheet positions at period end. Our principal consideration in evaluating this as a critical audit matter focused on the phase 3 studies due to the significant contractual obligations and the high degree of subjectivity and estimation required of management to determine the progress towards completion of specific tasks.
How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls over the Company's estimation of the clinical trial expenses, including the process of estimating the expenses incurred to date based on the progress of the phase 3 clinical trials. For example, we observed management's key review control which included quarterly interviews with Contract Research Organizations (CROs) and subsequent documentation which provided support for management's estimate of progress toward completion. We also tested controls over management's review of the clinical trial expense calculation including controls over the completeness and accuracy of data inputs. To test the clinical trial expense, we performed procedures that included, among others: 1) read each agreement and change order with the principal vendors supporting the phase 3 clinical study, 2) evaluated the significant assumptions related to enrollment, patient costs and other components of the study budget used to develop the clinical trial expense estimates and calculated the amounts that were accrued or prepaid at the balance sheet date, 3) tested the completeness and accuracy of invoicing activity associated with the Company's contractual obligations, 4) confirmed with the CRO the work orders, change orders, enrollment data and invoicing activity included in management's calculation, 5) assessed the historical accuracy of estimates previously made by management.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2002.
Baltimore, Maryland
March 1, 2023

Intra-Cellular Therapies, Inc. and Subsidiary

Consolidated Balance Sheets (in thousands except share and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	**$ 148,615**	$ 92,365
Investment securities, available-for-sale	**443,290**	319,968
Restricted cash	**1,750**	1,400
Accounts receivable, net	**75,189**	20,156
Inventory	**23,920**	7,948
Prepaid expenses and other current assets	**45,193**	25,444
Total current assets	**737,957**	467,281
Property and equipment, net	**1,913**	1,791
Right of use assets, net	**14,824**	20,764
Other assets	**86**	86
Total assets	**$ 754,780**	$ 489,922
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	**$ 10,395**	$ 8,691
Accrued and other current liabilities	**19,657**	11,073
Accrued customer programs	**25,621**	5,964
Accrued employee benefits	**22,996**	20,897
Operating lease liabilities	**4,567**	6,732
Total current liabilities	**83,236**	53,357
Operating lease liabilities, non-current,	**15,474**	18,675
Total liabilities	**98,710**	72,032
Stockholders' equity:		
Common stock, $0.0001 par value: 175,000,000 shares authorized at December 31, 2022 and December 31, 2021, respectively; 94,829,794 and 81,886,965 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	**9**	8
Additional paid-in capital	**2,137,737**	1,639,476
Accumulated deficit	**(1,477,486)**	(1,221,230)
Accumulated comprehensive loss	**(4,190)**	(364)
Total stockholders' equity	**656,070**	417,890
Total liabilities and stockholders' equity	**$ 754,780**	$ 489,922

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc. and Subsidiary

Consolidated Statements of Operations (in thousands except share and per share amounts)

	Years Ended December 31, 2022	2021	2020
Revenues			
Product sales, net	**$ 249,132**	$ 81,708	$ 22,531
Grant revenue	**1,182**	2,095	282
Total revenues, net	**250,314**	83,803	22,813
Operating expenses:			
Cost of product sales	**20,443**	8,035	1,895
Selling, general and administrative	**358,782**	272,611	186,364
Research and development	**134,715**	88,845	65,782
Total operating expenses	**513,940**	369,491	254,041
Loss from operations	**(263,626)**	(285,688)	(231,228)
Interest income	**7,376**	1,568	4,236
Loss before provision for income taxes	**(256,250)**	(284,120)	(226,992)
Income tax expense	**(6)**	(6)	(14)
Net loss	**$ (256,256)**	$ (284,126)	$ (227,006)
Net loss per common share:			
Basic & Diluted	**$ (2.72)**	$ (3.50)	$ (3.23)
Weighted average number of common shares:			
Basic & Diluted	**94,046,670**	81,253,394	70,364,800

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc. and Subsidiary

Consolidated Statements of Comprehensive Loss (in thousands)

	Years Ended December 31,		
	2022	**2021**	**2020**
Net loss	**$(256,256)**	$(284,126)	$(227,006)
Other comprehensive loss:			
Unrealized (loss) gain on investment securities	**(3,826)**	(845)	353
Comprehensive loss	**$(260,082)**	$(284,971)	$(226,653)

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc. and Subsidiary

Consolidated Statements of Stockholders' Equity (in thousands except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	55,507,497	$ 6	$ 904,971	$ (710,098)	$ 128	$ 195,007
Common shares issued	23,409,458	2	652,710	—	—	652,712
Exercise of stock options and issuances of restricted stock	1,536,797	—	11,465	—	—	11,465
Stock issued for services	9,337	—	214	—	—	214
Share-based compensation	—	—	24,115	—	—	24,115
Net loss	—	—	—	(227,006)	—	(227,006)
Other comprehensive income	—	—	—	—	353	353
Balance at December 31, 2020	80,463,089	$ 8	$1,593,475	$ (937,104)	$ 481	$ 656,860
Exercise of stock options and issuances of restricted stock	**1,419,331**	**—**	**11,519**	**—**	**—**	**11,519**
Stock issued for services	**4,545**	**—**	**179**	**—**	**—**	**179**
Share-based compensation	**—**	**—**	**34,303**	**—**	**—**	**34,303**
Net loss	**—**	**—**	**—**	**(284,126)**	**—**	**(284,126)**
Other comprehensive loss	**—**	**—**	**—**	**—**	**(845)**	**(845)**
Balance at December 31, 2021	**81,886,965**	**$ 8**	**$1,639,476**	**$(1,221,230)**	**$ (364)**	**$ 417,890**
Common shares issued January 7, 2022	**10,952,381**	**1**	**433,717**	**—**	**—**	**433,718**
Exercise of stock options and issuances of restricted stock	**1,988,775**	**—**	**21,441**	**—**	**—**	**21,441**
Stock issued for services	**1,673**	**—**	**90**	**—**	**—**	**90**
Share-based compensation	**—**	**—**	**43,013**	**—**	**—**	**43,013**
Net loss	**—**	**—**	**—**	**(256,256)**	**—**	**(256,256)**
Other comprehensive loss	**—**	**—**	**—**	**—**	**(3,826)**	**(3,826)**
Balance at December 31, 2022	**94,829,794**	**$ 9**	**$2,137,737**	**$(1,477,486)**	**$(4,190)**	**$ 656,070**

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc. and Subsidiary

Consolidated Statements of Cash Flows (in thousands)

	Years Ended December 31,		
	2022	2021	2020
Cash flows used in operating activities			
Net loss	**$(256,256)**	$(284,126)	$(227,006)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	**656**	533	528
Share-based compensation	**43,013**	34,303	24,115
Stock issued for services	**90**	179	214
Amortization of premiums and accretion of discounts on investment securities, net	**447**	(4,080)	(648)
Changes in operating assets and liabilities:			
Accounts receivable, net	**(55,033)**	(9,391)	(10,765)
Inventory	**(15,972)**	(892)	(7,056)
Prepaid expenses and other assets	**(19,749)**	(11,208)	(7,922)
Long term deferred tax asset, net	**—**	—	265
Accounts payable	**1,704**	3,189	(1,923)
Accrued and other current liabilities	**8,584**	3,177	(8,242)
Accrued customer programs	**19,657**	2,958	5,435
Accrued employee benefits	**2,099**	5,989	3,005
Lease liabilities, net	**574**	(175)	(73)
Net cash used in operating activities	**(270,186)**	(259,544)	(230,073)
Cash flows (used in) provided by investing activities			
Purchases of investments	**(759,209)**	(224,575)	(755,629)
Maturities of investments	**631,614**	505,244	275,601
Purchases of property and equipment	**(778)**	(325)	(267)
Net cash (used in) provided by investing activities	**(128,373)**	280,344	(480,295)
Cash flows provided by financing activities			
Proceeds of public offerings, net	**433,718**	—	652,712
Proceeds from exercise of stock options	**21,441**	11,519	11,465
Net cash provided by financing activities	**455,159**	11,519	664,177
Net increase (decrease) in cash, cash equivalents, and restricted cash	**56,600**	32,319	(46,191)
Cash, cash equivalents, and restricted cash at beginning of period	**93,765**	61,446	107,637
Cash, cash equivalents, and restricted cash at end of period	**$ 150,365**	$ 93,765	$ 61,446
Cash paid for taxes	**$ 6**	$ 6	$ 2
Non-cash investing and financing activities			
Right of use assets under operating leases	**$ 419**	$ 108	$ 8,918

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statements of cash flows:

Cash and cash equivalents	**$ 148,615**	$ 92,365	$ 60,046
Restricted cash	**1,750**	1,400	1,400
Total cash, cash equivalents and restricted cash	**$ 150,365**	$ 93,765	$ 61,446

See accompanying notes to consolidated financial statements.

1. Organization

Intra-Cellular Therapies, Inc. (the "Company"), through its wholly-owned operating subsidiary, ITI, Inc. ("ITI"), is a biopharmaceutical company focused on the discovery, clinical development and commercialization of innovative, small molecule drugs that address underserved medical needs primarily in neuropsychiatric and neurological disorders by targeting intracellular signaling mechanisms within the central nervous system. In December 2019, CAPLYTA® (lumateperone) was approved by the U.S. Food and Drug Administration ("FDA") for the treatment of schizophrenia in adults (42mg/day) and the Company initiated the commercial launch of CAPLYTA in March 2020. In December 2021, CAPLYTA was approved by the FDA for the treatment of bipolar depression in adults (42mg/day). The Company initiated the commercial launch of CAPLYTA for the treatment of bipolar depression in December 2021. Additionally, in April 2022, the FDA approved two new dosage strengths of CAPLYTA, 10.5 mg and 21 mg capsules, to provide dosage recommendations for patients concomitantly taking strong or moderate CYP3A4 inhibitors, and 21 mg for patients with moderate or severe hepatic impairment (Child-Pugh class B or C). The commercial launch of these special population doses occurred in August 2022. As used in these Notes to Consolidated Financial Statements, "CAPLYTA" refers to lumateperone approved by the FDA for the treatment of schizophrenia in adults and bipolar depression in adults, and "lumateperone" refers to, where applicable, CAPLYTA as well as lumateperone for the treatment of indications beyond schizophrenia and bipolar depression. Lumateperone is in Phase 3 clinical development as a novel treatment for major depressive disorder.

On January 7, 2022, the Company completed a public offering of common stock in which the Company sold 10,952,381 shares of common stock at a public offering price of $42.00 per share for aggregate gross proceeds of $460.0 million. After deducting underwriting discounts, commissions and offering expenses, the net proceeds to the Company were approximately $433.7 million. In order to further its commercial activities and research projects and support its collaborations, the Company may require additional financing until such time, if ever, that revenue streams are sufficient to generate consistent positive cash flow from operations. The Company currently projects that its cash, cash equivalents and investments will be sufficient to fund operating expenses and capital expenditures for at least one year from the date that these financial statements are filed with the Securities and Exchange Commission (the "SEC"). Possible sources of funds include public or private sales of the Company's equity securities, sales of debt or convertible debt securities, the incurrence of debt from commercial lenders, strategic collaborations, licensing a portion or all of the Company's products, product candidates and technology and, to a much lesser extent, grant funding.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements of Intra-Cellular Therapies, Inc. and its wholly own subsidiary have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States GAAP set forth in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB"). All intercompany accounts and transactions have been eliminated in consolidation. The Company currently operates in one operating segment. Operating segments are defined as components of an enterprise about which separate discrete information is available for the chief operating decision maker, or decision making group, in deciding how to allocate resources and assessing performance. The Company views its operations and manages its business in one segment, which is discovering, developing, and commercializing drugs primarily for the treatment of neurological and psychiatric disorders.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Although actual results could differ from those estimates, management does not believe that such differences would be material.

Reclassifications

Certain amounts reported in prior periods have been reclassified to conform to current period financial statement presentation. These reclassifications have no material effect on previously reported financial position, cash flows, or results of operations.

Cash and Cash Equivalents

The Company considers all highly liquid investments with a maturity of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents consist of checking accounts, money market accounts, money market mutual funds, and certificates of deposit with a maturity date of three months or less. The carrying values of cash and cash equivalents approximate the fair market value. Certificates of deposit, commercial paper, corporate notes and corporate bonds with a maturity date of more than three months are classified separately on the consolidated balance sheets.

Investment Securities

Investment securities may consist of investments in U.S. Treasuries, various U.S. governmental agency debt securities, corporate bonds, certificates of deposit, and other fixed income securities with an average maturity of approximately twelve months or less. Management classifies the Company's investments as available-for-sale. Such securities are carried at estimated fair value, with any unrealized holding gains or losses reported, net of any tax effects reported, as accumulated other comprehensive loss, which is a separate component of stockholders' equity. Realized gains and losses and declines in value judged to be other-than-temporary, if any, are included in consolidated results of operations. A decline in the market value of any available-for-sale security below cost that is deemed to be other-than-temporary results in a reduction in fair value, which is charged to earnings in that period, and a new cost basis for the security is established. Dividend and interest income are recognized as interest income on the consolidated statements of operations when earned. The cost of securities sold is calculated using the specific identification method.

The Company monitors its investment portfolio for overall risk, specifically credit loss, quarterly or more frequently if circumstances warrant. The Company has estimated the expected credit loss over the lifetime of the asset and has determined an allowance for credit losses is not material with respect to the investment portfolio.

Fair Value Measurements

The Company applies the fair value method under ASC Topic 820, *Fair Value Measurements and Disclosures*. ASC Topic 820 defines fair value, establishes a fair value hierarchy for assets and liabilities measured at fair value and requires expanded disclosures about fair value measurements. The ASC Topic 820 hierarchy ranks the quality and reliability of inputs, or assumptions, used in the determination of fair value and requires assets and liabilities carried at fair value to be classified and disclosed in one of the following categories based on the lowest level input used that is significant to a particular fair value measurement:

- Level 1—Fair value is determined by using unadjusted quoted prices that are available in active markets for identical assets and liabilities.
- Level 2—Fair value is determined by using inputs other than Level 1 quoted prices that are directly or indirectly observable. Inputs can include quoted prices for similar assets and liabilities in active

markets or quoted prices for identical assets and liabilities in inactive markets. Related inputs can also include those used in valuation or other pricing models, such as interest rates and yield curves that can be corroborated by observable market data.

- Level 3—Fair value is determined by inputs that are unobservable and not corroborated by market data. Use of these inputs involves significant and subjective judgments to be made by a reporting entity—e.g., determining an appropriate adjustment to a discount factor for illiquidity associated with a given security.

The Company evaluates financial assets and liabilities subject to fair value measurements on a recurring basis to determine the appropriate level at which to classify them each reporting period. This determination requires the Company to make subjective judgments as to the significance of inputs used in determining fair value and where such inputs lie within the ASC Topic 820 hierarchy.

Financial Instruments

The Company considers the recorded costs of its financial assets and liabilities, which consist of cash equivalents, restricted cash, accounts receivable, prepaid expenses, right of use asset, net, other assets, accounts payable, accrued liabilities, accrued employee benefits, and operating lease liabilities, current, to approximate their fair value because of their relatively short maturities at December 31, 2022 and 2021. Management believes that the risks associated with the Company's financial instruments are minimal as the counterparties are various corporations, financial institutions and government agencies of high credit standing.

Restricted Cash

Restricted cash is collateral used under the letter of credit arrangement for the Company's vehicle lease agreement (see Note 7). The Company adopted ASU No. 2016-18, "Restricted Cash" ("ASU 2016-18") and now includes restricted cash balances within the cash, cash equivalents and restricted cash balance on the statement of cash flows.

Accounts Receivable, net

The Company's accounts receivable, net, primarily arise from product sales. They are generally stated at the invoiced amount and do not bear interest. Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result primarily from chargebacks, prompt pay discounts, and distribution fees. All customers have standard payment terms which generally require payment within 60 days.

The Company monitors the financial performance and creditworthiness of its customers so that it can properly assess and respond to changes in the customers' credit profiles. The Company reserves against accounts receivable for estimated losses that may arise from a Customer's inability to pay and any amounts determined to be uncollectible are written off against the reserve when it is probable that the receivable will not be collected. The reserve amount for estimated collectability losses was not significant as of December 31, 2022 and 2021.

We are also subject to credit risk from our accounts receivable related to our product sales. We monitor our exposure within accounts receivable and record a credit loss reserve against uncollectible accounts receivable as necessary. We extend credit primarily to pharmaceutical wholesale distributors. Customer creditworthiness is monitored and collateral is not required. Historically, we have not experienced credit losses on our accounts receivable. As of December 31, 2022 and 2021, our credit loss reserve on receivables was not significant.

Concentration of Credit Risk

Financial instruments which potentially subject the Company to concentrations of credit risk consist of accounts receivable, net from customers and cash, cash equivalent and investments held at financial institutions. For the years ended December 31, 2022 and 2021, 97% and 96% of product sales were generated from three major industry wholesalers, respectively.

Three individual customers accounted for approximately 39%, 30%, and 28% and 40%, 28%, and 28% of product sales for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, the Company believes that these customers are of high credit quality.

Cash equivalents are held with major financial institutions in the United States. Certificates of deposit, cash and cash equivalents held with banks may exceed the amount of insurance provided on such deposits. Generally, these deposits may be redeemed upon demand and, therefore, bear minimal risk.

Inventory

The Company values its inventories at the lower of cost or estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out ("FIFO") basis. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated net realizable value in the period in which the impairment is first identified. Such impairment charges, if they occur, are recorded within cost of product sales.

The Company capitalizes inventory costs associated with the Company's products after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory acquired and manufactured prior to receipt of regulatory approval of a product candidate is expensed as research and development expense as incurred. Inventory that can be used in either the production of clinical or commercial product is expensed as research and development expense when selected for use in a clinical manufacturing campaign. Inventory that is used in the production of sample product is reclassified to prepaid and other current assets and is then expensed to selling, general and administrative expenses when the sample product is distributed.

Shipping and handling costs for product shipments to customers are recorded as part of cost of product sales along with costs associated with manufacturing the product, and any inventory write-downs.

Property and Equipment

Property and equipment is stated at cost and depreciated on a straight-line basis over estimated useful lives ranging from three to five years. Leasehold improvements are amortized using the straight-line method over the shorter of the estimated useful life of the assets or the term of the related lease. Expenditures for maintenance and repairs are charged to operations as incurred.

When indicators of possible impairment are identified, the Company evaluates the recoverability of the carrying value of its long-lived assets based on the criteria established in ASC Topic No. 360, *Property, Plant and Equipment*. The Company considers historical performance and anticipated future results in its evaluation of potential impairment. The Company evaluates the carrying value of those assets in relation to the operating performance of the business and undiscounted cash flows expected to result from the use of those assets. Impairment losses are recognized when carrying value exceeds the undiscounted cash flows, in which case management must determine the fair value of the underlying asset. No such impairment losses have been recognized to date.

Leases

In accordance with ASC 842, the Company elected the package of practical expedients, which permit the Company not to reassess under the new standard the historical lease classification. The Company made an accounting policy election to keep leases with an initial term of 12 months or less off of the consolidated balance sheets. The Company also elected the lessee component election, allowing the Company to account for the lease and non-lease components as a single lease component.

To determine whether a contract contains a lease, asset and service agreements are assessed at onset and upon modification for criteria of specifically identified assets, control and economic benefit. Payments for identified leases are recognized in the consolidated statements of operations on a straight-line basis over the lease term. The Company uses the rate implicit in the contract whenever possible when determining the applicable discount rate. As the majority of the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of lease payments.

Revenue Recognition

In accordance with ASC Topic 606, the Company recognizes revenue when the customer obtains control of a promised good or service, in an amount that reflects the consideration that the Company expects to receive in exchange for the good or service. The reported results for the years ended December 31, 2022 and 2021 reflect the application of ASC Topic 606.

To determine revenue recognition for arrangements that the Company determines are within the scope of ASC Topic 606, the Company performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to arrangements that meet the definition of a contract under ASC Topic 606, including when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For additional discussion of accounting for product sales, see *Product Sales, net* (below).

To date, the Company's only source of product sales has been from sales of CAPLYTA in the United States, which the Company began shipping to customers in March 2020.

Product Sales, net

The Company sells CAPLYTA to a limited number of customers which include a number of national and select regional distributors. These customers subsequently resell the Company's products to specialty pharmacy providers, as well as other retail pharmacies and certain medical centers or hospitals. In addition to distribution agreements with customers, the Company enters into arrangements with health care providers and payers that provide for government mandated and/or privately negotiated rebates, chargebacks, and discounts with respect to the purchase of the Company's products. The Company recognizes revenue on product sales when the customer obtains control of the Company's product, which occurs at a point in time (upon delivery). Product revenues are recorded net of applicable reserves for variable consideration, including rebates, discounts and allowances, among others. If taxes should be collected from customers relating to product sales and remitted to governmental authorities, they will be excluded from revenue.

Reserves for Variable Consideration

Revenues are calculated based on the wholesale acquisition cost that the Company charges to distributors for CAPLYTA less variable consideration for which reserves are established. Components of variable consideration may include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payer rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between the Company and its customers, payers, and other indirect customers relating to the Company's sales of its product.

These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, include the Company's best estimates that take into consideration a range of possible outcomes which are considered more likely in accordance with the expected value method in ASC Topic 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, and forecasted customer buying and payment patterns. The Company's estimates utilizing payer mix are based on CAPLYTA's actual channel mix in 2022. The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. The Company's analyses also contemplated application of the constraint in accordance with the guidance, under which it determined it was probable that a significant reversal of revenue would not occur in a future period for the estimates detailed below as of December 31, 2022 and 2021, therefore, the transaction price was not reduced further during the years ended December 31, 2022 and 2021. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product sales and earnings in the period such variances become known.

Trade Discounts and Allowances— The Company generally provides customers with discounts which include incentive fees that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company compensates (through trade discounts and allowances) its customers for sales order management, data, and distribution services. However, the Company has determined such services received to date are not distinct from the Company's sale of products to the Customer and, therefore, these payments have been recorded as a reduction of product sales, net within the consolidated statements of operations for the years ended December 31, 2022 and 2021, as well as a reduction to accounts receivable, net on the consolidated balance sheets.

Product Returns— Consistent with industry practice, the Company generally offers customers a limited right of return for product that has been purchased from the Company based on the product's expiration date, which lapses upon shipment to a patient. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as accrued expenses and other current liabilities on the consolidated balance sheets. The Company currently estimates product return liabilities using available industry data and its own sales information, including its visibility into the inventory remaining in the distribution channel. The Company has not received significant expired product returns to date.

Provider Chargebacks and Discounts— Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who purchase the product directly from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable, net. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and the Company generally issues credits for such amounts within a few weeks of the customer's notification to the Company of the resale. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at each reporting period-end that the Company expects will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit.

Government Rebates— The Company is subject to discount obligations under state Medicaid and Medicare programs. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability

under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Payer Rebates— The Company contracts with certain private payer organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its product. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability recorded as an accrued expenses and other current liabilities on the consolidated balance sheets.

Other Incentives— Other incentives which the Company offers include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payers. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue but remains in the distribution channel inventories at the end of each reporting period. The Company also has a voucher program whereby a patient can receive a prescription at no cost and whereby the Company reimburses the pharmacy for 100% of the sales price of the prescription. The Company applies the claims for vouchers for product that is in the distribution channel and reduces recognized revenue accordingly.

The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

Chargebacks, discounts, fees, and returns are recorded as reductions of trade receivables, net on the consolidated balance sheets. Government and other rebates are recorded as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

Cost of Product Sales

Our cost of product sales relates to sales of CAPLYTA. Cost of product sales primarily includes product royalty fees, overhead, and direct costs (inclusive of material, shipping, and manufacturing costs).

For the product royalty fees, the Company entered into an exclusive License Agreement with Bristol-Myers Squibb Company ("BMS"), for which the Company is obliged to make tiered single digit percentage royalty payments ranging between 5-9% on sales of licensed products. The related royalties are recorded within cost of product sales on the statement of operations.

Prior to the FDA approval of CAPLYTA, the Company expensed all costs associated with the manufacturing of lumateperone as part of research and development expenses. The cost of product sales in the years ended December 31, 2022, 2021 and 2020 are lower than incurred because of previously expensed inventory.

Research and Development, Including Clinical Trial Expenses

The Company recognizes its research and development expenses as the services are incurred. Research and development costs primarily consist of salaries and related expenses for personnel and resources and the costs of clinical trials. Other research and development expenses include nonclinical analytical testing, manufacturing of drug product for use in clinical and nonclinical trials, outside services, providers, materials and consulting fees.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to the Company by its vendors, among other factors with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

As part of the process of preparing its financial statements, the Company is required to estimate its expenses resulting from its obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company's objective is to reflect the appropriate clinical trial expenses in its financial statements by matching those expenses with the period in which services are performed and efforts are expended. The Company accounts for these expenses according to the progress of the clinical trial as measured by subject progression and the timing of various aspects of the trial. The Company determines accrual estimates through financial models taking into account various clinical information provided by vendors and discussion with applicable personnel and external service providers as to the progress or state of consummation of trials, or the services completed. During the course of a clinical trial, the Company adjusts its clinical expense recognition if actual results differ from its estimates. The Company makes estimates of its accrued expenses as of each balance sheet date based on the facts and circumstances known to it at that time. The Company's clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations, clinical sites and other third-party vendors. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in it reporting amounts that are too high or too low for any particular period.

Advertising Expense

Advertising costs are expensed when services are rendered. The Company incurred $85.8 million, $82.5 million and $36.3 million in advertising costs during the years ended December 31, 2022, 2021, and 2020, respectively, related to its marketed product, CAPLYTA.

Income Taxes

Income taxes are accounted for using the liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the year in which those temporary differences are expected to be recovered or settled.

The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Valuation allowances are established when necessary to reduce net deferred tax assets to the amount expected to be realized. Income tax expense is the tax payable for the period and the change during the period in deferred tax assets and liabilities. The Company accounts for uncertain tax positions pursuant to ASC Topic 740, *Income Taxes*. Financial statement recognition of a tax position taken or expected to be taken in a tax return is determined based on a more-likely-than-not threshold of that position being sustained. If the tax position meets this threshold, the benefit to be recognized is measured as the tax benefit having the highest likelihood of being realized upon ultimate settlement with the taxing authority. The Company recognizes interest accrued related to unrecognized tax benefits and penalties in the provision for income taxes.

The Company's effective tax rate for the years ended December 31, 2022, 2021 and 2020 was approximately 0%. This effective tax rate is substantially lower than the U.S. statutory rate of 21% due to valuation allowances recorded on current year losses where the Company is not more likely than not to recognize a future tax benefit.

On March 27, 2020, the United States enacted The Coronavirus Aid, Relief and Economic Security ("CARES") Act which includes several significant business tax provisions, of which the immediate relevance to the Company is the acceleration of refunds of previously generated corporate Alternative Minimum Tax ("AMT") credits. The CARES Act also adds an employee retention credit to encourage employers to maintain headcounts even if employees cannot report to work because of issues related to the coronavirus, and a temporary provision allowing companies to defer remitting to the government the employee share of some payroll taxes, among other things. On August 9, 2022, the United States enacted the CHIPS and Science Act which provides an investment tax credit for 25% of qualified investments primarily used for manufacturing of semiconductors and related equipment in the U.S. On August 16, 2022, the United States enacted the Inflation Reduction Act ("IRA") which includes a provision for a 15% corporate alternative minimum tax on companies with average annual adjusted financial statement income over $1 billion effective for tax years ending after December 31, 2022. The Company reviewed the provisions and there was not a material tax impact on its financial statements for the year ended December 31, 2022.

On December 31, 2022, ITI Limited, our wholly-owned Bermuda subsidiary, was merged into Intra-Cellular Therapies, Inc., a Delaware corporation. The intellectual property rights associated with lumateperone were transferred to the Delaware corporation as a result of this merger. This merger and the subsequent liquidation of ITI Limited does not have any material impact from a U.S. or Bermuda income tax perspective.

Comprehensive Loss

All components of comprehensive loss, including net loss, are reported in the financial statements in the period in which they are incurred. Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. In accordance with accounting guidance, the Company presents the impact of any unrealized gains or losses on its investment securities in a separate statement of comprehensive loss for each period.

Share-Based Compensation

Share-based payments are accounted for in accordance with the provisions of ASC Topic 718, *Compensation—Stock Compensation*. The fair value of share-based payments related to stock options is estimated, on the date of grant, using the Black-Scholes-Merton option-pricing model (the "Black-Scholes Model"). The resulting fair value is recognized ratably over the requisite service period, which is generally the vesting period of the option.

For all awards granted with time-based vesting conditions, expense is amortized using the straight-line attribution method. Share-based compensation expense recognized in the statements of operations for the years ended December 31, 2022, 2021 and 2020 accounts for forfeitures as they occur.

The Company utilizes the Black-Scholes Model for estimating fair value of its stock options granted. Option valuation models, including the Black-Scholes Model, require the input of subjective assumptions, and changes in the assumptions used can materially affect the grant date fair value of an award. These assumptions include the risk-free rate of interest, expected dividend yield, expected volatility and the expected life of the award.

The expected volatility rates are based entirely on the historical volatility of the Company's common stock. The expected life of stock options is the period of time for which the stock options are expected to be outstanding. Given the limited historical exercise data, the expected life is determined using the "simplified method," which defines expected life as the midpoint between the vesting date and the end of the contractual term.

The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. The Company has not paid dividends to its stockholders since its inception and does not plan to pay cash dividends in the foreseeable future. Therefore, the Company has assumed an expected dividend rate of zero. For stock options granted, the exercise price was determined by using the closing market price of the Company's common stock on the date of grant.

A restricted stock unit ("RSU") is a stock award that entitles the holder to receive shares of the Company's common stock as the award vests. The fair value of each RSU is based on the fair market value of the Company's common stock on the date of grant. In each fiscal year beginning in 2016, the Company has granted RSUs that vest in three equal annual installments provided that the employee remains employed with the Company. In each fiscal year beginning in 2020, the Company has granted select employees performance based RSUs which vest upon the Board's approval at the end of the three year service period based on the achievement of select clinical development performance milestones and comparative shareholder returns against the Company's peers.

Under ASC Topic 718, the cumulative amount of compensation cost recognized for instruments classified as equity that ordinarily would result in a future tax deduction under existing tax law is considered to be a deductible difference in applying ASC Topic 740, *Income Taxes*. The deductible temporary difference is based on the compensation cost recognized for financial reporting purposes; however, these provisions currently do not impact the Company, as all the deferred tax assets have a full valuation allowance.

Equity instruments issued to non-employees for services are accounted for under the provisions of ASC Topic 718 and ASC Topic 505-50, *Equity/Equity-Based Payments to Non-Employees*. Accordingly, the estimated fair value of the equity instrument is recorded on the earlier of the performance commitment date or the date the required services are completed and are marked to market during the service period.

In 2020, the Company's stockholders approved the Company's 2018 Amended and Restated Equity Incentive Plan (the "Amended 2018 Plan") pursuant to which 6,500,000 additional shares of common stock were reserved for future equity grants. In December 2019, the Company adopted the 2019 Inducement Award Plan (the "2019 Inducement Plan") for the grant of equity awards of up to 1,000,000 shares of common stock to newly hired employees.

Loss Per Share

Basic net loss per common share is determined by dividing the net loss by the weighted-average number of common shares outstanding during the period, without consideration of common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of common stock equivalents outstanding for the period. The treasury stock method is used to determine the dilutive effect of the Company's stock option grants and RSUs.

Recently Issued Accounting Standards

The Company considers the applicability and impact of any recent ASU issued by the FASB. Based on our assessment, there are no recent accounting pronouncements that have or are expected to have a material impact on the Company's consolidated financial statements or related disclosures.

3. Investment Securities

Investment securities consisted of the following (in thousands):

	December 31, 2022			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
U.S. Government Agency Securities	$188,465	$ 14	$(1,729)	$186,750
FDIC Certificates of Deposit	4,155	3	(72)	4,086
Certificates of Deposit	7,500	—	—	7,500
Commercial Paper	100,711	3	(269)	100,445
Corporate Notes/Bonds	189,588	1	(2,141)	187,448
	$490,419	**$ 21**	**$(4,211)**	**$486,229**

	December 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
U.S. Government Agency Securities	$ 71,752	$ —	$(100)	$ 71,652
Certificates of Deposit	26,232	1	—	26,233
Commercial Paper	55,955	—	(36)	55,919
Corporate Notes/Bonds	166,394	19	(249)	166,164
	$320,333	**$ 20**	**$(385)**	**$319,968**

The Company has classified all of its investment securities as available-for-sale, including those with maturities beyond one year, as current assets on the consolidated balance sheets based on the highly liquid nature of the investment securities and because these investment securities are considered available for use in current operations. As of December 31, 2022 and 2021, the Company held $71.5 million and $67.2 million, respectively, of available-for-sale investment securities with contractual maturity dates more than one year and less than two years, with the remainder of the available-for-sale investment securities having contractual maturity dates less than one year.

The aggregate related fair value of investments with unrealized losses as of December 31, 2022 was $438.3 million, which consisted of $153.1 million from U.S. government agency securities, $3.1 million of certificates of deposit, $96.6 million of commercial paper, and $185.5 million of corporate notes/bonds. $49.1 million of the aggregate fair value of investments with unrealized losses as of December 31, 2022 has been held in a continuous unrealized loss position for over than 12 months, with the remaining $389.2 million held in a continuous unrealized loss position for less than 12 months. As of December 31, 2022, $14.9 million of the commercial paper balance, $20.5 million of the U.S. Government Agency Securities balance, and $7.5 million of the certificates of deposit balance are listed as cash equivalents. As of December 31, 2021, the aggregate related fair value of investments with unrealized losses was $263.5 million. $9.5 million of the aggregate fair value of investments with unrealized losses as of December 31, 2021 has been held in a continuous unrealized loss position for over than 12 months, with the remaining $254.1 million held in a continuous unrealized loss position for less than 12 months.

The Company reviewed all of the investments which were in a loss position at the respective balance sheet dates, as well as the remainder of the portfolio. The Company has analyzed the unrealized losses and determined that market conditions were the primary factor driving these changes. After analyzing the securities in an unrealized loss position, the portion of these losses that relate to changes in credit quality is insignificant. The Company does not intend to sell these securities, nor is it more likely than not that the Company will be required to sell them prior to the end of their contractual terms. Furthermore, the Company does not believe that these securities expose the Company to undue market risk or counterparty credit risk.

4. Fair Value Measurements

The Company has no assets or liabilities that were measured for significant unobservable inputs (Level 3 assets and liabilities) as of December 31, 2022 and 2021. The carrying value of cash held in money market funds of approximately $12.2 million as of December 31, 2022 and $56.5 million as of December 31, 2021 is included in cash and cash equivalents and approximates market value based on quoted market price or Level 1 inputs. The carrying value of cash held in commercial paper of approximately $14.9 million, U.S. Government Agency Securities of $20.5 million, and certificates of deposit of $7.5 million as of December 31, 2022 are included in cash and cash equivalents. The carrying value of cash held in investment securities of $0 as of December 31, 2021 is included in cash and cash equivalents.

The fair value measurements of the Company's cash equivalents and available-for-sale investment securities are identified in the following tables (in thousands):

		Fair Value Measurements at Reporting Date Using		
	December 31, 2022	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money Market Funds	$ 12,203	$12,203	$ —	$ —
U.S. Government Agency Securities	186,750	—	186,750	—
FDIC Certificates of Deposit	4,086	—	4,086	—
Certificates of Deposit	7,500	—	7,500	—
Commercial Paper	100,445	—	100,445	—
Corporate Notes/Bonds	187,448	—	187,448	—
	$498,432	**$12,203**	**$486,229**	**$ —**

		Fair Value Measurements at Reporting Date Using		
	December 31, 2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money Market Funds	$ 56,539	$56,539	$ —	$ —
U.S. Government Agency Securities	71,652	—	71,652	—
Certificates of Deposit	26,233	—	26,233	—
Commercial Paper	55,919	—	55,919	—
Corporate Notes/Bonds	166,164	—	166,164	—
	$376,507	**$56,539**	**$319,968**	**$ —**

5. Inventory

Inventory consists of the following (in thousands):

	December 31, 2022	December 31, 2021
Raw materials	**$17,227**	$2,484
Work in process	**2,594**	2,407
Finished goods	**4,099**	3,057
	$23,920	$7,948

6. Property and Equipment

Property and equipment consist of the following (in thousands):

	December 31, 2022	December 31, 2021
Computer equipment	**$ 409**	$ 409
Furniture and fixtures	**423**	423
Scientific equipment	**5,065**	4,287
Leasehold improvements	**1,240**	1,240
	7,137	6,359
Less accumulated depreciation	**(5,224)**	(4,568)
	$ 1,913	$ 1,791

Depreciation expense for the year ended December 31, 2022, 2021 and 2020 was $0.7 million, $0.5 million and $0.5 million, respectively.

7. Right of Use Assets and Lease Liabilities

In 2014, the Company entered into a long-term lease with a related party which, as amended, provided for a lease of useable laboratory and office space located in New York, New York. A member of the Company's board of directors is the Executive Chairman of the parent company to the landlord under this lease. Concurrent with this lease, the Company entered into a license agreement to occupy certain vivarium related space in the same facility for the same term and rent escalation provisions as the lease. This license has the primary characteristics of a lease and is characterized as a lease in accordance with ASU 2016-02 for accounting purposes. In September 2018, the Company further amended the lease to obtain an additional office space beginning October 1, 2018 and to extend the term of the lease for previously acquired space. The lease, as amended, has a term of 14.3 years ending in May 2029.

On May 17, 2019, the Company entered into an agreement (the "Vehicle Lease") with a company (the "Lessor") to acquire motor vehicles for certain employees. The Vehicle Lease provides for individual leases for the vehicles, which at each lease commencement was determined to qualify for operating lease treatment. The Company began leasing vehicles under the Vehicle Lease in March 2020.

The contractual period of each lease is 12 months, followed by month-to-month renewal periods. The Company estimates the lease term for each vehicle to be between 12 and 30 months. Leases which the Company determined to have a lease term of 12 months or less will be treated as short-term in accordance with the accounting policy election and are not recognized on the balance sheet. The lease permits either party to terminate the lease at any time via written notice to the other party. The Company neither acquires ownership of, nor has the option to purchase the vehicles at any time. The Company is required to maintain an irrevocable $1.75 million letter of credit that the Lessor may draw upon in the event the Company defaults on the Vehicle Lease, which has been recorded as restricted cash on the consolidated balance sheets.

The following tables present the lease balances within the consolidated balance sheet, operating cash outflows, weighted average remaining lease term, and the weighted average discount rates related to leases as of December 31, 2022 and 2021 (in thousands, except years and percentages):

	December 31, 2022	December 31, 2021
Operating lease balance sheet classification		
Right of use assets, net	**$ 14,824**	$ 20,764
Lease liabilities, short term	**4,567**	6,732
Lease liabilities, noncurrent	**15,474**	18,675
Total lease liabilities	**$ 20,041**	$ 25,407
Lease cost		
Operating lease cost	**$ 4,719**	$ 5,774
Variable lease cost	**1,612**	2,676
Short-term lease cost	**873**	—
	$ 7,204	$ 8,450
Other information		
Weighted average remaining lease term	**5.9 years**	6.1 years
Weighted average discount rate	**8.76%**	8.46%

Maturity analysis under the lease agreements are as follows:

Year ending December 31, 2023	$ 4,741
Year ending December 31, 2024	3,792
Year ending December 31, 2025	3,907
Year ending December 31, 2026	3,974
Year ending December 31, 2027	4,022
Thereafter	5,915
Total	26,351
Less: Present value discount	(6,310)
Total Lease liability	20,041
Less: Current portion	(4,567)
Long-term lease liabilities	$15,474

8. Share-Based Compensation

The Board of Directors determines who will receive options, the vesting periods (which are generally one to three years) and the exercise prices of such options. Options have a maximum term of 10 years. The exercise price of stock options granted under the Amended 2018 Plan and the 2019 Inducement Plan must be at least equal to the fair market value of the common stock on the date of grant.

Total share-based compensation expense related to all of the Company's share-based awards, including stock options and RSUs granted to employees and directors recognized during the years ended December 31, 2022, 2021, and 2020, was comprised of the following (in thousands):

	Years Ended December 31,		
	2022	**2021**	**2020**
Inventoriable costs	**$ 1,791**	$ 1,624	$ 1,342
Research and development	**15,387**	9,832	7,073
Selling, general and administrative	**25,835**	22,847	15,700
Total share-based compensation expense	**$43,013**	$34,303	$24,115

The following table describes the assumptions used for calculating the value of options granted during the years ended December 31, 2022, 2021 and 2020:

	2022	**2021**	**2020**
Dividend yield	**0%**	0%	0%
Expected volatility	**78.7%-88.7%**	89.4-94.9%	91.6-95.5%
Weighted-average risk-free interest rate	**2.22%**	0.87%	1.29%
Expected term (in years)	**5.9**	5.9	6.0

Information regarding the stock options activity, including with respect to grants to employees, directors and consultants under the Amended 2018 Plan and 2019 Inducement Plan as of December 31, 2022, and changes during the year then ended, are summarized as follows:

	Number of Shares	**Weighted-Average Exercise Price**	**Weighted-Average Contractual Life**
Outstanding at December 31, 2021	5,451,398	$21.09	6.1 years
Options granted 2022	612,945	$56.65	
Options exercised 2022	(1,219,421)	$17.58	
Options canceled 2022	(56,792)	$41.01	
Options expired 2022	(2,158)	$12.73	
Outstanding at December 31, 2022	4,785,972	$26.27	5.8 years
Vested and expected to vest at December 31, 2022	4,785,972	$26.27	
Exercisable at December 31, 2022	3,628,867	$20.38	5.0 years

The weighted-average grant date fair value for awards granted during the years ended December 31, 2022, 2021 and 2020 was $41.71, $29.01 and $17.98 per share, respectively. The total intrinsic value of the options exercised during the years ended December 31, 2022, 2021 and 2020 was $48.3 million, $19.6 million and $11.1 million, respectively. The total intrinsic value of the options outstanding as of December 31, 2022 was $130.1 million. The total intrinsic value of the options exercisable as of December 31, 2022 was $118.3 million. The total fair value of shares vested during the years ended December 31, 2022, 2021 and 2020 was $17.1 million, $10.6 million and $13.4 million, respectively.

The unrecognized share-based compensation expense related to stock option awards at December 31, 2022 was $23.6 million, and will be recognized over a weighted-average period of 1.3 years.

Information regarding time based RSU activity, including with respect to grants to employees under the Amended 2018 Plan and 2019 Inducement Plan as of December 31, 2022, and changes during the year then ended, is summarized as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value Per Share	Weighted-Average Contractual Life
Outstanding at December 31, 2021	1,529,652	$26.95	1.5 years
Time based RSUs granted in 2022	601,055	$57.53	
Time based RSUs vested in 2022	(769,355)	$23.23	
Time based RSUs cancelled in 2022	(86,688)	$39.73	
Outstanding at December 31, 2022	1,274,664	$42.76	0.8 years

The total intrinsic value of the time based RSUs vested during the years ended December 31, 2022, 2021 and 2020 was $40.7 million, $25.0 million and $14.6 million, respectively. The total intrinsic value of the time based RSU's outstanding as of December 31, 2022 was $67.5 million. The total fair value of time based RSUs vested during the years ended December 31, 2022, 2021 and 2020 was $17.9 million, $12.4 million and $7.2 million, respectively. The fair value of time based RSUs is based on the closing price of the Company's common stock on the date of grant.

The Company did not issue any options or RSUs under the 2019 Inducement Plan in 2022 or 2021. As of December 31, 2022, there was approximately $0.3 million of unrecognized compensation costs related to unvested options and RSUs under the 2019 Inducement Plan, and $1.2 million was recognized during 2022 under this plan. As of December 31, 2022, 11,126 options and 64,302 RSUs are expected to vest in the future.

As of December 31, 2022, there was $34.7 million of unrecognized compensation costs related to unvested time based RSUs which will be recognized over a weighted-average period of 1.4 years.

9. Loss per Share

The following common stock equivalents were excluded in the calculation of diluted loss per share because their effect could be anti-dilutive as applied to the net loss for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
Stock options	4,785,972	5,451,398	5,517,622
RSUs	1,469,678	1,666,848	1,636,422

10. Income Taxes

Loss before income taxes is as follows (in thousands):

	2022	2021	2020
U.S.	**$(223,465)**	$(221,216)	$(155,616)
Non-U.S.	**(32,785)**	(62,904)	(71,376)
Total loss before taxes	**$(256,250)**	$(284,120)	$(226,992)

Total income tax expense for the years ended December 31, 2022, 2021 and 2020 is allocated as follows:

	2022	2021	2020
Current	**$ 6**	$ 6	$ 14
Deferred	**(52,789)**	(53,070)	(40,049)
Valuation allowance	**52,789**	53,070	40,049
Provision for income taxes	**$ 6**	$ 6	$ 14

A reconciliation of the difference between the statutory federal income tax rate and the effective income tax rate for the years ended December 31, 2022, 2021 and 2020 is as follows:

	December 31,		
	2022	2021	2020
Income tax at statutory federal rate	**21.00%**	21.00%	21.00%
Executive and share-based compensation	**1.92**	0.60	(1.01)
Subpart F Inclusion	**(3.38)**	0.0	0.0
Foreign rate differential	**(2.69)**	(4.63)	(6.60)
Change in effective state tax rates	**0.17**	(0.31)	1.12
State income tax expense	**3.58**	2.04	3.14
Change in valuation allowance	**(20.60)**	(18.70)	(17.65)
Provision for income taxes	**0.0%**	0.0%	0.0%

Deferred income taxes reflect the net tax effect of temporary differences that exist between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, using enacted tax rates in effect for the year in which the differences are expected to reverse. As of December 31, 2022, the Company had $663.2 million of federal net operating loss carryforwards, of which $131.1 million expire at various dates through 2037 and $532.1 million do not expire. The gross amount of the state net operating loss carryforwards is equal to or less than the federal net operating loss carryforwards and expires over various periods based on individual state tax law. In general, businesses with U.S. net operating losses (“NOLs”) are considered loss corporations for U.S. federal income tax purposes. Pursuant to Section 382 of the Code, loss corporations that undergo an ownership change, as defined under the Code, may be subject to an annual limitation on the amount of NOLs (and certain other tax attributes) available to offset taxable income earned after such ownership change. For the years ended December 31, 2015 through 2022, the Company performed a Section 382 ownership analysis and determined that an ownership change occurred (within the meaning of Section 382 of the Code) in 2015 but not in subsequent periods. Based on the analysis performed through December 31, 2022, however, the Company does not believe that the Section 382 annual limitation will impact the Company’s ability to utilize the tax attributes that existed as of the date of the ownership change in a material manner. If the Company experiences an ownership change in the future, the tax benefits related to the NOLs and tax credit carryforwards may be further limited or lost.

The following summarizes the significant components of the Company's deferred tax assets and liabilities as of December 31, 2022 and 2021, respectively (in thousands):

	December 31, 2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 168,606	$ 137,561
Accrued expenditures	9,169	2,723
Research and development credit, net	9,321	9,321
Research and development expenditures	13,525	—
Share-based compensation	17,085	15,947
Other	1,466	93
Capital lease	4,980	6,178
Deferred tax liabilities:		
Right of use asset—capital lease	(3,684)	(5,049)
Depreciation	(154)	(201)
Net deferred tax asset before valuation allowance	220,314	166,573
Valuation allowance	(220,314)	(166,573)
Net deferred tax asset	$ —	$ —

Based upon the Company's historical operating performance and the reported cumulative net losses to date, the Company presently does not have sufficient objective evidence to support the recovery of its net deferred tax assets. Accordingly, the Company has established a full valuation allowance against its net deferred tax assets in 2022 and 2021, for financial reporting purposes because it is not more likely than not that these deferred tax assets will be realized.

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. The open years subject to tax audits vary depending on the tax jurisdictions. In the U.S. federal jurisdiction, we are no longer subject to income tax audits by taxing authorities for years before 2014.

The total amount of unrecognized tax benefits was $1.7 million as of December 31, 2022 and 2021. If recognized, none of these tax benefits would affect the effective tax rate due to valuation allowances.

11. Commitments and Contingencies

License and Royalty Commitments

On May 31, 2005, the Company entered into a worldwide, exclusive License Agreement with Bristol-Myers Squibb Company, pursuant to which the Company holds a license to certain patents and know-how of BMS relating to lumateperone and other specified compounds. The agreement was amended on November 3, 2010. The licensed rights are exclusive, except BMS retains rights in specified compounds in the fields of obesity, diabetes, metabolic syndrome and cardiovascular disease. However, BMS has no right to use, develop, or commercialize lumateperone and other specified compounds in any field of use. The Company has the right to grant sublicenses of the rights conveyed by BMS. The Company is obliged under the agreement to use commercially reasonable efforts to develop and commercialize the licensed technology. The Company is also prohibited from engaging in the clinical development or commercialization of specified competitive compounds.

Under the agreement, the Company made an upfront payment of $1.0 million to BMS in 2005, a milestone payment of $1.25 million in December 2013, and a milestone payment of $1.5 million in December 2014 following the initiation of the Company's first Phase 3 clinical trial for lumateperone for patients with exacerbated schizophrenia. Upon FDA acceptance of an NDA filing for lumateperone, the Company was obligated to pay BMS a $2.0 million milestone payment, which was paid in January 2019. The FDA approved

the NDA filing on December 20, 2019 and as a result the Company accrued an additional milestone liability of $5.0 million in the fourth quarter of 2019 which was paid in January 2020. Possible milestone payments remaining total $5.0 million. Under the agreement, the Company may be obliged to make other milestone payments to BMS for each licensed product of up to an aggregate of approximately $14.75 million. The Company is also obliged to make tiered single digit percentage royalty payments ranging between 5 – 9% on sales of licensed products. The Company is obliged to pay to BMS a percentage of non-royalty payments made in consideration of any sublicense.

The agreement extends, and royalties are payable, on a country-by-country and product-by-product basis, through the later of 10 years after first commercial sale of a licensed product in such country, expiration of the last licensed patent covering a licensed product, its method of manufacture or use, or the expiration of other government grants providing market exclusivity, subject to certain rights of the parties to terminate the agreement on the occurrence of certain events. On termination of the agreement, the Company may be obliged to convey to BMS rights in developments relating to a licensed compound or licensed product, including regulatory filings, research results and other intellectual property rights.

In September 2016, the Company transferred certain of its rights under the BMS agreement to its wholly owned subsidiary, ITI Limited. However, in December 2022, ITI Limited merged into Intra-Cellular Therapies, Inc. The Company expensed approximately $12.5 million, $4.1 million, and $1.1 million in cost of product sales to satisfy its obligation under the BMS agreement for the years ended December 31, 2022, 2021 and 2020, respectively.

Purchase Commitments

The Company enters into certain other long-term commitments for goods and services that are outstanding for periods greater than one year. The Company recently amended the significant manufacturing service agreements with Siegfried Evionnaz SA and Lonza Ltd, committing to certain minimum annual purchase commitments which the Company anticipates making payments for within the years 2025 through 2029. As of December 31, 2022, the Company has committed to purchasing production campaigns for various raw materials including active pharmaceutical ingredients (API) and its intermediates from each of its supply vendors. The campaigns are expected to be received into inventory during 2023 and 2024. The Company has paid deposits of $21.6 million and $9.5 million as of December 31, 2022 and 2021, respectively, for the various campaigns, which are recorded within prepaid expenses and other current assets. Over the course of the vendors' manufacturing period, the Company will remit payments to each vendor based on the payment plan within the executed agreements.

Retirement savings plan 401(k) contributions

The Company sponsors a defined contribution 401(k) plan covering all full-time employees. Participants may elect to contribute their annual pre-tax earnings up to the federally allowed maximum limits. The Company made a matching contribution of 100% on the first 6% of contributions made by participants in the year ended December 31, 2022, 2021 and 2020. Participant and company contributions vest immediately. During the years ended December 31, 2022, 2021 and 2020, the Company recorded matching contribution expense of $3.9 million, $3.0 million and $1.8 million, respectively.

Contingencies

During the normal course of our business, we are occasionally involved with various claims and litigation. Reserves are established in connection with such matters when a loss is probable and the amount of such loss can be reasonably estimated. At December 31, 2022 and 2021, no material reserves were recorded. The determination of probability and the estimation of the actual amount of any such loss are inherently unpredictable, and it is therefore possible that the eventual outcome of such claims and litigation could exceed the estimated reserves, if any. However, we believe that the likelihood that any such excess might have a material adverse effect on our financial statements is remote.

12. Unaudited Quarterly Financial Information

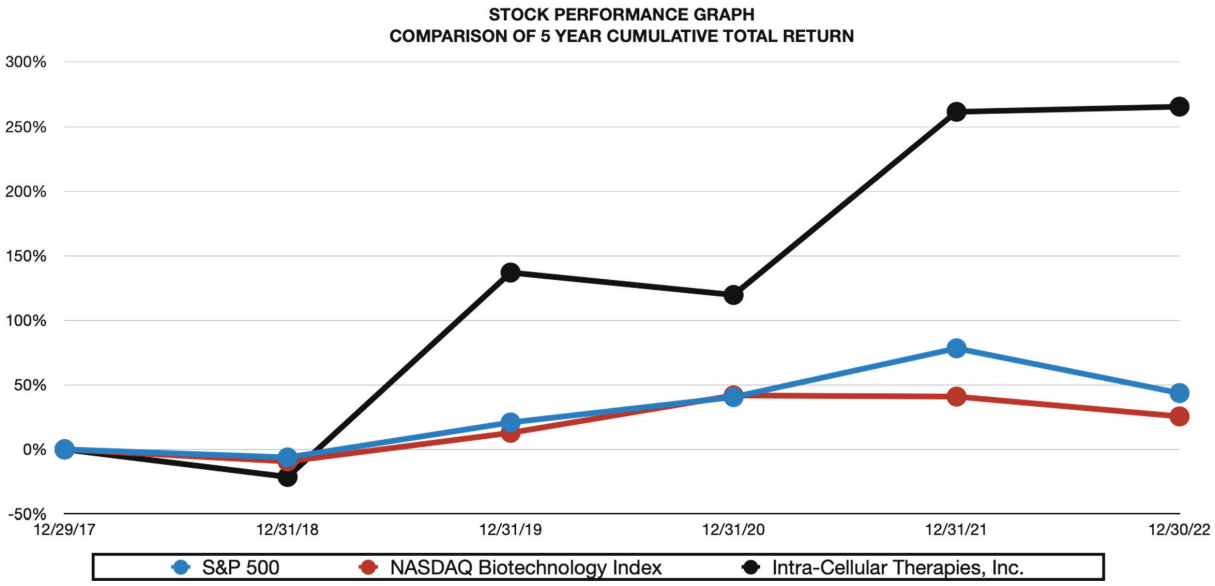
The tables herein set forth the Company's unaudited condensed consolidated 2022 and 2021 quarterly statements of operations.

The following table sets forth the Company's unaudited condensed consolidated statements of operations for the 2022 quarters ended (in thousands):

2022 Quarter Ended	December 31,	September 30,	June 30,	March 31,
Revenue, net	$ 87,869	$ 71,870	$ 55,579	$ 34,996
Operating expenses	(135,281)	(127,499)	(143,502)	(107,658)
Interest income	3,386	2,122	1,320	548
Income tax expense	—	(1)	—	(5)
Net loss	(44,026)	(53,508)	(86,603)	(72,119)
Basic and diluted net loss per share	$ (0.45)	$ (0.57)	$ (0.92)	$ (0.78)

The following table sets forth the Company's unaudited condensed consolidated statements of operations for the 2021 quarters ended (in thousands):

2021 Quarter Ended	December 31,	September 30,	June 30,	March 31,
Revenue, net	$ 25,671	$ 22,207	$ 20,047	$ 15,878
Operating expenses	(111,675)	(99,531)	(89,188)	(69,097)
Interest income	270	393	421	484
Income tax benefit (expense)	—	23	(24)	(5)
Net loss	(85,734)	(76,908)	(68,744)	(52,740)
Basic and diluted net loss per share	$ (1.05)	$ (0.95)	$ (0.85)	$ (0.65)


STOCK PERFORMANCE GRAPH
COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN
300%
250%
200%
150%
100%
50%
0%
-50%
12/29/17
12/31/18
12/31/19
12/31/20
12/31/21
12/30/22
S&P 500
NASDAQ Biotechnology Index
Intra-Cellular Therapies, Inc.

Directors

Sharon Mates, Ph.D.
Chairman of the Board

Joel S. Marcus
Executive Chairman and Founder, Alexandria Real Estate Equities, Inc.

Rory B. Riggs
Co-founder and Director, Royalty Pharma

E. Rene Salas
Former Senior Client Partner, Ernst & Young LLP

Robert L. Van Nostrand
Former Executive Vice President and Chief Financial Officer, Aureon Biosciences, Inc.

Executive Officers

Sharon Mates, Ph.D.
Chairman, President and Chief Executive Officer

Mark Neumann
Executive Vice President, Chief Commercial Officer

Suresh Durgam, M.D.
Executive Vice President, Chief Medical Officer

Michael I. Halstead
Executive Vice President, General Counsel and Secretary

Lawrence J. Hineline
Senior Vice President of Finance, Chief Financial Officer, Treasurer and Assistant Secretary

Shareholders and Stock Listing

Our common stock is traded on the Nasdaq Global Select Market under the symbol ITCI. On March 31, 2023, the closing price of our common stock was $54.15 per share and our common stock was held by 78 stockholders of record.

Investor Information

You may obtain a copy of any of the exhibits to our Annual Report on Form 10-K free of charge. These documents are available on our website at www.intracellulartherapies.com or by contacting Investor Relations at Intra-Cellular Therapies, Inc.

Requests for information about Intra-Cellular Therapies, Inc. should be directed to:

Investor Relations
Intra-Cellular Therapies, Inc.
430 East 29th Street
New York, New York 10016
Telephone: (646) 440-9333

Annual Meeting

The annual meeting of stockholders will be held virtually via the internet at https://meetnow.global/MKSPA7Y at the time stated below.

Friday, June 23, 2023
10:00 a.m., Eastern Time

Internet Website

www.intracellulartherapies.com

Legal Counsel

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
Boston, Massachusetts

Independent Registered Public Accounting Firm

Ernst & Young LLP, Baltimore, Maryland

Transfer Agent and Registrar

Computershare Investor Services
P.O. Box 43006
Providence, RI 02940-3006
1-877-373-6374
www.computershare.com/investor

Forward-Looking Statements. The Letter to Shareholders contained in this annual report contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements concern, among other things, CAPLYTA and our other product candidates, our expectations about the commercialization of CAPLYTA, potential regulatory approval of our product candidates, potential benefits of our product and our product candidates, and our plans and our development programs. These statements involve risks, uncertainties and assumptions and are based on the current estimates and assumptions of the management of Intra-Cellular Therapies, Inc. (the "Company") as of the date of the Letter to Shareholders and are subject to uncertainty and changes. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, those set forth under the heading "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2022 filed with the Securities and Exchange Commission, as well as any updates to those risk factors filed from time to time in our periodic and current reports. All information in the Letter to Shareholders is as of the date of the Letter to Shareholders, and the Company undertakes no duty to update this information unless required by law.

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