Intra-Cellular Therapies, Inc.
Form 10-K
February 27, 2019
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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, 2018

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	Name of each exchange on which registered
Common Stock, $0.0001 Par Value Per Share	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 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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 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 $793 million.

As of February 25, 2019, the registrant had 55,116,739 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 2019 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission.

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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 subsidiaries, ITI, Inc. and ITI Limited.

Item 1. BUSINESS

Overview

We are a biopharmaceutical company focused on the discovery and clinical development 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. Lumateperone (also known as ITI-007) is our lead product candidate with mechanisms of action that, we believe, may represent an effective treatment across multiple therapeutic indications. In our preclinical and clinical trials to date, lumateperone combines potent serotonin 5-HT2A receptor antagonism, dopamine receptor phosphoprotein modulation, or DPPM, glutamatergic modulation, and serotonin reuptake inhibition into a single drug candidate for the treatment of acute and residual schizophrenia and for the treatment of bipolar disorder, including bipolar depression. At dopamine D2 receptors, lumateperone has been demonstrated to have dual properties and to act as both a pre-synaptic partial agonist and a post-synaptic antagonist. Lumateperone has also been demonstrated to have affinity for dopamine D1 receptors and indirectly stimulate phosphorylation of glutamatergic NMDA GluN2B receptors in a mesolimbic specific manner. We believe that this regional selectivity in brain areas thought to mediate the efficacy of antipsychotic drugs, together with serotonergic, glutamatergic, and dopaminergic interactions, may result in efficacy for a broad array of symptoms associated with schizophrenia and bipolar disorder with improved psychosocial function. The serotonin reuptake inhibition potentially allows for antidepressant activity in the treatment of schizoaffective disorder, other disorders with co-morbid depression, and/or as a stand-alone treatment for major depressive disorder, or MDD. We believe lumateperone may also be useful for the treatment of other psychiatric and neurodegenerative disorders, particularly behavioral disturbances associated with dementia, autism, and other CNS diseases. In the fourth quarter of 2018, the FDA accepted for review our new drug application, or NDA, for lumateperone for the treatment of schizophrenia, and assigned a Prescription Drug User Fee Act, or PDUFA, target action date of September 27, 2019. Lumateperone is also in Phase 3 clinical development as a novel treatment bipolar depression and agitation associated with dementia, including Alzheimer s disease, or AD.

Lumateperone for the Treatment of Schizophrenia

In September 2015, we announced top-line clinical results from our first Phase 3 clinical trial of lumateperone for the treatment of patients with schizophrenia. This randomized, double-blind, placebo-controlled Phase 3 clinical trial was conducted at sites in the United States with 450 patients randomized. The pre-specified primary efficacy measure was change from baseline versus placebo at study endpoint (4 weeks) on the centrally rated Positive and Negative Syndrome Scale, or PANSS, total score. In this trial, the once-daily dose of 60 mg of ITI-007 met the primary endpoint and demonstrated antipsychotic efficacy with statistically significant superiority over placebo at week 4 (study endpoint). Consistent with previous studies, lumateperone had a favorable safety and tolerability profile as evidenced by motoric, metabolic, and cardiovascular characteristics similar to placebo, and no clinically significant changes in akathisia, extrapyramidal symptoms, prolactin, body weight, glucose, insulin, or lipids.

The results from our first Phase 3 clinical trial of lumateperone confirmed the earlier Phase 2 results that we announced in December 2013, in which lumateperone exhibited antipsychotic efficacy in a randomized, double-blind, placebo and active controlled clinical trial in patients with schizophrenia. In this study, lumateperone

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(ITI-007 60 mg) met the trial s pre-specified primary endpoint, improving symptoms associated with schizophrenia as measured by a statistically significant and clinically meaningful decrease in the PANSS total score. The trial also met key secondary outcome measures related to efficacy on PANSS subscales and safety.

In September 2016, we announced top-line results from the second Phase 3 clinical trial (ITI-007-302) of lumateperone for the treatment of patients with schizophrenia. In this trial, neither dose of lumateperone separated from placebo on the primary endpoint, change from baseline on the PANSS total score, in the pre-defined patient population. The active control, risperidone, did separate from placebo. In this trial, lumateperone was statistically significantly better than risperidone on key safety and tolerability parameters and exhibited a safety profile similar to placebo. We believe lumateperone did not separate from placebo on the pre-specified primary endpoint in the ITI-007-302 study in part due to an unusually high placebo response at certain sites which disproportionately affected the trial results and contributed to the efficacy outcome of this study compared to our two previous positive efficacy studies. In addition, we believe other confounding factors may have played a role in the efficacy outcome of ITI-007-302, including an expectation bias and the potential for functional unblinding. We believe the lumateperone late-stage clinical development program, including two large, well-controlled positive studies and supportive evidence from this second Phase 3 study, collectively provide evidence of the efficacy and safety of lumateperone for the treatment of schizophrenia. Across all three of our efficacy trials, ITI-007 60 mg improved symptoms of schizophrenia with the same trajectory and magnitude of change from baseline in the primary endpoint, the PANSS total score.

As part of our ongoing dialogue with the U.S. Food and Drug Administration, or FDA, regarding our lumateperone development program in schizophrenia, we requested guidance from the FDA on the acceptability of the two positive well controlled clinical trials we have conducted (Study ITI-007-005 and Study ITI-007-301), with supportive evidence from Study ITI-007-302, as the basis for the submission of a new drug application, or NDA, for the treatment of schizophrenia. In connection with this request we provided extensive information and data analyses to the FDA relating to the three studies. The FDA confirmed that the results of Study ITI-007-302 do not preclude us from submitting an NDA based on the efficacy studies we have conducted to date. We completed our NDA for lumateperone for the treatment of schizophrenia in the third quarter of 2018 and the FDA accepted for review the NDA in the fourth quarter of 2018. We believe our schizophrenia clinical development program collectively provides evidence of the efficacy and safety of lumateperone for the treatment of schizophrenia.

Lumateperone for the Treatment of Depressive Episodes Associated with Bipolar Disorder (Bipolar Depression)

Our bipolar depression program consists of three Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials. In the ITI-007-401 and the ITI-007-404 trials, lumateperone is being evaluated as a monotherapy and in the ITI-007-402 trial, lumateperone is being evaluated as an adjunctive therapy with lithium or valproate. All three trials are evaluating lumateperone in patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode. We have completed patient enrollment in the ITI-007-401 trial conducted in the United States and the ITI-007-404 trial conducted globally. We anticipate reporting topline results from the ITI-007-401 and ITI-007-404 trials simultaneously in the second quarter of 2019. Subject to the outcome of these trials, we expect to submit an NDA for bipolar depression in the second half of 2019. Our global ITI-007-402 trial evaluating adjunctive lumateperone in bipolar depression is ongoing. In connection with the global strategy of this program we are adding sites outside the U.S. to the ITI-007-402 trial and we expect to provide anticipated timelines for this trial after completing the expansion.

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Lumateperone for the Treatment of Behavioral Disturbances Associated with Dementia, Including Alzheimer s Disease

In the fourth quarter of 2014, we announced the top-line data from ITI-007-200, a Phase 1/2 clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of lumateperone in healthy geriatric subjects and in patients with dementia, including AD. The completion of this study marked an important milestone in our strategy to develop low doses of lumateperone for the treatment of behavioral disturbances associated with dementia and related disorders. The ITI-007-200 trial results indicate that lumateperone is safe and well-tolerated across a range of low doses, has linear- and dose-related pharmacokinetics and may improve cognition in the elderly. The most frequent adverse event was mild sedation at the higher doses. We believe these results further position lumateperone as a development candidate for the treatment of behavioral disturbances in patients with dementia and other neuropsychiatric and neurological conditions.

In the second quarter of 2016, we initiated Phase 3 development of lumateperone for the treatment of agitation in patients with dementia, including AD. Our ITI-007-201 trial is a Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trial in patients with a clinical diagnosis of probable AD and clinically significant symptoms of agitation. In the fourth quarter of 2018, an independent data monitoring committee, or DMC, completed a pre-specified interim analysis of the ITI-007-201 trial, concluded that the trial is not likely to meet its primary endpoint upon completion and therefore recommended the study should be stopped for futility. As a result, we determined to discontinue the ITI-007-201 trial. Lumateperone was generally well tolerated in the ITI-007-201 trial and the decision to discontinue the study was not related to safety. We are analyzing the results of this trial and, following completion of this analysis, we will determine the next steps in this program.

Other Indications for Lumateperone

We are also pursuing clinical development of lumateperone for the treatment of additional CNS diseases and disorders. At the lowest doses, lumateperone has been demonstrated to act primarily as a potent 5-HT2A serotonin receptor antagonist. As the dose is increased, additional benefits are derived from the engagement of additional drug targets, including modest dopamine receptor modulation and modest inhibition of serotonin transporters. We believe that combined interactions at these receptors may provide additional benefits above and beyond selective 5-HT2A antagonism for treating agitation, aggression and sleep disturbances in diseases that include dementia, AD, Huntington s disease and autism spectrum disorders, while avoiding many of the side effects associated with more robust dopamine receptor antagonism. As the dose of lumateperone is further increased, leading to moderate dopamine receptor modulation, inhibition of serotonin transporters, and indirect glutamate modulation, these actions complement the complete blockade of 5-HT2A serotonin receptors. At a dose of 60 mg, ITI-007 has been shown effective in treating the symptoms associated with schizophrenia, and we believe this higher dose range will be useful for the treatment of bipolar disorder, depressive disorders and other neuropsychiatric diseases.

We have commenced our program of lumateperone in MDD. In previous studies, schizophrenia patients with co-morbid depression experienced improvements in depressive symptoms. Additionally, recent preclinical data support the potential for rapid-acting antidepressant effects. In order to explore the effect of different modes of drug administration and the potential for rapid-onset antidepressant activity, our program includes the assessment of novel formulations of lumateperone. Pharmacokinetic studies evaluating these novel formulations are currently ongoing.

Within the lumateperone portfolio, we are also developing a long-acting injectable (LAI) formulation to provide more treatment options to patients suffering from mental illness. Given the encouraging tolerability data to date with oral lumateperone, we believe that a long-acting injectable option, in particular, may lend itself to being an important formulation choice for patients.

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Given the potential utility for lumateperone and follow-on compounds to treat these additional indications, we may investigate, either on our own or with a partner, agitation, aggression and sleep disturbances in additional diseases that include autism spectrum disorders, depressive disorder, intermittent explosive disorder, non-motor symptoms and motor complications associated with Parkinson s disease, and post traumatic stress disorder. 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 have a second major program called ITI-002 that has yielded a portfolio of compounds that selectively inhibits the enzyme phosphodiesterase type 1, or PDE1. On February 25, 2011, we (through our wholly owned operating subsidiary, ITI) and Takeda Pharmaceutical Company Limited, or Takeda, entered into a license and collaboration agreement, or the Takeda License Agreement, under which we agreed to collaborate to research, develop and commercialize our proprietary compound ITI-214 and other selected compounds that selectively inhibit PDE1 for use in the prevention and treatment of human diseases. On October 31, 2014, we entered into an agreement with Takeda terminating the Takeda License Agreement, or the Termination Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. On September 15, 2015, Takeda completed the transfer of the Investigational New Drug application, or IND, for ITI-214 to us. We believe ITI-214 is the first compound in its class to successfully advance through Phase 1 clinical trials. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, including cardiovascular disease. Following the positive safety and tolerability results in our Phase 1 program, we initiated our development program for ITI-214 for Parkinson s disease and commenced patient enrollment in the third quarter of 2017 in a Phase 1/2 clinical trial of ITI-214 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 the fourth quarter of 2018, we announced that the Phase 1/2 clinical trial of ITI-214 had been completed and topline results demonstrated ITI-214 was generally well-tolerated with a favorable safety profile and clinical signs consistent with improvements in motor symptoms and dyskinesias. In addition, in the first quarter of 2018, the investigational new drug application, or IND, went into effect for ITI-214 for the treatment of heart failure. We have initiated clinical conduct of the first clinical study in this program, a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 to evaluate safety and hemodynamic effects in patients with systolic heart failure.

Our pipeline also includes preclinical programs that are focused on advancing drugs for the treatment of schizophrenia, Parkinson s disease, AD and other neuropsychiatric and neurodegenerative disorders. We are also investigating the development of treatments for disease modification of neurodegenerative disorders and non-CNS diseases, including our ITI-333 development program. ITI-333 is designed 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. We believe the potential exists for ITI-333 to address these challenges. In preclinical studies, ITI-333 functions as a partial agonist at mu opiate receptors, attenuating the behavioral effects of morphine while displaying full analgesic efficacy that is reversible by the mu opiate antagonist, naloxone. ITI-333 also acts as a 5-HT2A antagonist with interactions at D1 receptors. Preclinical safety studies are currently ongoing. If successfully translated to humans, this unique pharmacological profile may yield clinical utility for the treatment of substance use disorders and pain. Preclinical safety studies with ITI-333 are currently ongoing and we expect to initiate a clinical program in 2019.

We have assembled a management team with significant industry experience to lead 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 and other CNS disorders, including Nobel laureate, Dr. Paul Greengard, one of our co-founders.

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We were originally incorporated in the State of Delaware in August 2012 under the name Oneida Resources Corp. Prior to a reverse merger that occurred on August 29, 2013, or the Merger, Oneida Resources Corp. was a shell company registered under the Securities Exchange Act of 1934, or the Exchange Act, with no specific business plan or purpose until it began operating the business of ITI, Inc., or ITI, through the Merger transaction on August 29, 2013. 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 CNS. Effective upon the Merger, a wholly-owned subsidiary of the Company merged with and into ITI, and ITI continues as the operating subsidiary of the Company and ITI s business continues as the business of the Company. As used herein, the words the Company, we, us, and our refer to the current Delaware Corporation and its wholly owned subsidiaries, ITI, Inc. and ITI Limited

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. Our filings with the SEC will be available free of charge through the Investors section of our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website does not constitute a part of this report or our other filings with the SEC.

Our Strategy

Our goal is to discover and develop 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:

- complete the development of lumateperone for its lead indication, treatment of schizophrenia, and for additional neuropsychiatric indications, such as bipolar disorder, behavioral disturbances in dementia, including AD, residual symptoms in schizophrenia and MDD;

- expand the commercial potential of lumateperone by investigating its usefulness in additional neurological areas, such as autism spectrum disorder, and in additional neuropsychiatric indications, such as sleep disorders associated with neuropsychiatric and neurological disorders;

continue to develop PDE inhibitor compounds, such as ITI-214, for the treatment of CNS and other disorders; and

advance earlier stage product candidates in our pipeline, such as ITI-333, for substance use disorders, pain and psychiatric comorbidities including depression and anxiety.

Our Drug Discovery Platform and Capabilities

Based on the pioneering efforts of our 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

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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 preclinical 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. Current antipsychotic medications provide some relief for the symptoms associated with the acute phase of the disorder, but they do not effectively treat the residual phase symptoms associated with chronic schizophrenia. Currently available medications used to treat acute schizophrenia are limited in their use due to side effects that can include movement disorders, weight gain, metabolic disturbances, and cardiovascular disorders. Indeed, the side effects associated with current antipsychotic medications often make some of the residual phase symptoms, such as negative symptoms and social function, worse. There is an unmet medical need for new therapies that have improved side effect and efficacy profiles.

According to the Alliance on Mental Illness and National Institute of Mental Health, about 1% of the population suffers from schizophrenia, and 2.4 million Americans suffer from the illness in any given year. US market value of antipsychotic drugs exceeded $10 billion in 2018. These drugs have been increasingly used by physicians to address a range of disorders in addition to schizophrenia, including bipolar disorder and a variety of psychoses and related conditions in elderly patients. Despite their commercial success, current antipsychotic drugs have substantial limitations, including inadequate efficacy and severe side effects.

The first-generation, or typical, antipsychotics that were introduced in the late-1950s block dopamine receptors. While typical antipsychotics are effective against positive symptoms of schizophrenia in many patients, these drugs often induce disabling motor disturbances, and they fail to address or worsen most of the negative symptoms and cognitive disturbances associated with schizophrenia.

Most schizophrenia patients in the United States are treated today with second-generation, or atypical, antipsychotics, which induce fewer motor disturbances than typical antipsychotics, but still fail to address most of the negative symptoms of schizophrenia and other symptoms associated with social function impairment. Many patients with

schizophrenia have deficits in social function. Social function is the ability to recognize, understand, process and use external cues to solve problems, maintain work performance, and conduct interpersonal relationships. Deficits in social function often remain after positive symptoms, such as

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hallucinations and delusions, have resolved in these patients. In addition, currently prescribed treatments do not effectively address or may exacerbate cognitive disturbances associated with schizophrenia. It is believed that the efficacy of atypical antipsychotics is due to their interactions with dopamine and 5-HT2A receptors. The side effects induced by the atypical agents may include weight gain, non-insulin dependent (type II) diabetes, cardiovascular side effects, sleep disturbances, and motor disturbances. We believe that these side effects generally arise either from non-essential receptor interactions or from excessive dopamine blockade.

The limitations of currently available antipsychotics result in poor patient compliance. 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. We believe there is a large underserved medical need for new therapies that have improved side effect and efficacy profiles.

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, and 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.

Bipolar disorder affects approximately 6 million adults in the United States in any given year, or about 2.8 percent of the adult U.S. population. According to Decision Resources Group, therapeutics used to treat bipolar disorder had global sales of approximately $6 billion in 2018.

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.

Behavioral Disturbances in Dementia, Including Alzheimer s Disease

It has been estimated that 46 million people worldwide were living with dementia in 2015, and this number is expected to increase to 132 million by 2050. The Alzheimer s Association estimates 5.7 million Americans are living with Alzheimer s dementia in 2018. 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. In view of the potential multiple effects of lumateperone on aggression, agitation, sleep disorders and depression, and its safety profile to date, we believe that lumateperone 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. As symptoms progress and become more severe, physicians often resort to off-label use of antipsychotic medications in these patients. Current antipsychotic drugs are associated with a number of side effects, which can be problematic for

elderly patients with dementia. In addition, antipsychotic drugs may exacerbate the cognitive disturbances associated with dementia. 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.

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Alzheimer s Disease

AD is a progressive neurodegenerative disorder that slowly destroys memory and thinking skills, and eventually even the ability to carry out simple tasks. Its symptoms include cognitive dysfunction, memory abnormalities, progressive impairment in activities of daily living, and a host of behavioral and neuropsychiatric symptoms. AD primarily affects older people and, in most cases, symptoms first appear after age 60. AD gets worse over time and is fatal.

The market for AD therapeutics is categorized into two segments: acetylcholinesterase inhibitors and NMDA receptor antagonists, which include donepezil, memantine and rivastigmine.

While the diagnostic criteria for AD 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. These symptoms include agitation, aggressive behaviors, depression, sleep disorders, and psychosis. Studies have suggested that approximately 60% of patients with AD experience agitation/aggression, up to 87% of patients experience depression, approximately 60% of patients experience sleep disturbances, particularly as an increased likelihood of day-night reversal, and approximately 20% to 50% of AD patients may develop psychosis at some point in the disease process, commonly consisting of hallucinations and delusions. The diagnosis of AD psychosis is associated with more rapid cognitive and functional decline and institutionalization. Sleep disturbances increase the likelihood of day-night reversal, increased agitation and increased caregiver stress that strongly influences decisions for nursing home placement.

The FDA has not approved any drug to treat the behavioral symptoms of AD. As symptoms progress and become more severe, physicians often resort to off-label use of antipsychotic medications in these patients. Current antipsychotic drugs are associated with a number of side effects, which can be problematic for elderly patients with AD. In addition, antipsychotic drugs may exacerbate the cognitive disturbances associated with AD. Current antipsychotic drugs also have a boxed warning for use in elderly patients with dementia-related psychosis due to increased mortality and morbidity. There is a large unmet medical need for a safe and effective therapy to treat the behavioral symptoms in patients with 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.

Parkinson s disease is the second most common neurodegenerative disorder after AD. According to the National Parkinson Foundation, about 1 million people in the United States and approximately 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. According to Decision Resources Group, sales of therapeutics such as L-DOPA and dopamine agonists used to treat the disease had global sales of approximately $3 billion in 2018.

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

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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. No drugs are currently approved by the FDA for treating the broad non-motor symptoms associated with Parkinson s disease, and this remains a large unmet medical need.

Major Depressive Disorder

Major depressive disorder, or MDD, is a brain 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 7% of adults experience MDD each year. Worldwide sales of antidepressant drugs reached $9.5 billion in 2015. 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 and Rexulti® (marketed jointly by Otsuka Pharmaceutical and Lundbeck) 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 were considered treatment-resistant.

Heart Failure

Heart failure is a chronic, progressive condition in which the heart muscle is unable to pump enough blood to meet the body s needs for blood and oxygen. In some types of heart failure, the left ventricle loses its ability to contract normally. The heart can t pump with enough force to push enough blood into circulation (heart failure with reduced ejection fraction). Eventually the heart and body cannot compensate, and the person experiences fatigue, breathing problems or other symptoms.

Approximately 5.7 million adults in the United States have heart failure. One in 9 deaths in 2009 included heart failure as contributing cause. About half of people who develop heart failure die within 5 years of diagnosis. Heart failure costs the nation an estimated $30.7 billion each year. This total includes the cost of health care services, medications to treat heart failure, and missed days of work. Current treatments prolong life and improve the heart s function, but there is no cure. There is a pressing need for improved treatments to improve and reverse these changes in cardiac function.

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Our Clinical Programs

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

OUR THERAPEUTIC PIPELINE

Lumateperone Program

Our lead product candidate, lumateperone, possesses mechanisms of action that, we believe, may represent an effective treatment across multiple therapeutic indications. We completed the submission of the NDA for lumateperone for the treatment of schizophrenia in the third quarter of 2018 and the FDA accepted for review the NDA in the fourth quarter of 2018. In our preclinical and clinical trials to date, lumateperone combines potent serotonin 5-HT2A receptor antagonism, dopamine receptor phosphoprotein modulation, or DPPM, glutamatergic modulation, and serotonin reuptake inhibition into a single drug candidate for the treatment of acute and residual schizophrenia. At dopamine D2 receptors, lumateperone has been demonstrated to have dual properties and to act as both a pre-synaptic partial agonist and a post-synaptic antagonist. Lumateperone has also been demonstrated to have affinity for dopamine D1 receptors and indirectly stimulate phosphorylation of glutamatergic NMDA NR2B, or GluN2B, receptors in a mesolimbic specific manner, resulting in enhanced glutamatergic function through both NDMA and AMPA current. We believe that this regional selectivity in brain areas thought to mediate the efficacy of antipsychotic drugs, together with serotonergic, glutamatergic, and dopaminergic interactions, may result in efficacy for a broad array of symptoms associated with schizophrenia. The serotonin reuptake inhibition potentially allows for antidepressant activity in the treatment of schizoaffective disorder, other disorders with co-morbid depression, and/or as a stand-alone treatment for MDD. We believe lumateperone may also be useful for the treatment of bipolar disorder and other psychiatric and neurodegenerative disorders, particularly behavioral disturbances associated with dementia, autism, and other CNS diseases.

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We believe these features of lumateperone may be able to improve the quality of life of patients with schizophrenia and enhance social function to allow them to integrate more fully into their families and their workplaces. In addition, lumateperone may be shown to treat disorders at either low-doses (*e.g.,* sleep, aggression and agitation) or high-doses (*e.g.*, acute exacerbated and residual schizophrenia, bipolar disorders, and mood disorders).

Lumateperone for the treatment of exacerbated and residual schizophrenia

In multiple clinical trials of lumateperone in patients with schizophrenia, the drug candidate has demonstrated clinical signals consistent with reductions in psychosis, depression and insomnia. Reductions in psychosis are consistent with the potential to treat acute schizophrenia, whereas reductions in depression and insomnia are consistent with the potential to treat residual phase schizophrenia. Lumateperone has demonstrated a positive safety profile and been well-tolerated across a wide range of doses in these studies. Further, at doses that have demonstrated clinical activity, lumateperone has caused fewer adverse effects than those typically associated with antipsychotic drug treatment, such as impaired motor function. These adverse side effects can be a major cause of patient noncompliance with current antipsychotic therapies and can lead to poorer social function.

Phase 2 Clinical Trial (ITI-007-005)

Lumateperone exhibited antipsychotic efficacy in ITI-007-005, a randomized, double-blind, placebo and active controlled Phase 2 clinical trial in patients with an acutely exacerbated episode of schizophrenia. In December 2013, we announced the clinical results from this Phase 2 trial. In this Phase 2 trial, 335 patients were randomized to receive one of four treatments: 60 mg of ITI-007, 120 mg of ITI-007, 4 mg of risperidone (active control) or placebo in a 1:1:1:1 ratio. Patients received study treatment orally once daily in the morning for 28 days. Of those randomized, 311 patients were included in the intent-to-treat primary analysis. Subject participation lasted approximately 7 to 8 weeks, including a one week screening period, a four week treatment period followed by stabilization on standard of care, and a safety follow up visit approximately two weeks after stabilization. The primary endpoint for this clinical trial was change from baseline to Day 28 on the PANSS total score. The PANSS is a well-validated 30-item rating scale that measures the ability of a drug to reduce schizophrenia symptom severity. The PANSS measures positive symptoms, such as delusions, suspiciousness, and hallucinations; negative symptoms, such as blunted affect, social and emotional withdrawal, and stereotyped thinking; and general psychopathology, such as anxiety, tension, depression, and active social avoidance.

Secondary endpoints in this trial included weekly assessments of the PANSS total score as well as its subscales (Positive Symptom Subscale, Negative Symptom Subscale, and General Psychopathology Subscale) and the Negative Symptom Factor (based on a subset of PANSS questions), individual item response on the PANSS, and the Calgary Depression Scale for Schizophrenia. Safety and tolerability were also assessed.

In December 2013, we announced that topline results from the ITI-007-005 study indicated that lumateperone (ITI-007 60 mg) met the trial s pre-specified primary endpoint, improving symptoms associated with schizophrenia as measured by a statistically significant and clinically meaningful decrease in the PANSS total score. The trial also met key secondary outcome measures related to efficacy on PANSS subscales and safety.

Many patients with schizophrenia have deficits in social function. Social function is the ability to recognize, understand, process and use external cues to solve problems, maintain work performance and conduct interpersonal relationships. Deficits in social function often remain after positive symptoms, such as hallucinations and delusions, have resolved in these patients. In the Phase 2 trial, lumateperone exhibited a differentiating response profile across a broad range of symptoms that we believe is consistent with improvements in these social functioning deficits. The study also showed that lumateperone was well-tolerated at the tested doses. Lumateperone demonstrated a favorable

safety profile in the study without characteristic antipsychotic drug side effects or any serious adverse events.

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ITI-007 at a dose of 60 mg demonstrated a statistically significant improvement in psychosis ($p = 0.017$) on the trial s pre-specified primary endpoint, which was change from baseline on the PANSS total score, compared to placebo. The primary statistical analysis was pre-specified and used a Mixed-Effect Model Repeated Measure method for handling missing data in the intent-to-treat, or ITT, study population and a Bonferroni procedure to correct for multiple two-sided comparisons (each dose of ITI-007 compared to placebo). The trial s pre-specified sensitivity analysis on the primary endpoint used the analysis of covariance, or ANCOVA, model and last observation carried forward, or LOCF, method for handling missing data for the ITT population and confirmed the positive outcome with statistically significant improvements compared to placebo in patients receiving the 60 mg dose of ITI-007 ($p = 0.011$). ITI-007 at a dose of 60 mg also significantly improved the positive symptom subscale ($p < 0.05$) and the general psychopathology subscale ($p < 0.05$) on the PANSS after 28 days of treatment using the ANCOVA-LOCF on the ITT population.

The improvement in the PANSS total score in the 120 mg dose group did not reach statistical significance. We believe that it is possible that sedation, the most frequent side effect in the 120 mg dose group, interfered with the ability to detect an efficacy signal at this dose administered once daily in the morning. Approximately 32.5% of subjects randomized to 120 mg of ITI-007 experienced sedation/somnolence, compared to 21% of subjects randomized to risperidone, 17% of subjects randomized to 60 mg of ITI-007, and 13% randomized to placebo. We believe that nighttime administration may be more appropriate for testing the effectiveness of the 120 mg dose of ITI-007 in this patient population. In the trial, the 60 mg dose of ITI-007 was effective when administered once daily in the morning.

Consistent with preliminary indications from the interim analysis and with the drug candidate s pharmacological profile, ITI-007 at a dose of 60 mg significantly improved certain items on the negative symptom and general psychopathology subscales consistent with improved social function. The study was statistically powered only on the primary endpoint. Lumateperone did significantly improve many secondary endpoints, although the study was not designed for significance on secondary endpoints and was not powered to detect statistical differences in subgroup analyses.

A high percentage (74%) of randomized subjects completed trial participation. Only 19% of subjects discontinued from study treatment during the 28 day study treatment period, and an additional 7% of subjects completed study treatment but were lost to follow up.

In the Phase 2 trial, lumateperone was well-tolerated. The most frequent AE was sedation, as described above. There were no serious adverse events related to lumateperone. There were no clinically meaningful changes in safety measures with lumateperone. Notably, lumateperone demonstrated a favorable metabolic profile with no increase of blood levels of glucose, insulin, cholesterol or triglycerides over a four week treatment period. Moreover, in contrast to risperidone, 60 mg of ITI-007 was effective with no difference from placebo on weight change parameters, prolactin levels, extrapyramidal symptoms (EPS) or akathisia. Lumateperone was not associated with EPS as measured by the Simpson-Angus Scale, Barnes Akathisia Rating Scale, or Abnormal Involuntary Movement Scale. There was no increase in suicidal ideation or behavior with lumateperone.

Phase 3 Clinical Trials and Regulatory Plans

We have conducted two randomized, double-blind, placebo-controlled Phase 3 clinical trials of lumateperone in patients with acutely exacerbated schizophrenia. In September 2015, we announced top-line clinical results from our first Phase 3 clinical trial of lumateperone for the treatment of patients with schizophrenia. This randomized, double-blind, placebo-controlled Phase 3 clinical trial was conducted at 12 sites in the United States with 450 patients randomized (1:1:1) to receive either 60 mg of ITI-007, 40 mg of ITI-007 or placebo once daily in the morning for 28 days. The pre-specified primary efficacy measure was change from baseline versus placebo at study endpoint (4

weeks) on the centrally rated Positive and Negative Syndrome Scale, or PANSS, total score. In this trial, the once-daily dose of 60 mg of ITI-007 met the primary endpoint and

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demonstrated antipsychotic efficacy with statistically significant superiority over placebo at week 4 (study endpoint) with additional improvements observed in social function. Moreover, the 60 mg dose of ITI-007 showed significant antipsychotic efficacy as early as week 1, which was maintained at every time point throughout the entire study. ITI-007 showed a dose-related improvement in symptoms of schizophrenia with the 40 mg dose approximating the trajectory of improvement seen with the 60 mg dose, but the effect with 40 mg did not reach statistical significance on the primary endpoint. In addition, the 60 mg dose of ITI-007 met the key secondary endpoint of statistically significant improvement on the Clinical Global Impression Scale for Severity of Illness, or CGI-S. The 40 mg dose of ITI-007 also demonstrated a statistically significant improvement versus placebo on the CGI-S, though not formally tested against placebo as a key secondary endpoint since it did not separate on the primary endpoint. A high treatment completion rate was observed with ITI-007 (87% of patients completed treatment on ITI-007 60 mg, 82% completed on ITI-007 40 mg, and 75% completed on placebo). Patients randomized to ITI-007 60 mg demonstrated a statistically significant longer time to treatment discontinuation due to any reason compared to placebo ($p=0.006$) and a statistically significant longer time to treatment discontinuation due to lack of efficacy ($p=0.01$). Consistent with previous studies, lumateperone had a favorable safety and tolerability profile as evidenced by motoric, metabolic, and cardiovascular characteristics similar to placebo, and no clinically significant changes in akathisia, extrapyramidal symptoms, prolactin, body weight, glucose, insulin, or lipids. The number of patients who discontinued treatment in this study due to an adverse event was low and the time to treatment discontinuation due to an adverse event was not statistically significantly different from placebo for either dose of lumateperone.

In September 2016, we announced top-line results from the second Phase 3 clinical trial (ITI-007-302) of lumateperone for the treatment of patients with schizophrenia. In this trial, neither dose of lumateperone separated from placebo on the primary endpoint, change from baseline on the PANSS total score, in the pre-defined patient population. The active control, risperidone, did separate from placebo. In this trial, lumateperone was statistically significantly better than risperidone on key safety and tolerability parameters and exhibited a safety profile similar to placebo. This replicates the safety and tolerability findings of our Phase 2 study (ITI-007-005) in which the efficacy of ITI-007 60 mg and risperidone, the active control, were similar. We believe lumateperone did not separate from placebo on the pre-specified primary endpoint in the ITI-007-302 study in part due to an unusually high placebo response at certain sites which disproportionately affected the trial results and contributed to the efficacy outcome of this study compared to our two previous positive efficacy studies. In addition, we believe other confounding factors may have played a role in the efficacy outcome of ITI-007-302, including an expectation bias and the potential for functional unblinding. We believe the lumateperone late-stage clinical development program, including two large, well-controlled positive studies and supportive evidence from this second Phase 3 study, collectively provide evidence of the efficacy and safety of lumateperone for the treatment of schizophrenia. Across all three of our efficacy trials, ITI-007 60 mg improved symptoms of schizophrenia with the same trajectory and magnitude of change from baseline in the primary endpoint, the PANSS total score.

As part of our ongoing dialogue with the FDA regarding our lumateperone development program in schizophrenia, we requested guidance from the FDA on the acceptability of the two positive well controlled clinical trials we have conducted (Study ITI-007-005 and Study ITI-007-301), with supportive evidence from Study ITI-007-302, as the basis for the submission of an NDA, for the treatment of schizophrenia. In connection with this request we provided extensive information and data analyses to the FDA relating to the three studies. The FDA has confirmed that the results of Study ITI-007-302 do not preclude us from submitting an NDA based on the efficacy studies we have conducted to date. We completed our NDA for lumateperone for the treatment of schizophrenia in the third quarter of 2018 and the FDA accepted for review the NDA in the fourth quarter of 2018. We believe our schizophrenia clinical development program collectively provides evidence of the efficacy and safety of lumateperone for the treatment of schizophrenia.

In addition, the FDA had raised questions relating to certain findings observed in nonclinical toxicology studies of lumateperone in an animal species and requested additional information to confirm that the nonclinical findings are not indicative of a safety risk associated with long term exposure in humans. The data we presented

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supports the position that there are significant species differences in the metabolism of lumateperone. Based on the FDA s agreement that we presented adequate data indicating that the toxicity seen in the animal species is not relevant to humans, we proceeded with our long-term safety study of lumateperone in patients with schizophrenia. Further, based on feedback from the FDA, we incorporated additional monitoring in our long-term safety study for metabolites seen in animal species but not seen to date in humans, and also will continue to monitor for toxicities in our nonclinical studies. With over 1,900 people exposed to date, lumateperone has been well-tolerated with a safety profile similar to placebo.

In November 2017, we announced that the FDA has granted Fast Track designation for lumateperone for the treatment of schizophrenia. We requested Fast Track designation for lumateperone based on clinical evidence that lumateperone has the potential to address the unmet medical need for the treatment of schizophrenia with significant improvements on several clinically significant safety parameters, including with respect to metabolic, motor and cardiovascular issues associated with many currently available antipsychotic agents. The FDA s Fast Track designation is designed to facilitate the development and expedite the review of drug candidates to treat serious and life-threatening conditions. Fast Track designation may allow for more frequent meetings and communications with the FDA to discuss a drug candidate s development plans and review process. Drug candidates with Fast Track designation may also qualify for priority review to expedite the FDA review process, if relevant criteria are met.

We had a pre-NDA meeting with the FDA in the first quarter of 2018 and reached agreement on the timing and content of a rolling NDA submission for lumateperone for the treatment of schizophrenia. We initiated the rolling submission of our NDA with the FDA for lumateperone for the treatment of schizophrenia in the second quarter of 2018, we completed this NDA submission in the third quarter of 2018 and the FDA accepted for review the NDA in the fourth quarter of 2018. The FDA assigned a PDUFA target action date of September 27, 2019. Meetings with the FDA may be requested, as needed, to discuss in greater detail our plans for schizophrenia, and other elements of our regulatory strategy, including additional therapeutic indications, as the program progresses. Our clinical plans may change based on any discussions with the FDA, the relative success and cost of our research, preclinical and clinical development programs, whether we are able to enter into future collaborations, and any unforeseen delays or cash needs. If the FDA does not agree with our clinical development plans for lumateperone, our development of lumateperone may be delayed and the costs of our development of lumateperone could increase, which would have a material adverse effect on our business, financial condition and results of operations.

We are also developing long acting injectable formulations of ITI-007 for the treatment of schizophrenia. This is a preclinical stage development program.

PET study of lumateperone in patients with stable schizophrenia

On September 16, 2015, we announced top-line data from an open-label PET study of lumateperone examining brain occupancy of striatal D2 receptors. This study was conducted in patients diagnosed with schizophrenia who were otherwise healthy and stable with respect to their psychosis. After washout from their previous antipsychotic medication for at least two weeks, PET was used to determine target occupancy in brain regions at baseline (drug-free) and again after two weeks of once daily lumateperone oral administration. In this trial, the 60 mg dose of ITI-007 was associated with a mean of approximately 40% striatal dopamine D2 receptor occupancy. As predicted by preclinical and earlier clinical data, lumateperone demonstrated antipsychotic effect at relatively low striatal D2 receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D2 receptors. We believe this mechanism likely contributes to the favorable safety profile of lumateperone, with reduced risk for hyperprolactinemia, akathisia, extrapyramidal symptoms, and other motoric side effects.

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Open-label safety switching study

In September 2017, we announced positive top-line data from the first part of an open-label safety switching study in which 302 patients with stable symptoms of schizophrenia were switched from standard-of-care antipsychotic medications to lumateperone (ITI-007 60 mg) with no dose titration of lumateperone required for a six-week treatment duration, then switched back to standard-of-care. Many currently available antipsychotic agents are associated with motor side effects and/or weight gain, cardiovascular liabilities, dyslipidemia, and hyperglycemia. In this study, lumateperone was generally well tolerated with a favorable safety profile. Statistically significant improvements from standard-of-care baseline were observed in body weight, cardiometabolic and endocrine parameters in patients with stable symptoms of schizophrenia when switched to lumateperone and worsened again when switched back to standard-of-care medication. Additionally, treatment with lumateperone was not associated with the motor or cardiovascular disturbances often associated with other antipsychotic medications. These data are consistent with previous study results reflecting a safety profile similar to placebo in placebo-controlled trials with lumateperone in patients with acutely exacerbated schizophrenia and extend this favorable safety profile to this stable patient population. Symptoms of schizophrenia did not worsen upon switch to lumateperone from standard-of-care. Rather, statistically significant improvement from baseline was observed in the PANSS mean total score. Notably, greater improvements were observed in subgroups of patients with elevated symptomatology such as those with comorbid symptoms of depression and those with prominent negative symptoms.

In December 2018, we announced positive results from our ongoing long-term safety switching study. In the second part of the study, 603 patients with stable symptoms of schizophrenia were switched from standard-of-care antipsychotic medications to lumateperone (ITI-007 60 mg) for up to one year with no dose titration of lumateperone required. In contrast to many other antipsychotics that are associated with weight gain, in this study, mean body weight significantly decreased after switch from standard-of-care antipsychotic treatment at six months (-1.82 kg at Day 175, $p < 0.001$) and one year (-3.16 kg at Day 350, $p < 0.001$) of treatment with lumateperone. Of the 603 patients in the trial, 24% experienced a decrease of ³7% from their standard-of-care baseline body weight over the course of the study, while only 8% experienced a body weight increase of ³7%. Long-term treatment with lumateperone also demonstrated a favorable cardiometabolic and endocrine safety profile with stable blood levels of glucose, insulin, and HDL cholesterol and statistically significant ($p < 0.001$) reductions from standard-of-care baseline in total cholesterol, LDL cholesterol and prolactin. With long-term administration, the most frequent (occurring in ³ 5% of patients) treatment-emergent adverse events, regardless of whether such adverse event was related to treatment, were decrease in weight (9.5%), dry mouth (7.6%), diarrhea (7.0%), and headache (5.1%). The proportion of patients experiencing motor side effects while on lumateperone was low: any adverse event related to extrapyramidal side effects combined including akathisia (5.3%); and akathisia specifically (0.5%). There were no signs of treatment-emergent extrapyramidal side effects, akathisia, or dyskinesia as measured by the Simpson Angus Scale, or SAS, the Barnes Akathisia Rating Scale, or BARS, or the Abnormal Involuntary Movement Scale or AIMS, respectively. In addition, there were no signs of treatment-emergent suicidal ideation or behavior as measured by the Columbia-Suicide Severity Rating Scale, or C-SSRS. As observed in the first part of the study (6 weeks of treatment), patients treated with lumateperone in the second part of the study (up to one year of treatment) did not worsen with respect to their symptoms of schizophrenia upon switch from standard of care. Rather, statistically significant ($p < 0.001$) improvements from a baseline score of 62.9 were observed on the PANSS. Given the favorable safety profile of lumateperone observed to date, the study has been extended to allow patients to stay on lumateperone for more than one year and study conduct is ongoing.

Lumateperone for the treatment of depressive episodes associated with bipolar disorder (bipolar depression)

The pharmacological profile of lumateperone offers the potential to treat bipolar mania, depression, and mixed symptoms at doses similar to those targeted for the treatment of schizophrenia. We believe that lumateperone may be

effective alone or in combination with mood stabilizers. Given that many patients with

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bipolar disorder also experience disturbed sleep and cognitive impairment similar to that observed in schizophrenia, we believe that lumateperone may treat a wide array of symptoms in patients with bipolar disorder, including improvement of cognition and sleep.

Our bipolar depression program consists of three Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials. In the ITI-007-401 and the ITI-007-404 trials, lumateperone is being evaluated as a monotherapy and in the ITI-007-402 trial, lumateperone is being evaluated as an adjunctive therapy with lithium or valproate. All three trials are evaluating lumateperone in patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode. In the ITI-007-401 and the ITI-007-402 trials, patients are randomized to receive one of three treatments: 60 mg ITI-007, 40 mg ITI-007, or placebo in a 1:1:1 ratio orally once daily for 6 weeks. In the ITI-007-404 trial, patients are randomized to receive 60 mg ITI-007 or placebo in a 1:1 ratio orally once daily for 6 weeks. In the ITI-007-401 and the ITI-007-404 trials, patients receive lumateperone or placebo as a monotherapy. In the ITI-007-402 trial, patients receive lumateperone or placebo adjunctive to their existing mood stabilizer lithium or valproate. In each of these trials, we are employing a number of strategies designed to ensure we recruit appropriately diagnosed patients in an effort to reduce the risk of a high placebo response. We have completed patient enrollment in the ITI-007-401 trial conducted in the United States and in the ITI-007-404 trial conducted globally. We anticipate reporting topline results from the ITI-007-401 and ITI-007-404 trials simultaneously in the second quarter of 2019. Subject to the outcome of these trials, we expect to submit an NDA for bipolar depression in the second half of 2019. Our global ITI-007-402 trial evaluating adjunctive lumateperone in bipolar depression is ongoing. In connection with the global strategy of this program we are adding sites outside the U.S. to the ITI-007-402 trial and we expect to provide anticipated timelines for this trial after completing the expansion.

The primary endpoint for these clinical trials is change from baseline at Day 42 on the Montgomery-Åsberg Depression Rating Scale (MADRS) total score versus placebo. The MADRS is a well-validated 10-item checklist that measures the ability of a drug to reduce overall severity of depressive symptoms. Individual items are rated by an expert clinician on a scale of 0 to 6 in which a score of 6 represents the most depressed evaluation for each item assessed. The total score ranges from 0 to 60. Secondary endpoints include measures of social function and quality of life that may illustrate the differentiated clinical profile of lumateperone. Safety and tolerability are also assessed in these clinical trials.

Lumateperone for the treatment of behavioral disturbances associated with dementia, including Alzheimer s disease

Behavioral disturbances are common in dementia and AD. These disturbances are a major component of the burden to caregivers, and often lead to institutionalization. Although currently available treatments for patients with dementia mainly address cognitive disturbances, behavioral disturbances are considerably more problematic and likely more amenable to drug treatment. Several behavioral symptoms are quite prevalent in patients with dementia, including patients with AD. In the fourth quarter of 2014, we announced the top-line data from ITI-007-200, a Phase 1/2 clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of lumateperone in healthy geriatric subjects and in patients with dementia, including AD. The ITI-007-200 clinical trial was conducted in two parts. Part 1 was a randomized, double-blind, placebo-controlled multiple ascending dose evaluation of lumateperone in healthy geriatric subjects. In each of three cohorts in Part 1, approximately 10 subjects were randomized to receive lumateperone (N=8) or placebo (N=2) orally once daily in the morning for seven days. Doses of ITI-007 up to and including 30 mg were evaluated in three cohorts in Part 1. In Part 2, eight patients with dementia were randomized to receive 9 mg ITI-007 (N=5) or placebo (N=3) orally once a day in the evening for seven days. The primary objectives of the study were to evaluate the safety, tolerability and pharmacokinetics of lumateperone in the elderly and in the target dementia patient population. Secondary measures were included to explore the effects of lumateperone on cognition and agitation. The Hopkins Verbal Learning Test-R, or HVLT-R, was used to assess cognition in healthy geriatric subjects and dementia patients. The results demonstrated impaired verbal learning and memory (recall and

recognition memory) by dementia patients relative to healthy geriatric subjects. Moreover, the data indicated that healthy

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geriatric subjects treated with lumateperone for approximately one week experienced an improvement in verbal learning and memory relative to placebo-treated subjects. Dementia patients treated with lumateperone showed enhanced recognition memory, making fewer false positive errors (i.e., responding yes to non-target words) than patients treated with placebo. Other secondary endpoints in the ITI-007-200 clinical trial included the assessment of agitation. However, none of the study participants experienced agitation at baseline or during the study, and therefore no signals on this behavioral endpoint could be assessed. The completion of this study marked an important milestone in our strategy to develop low doses of lumateperone for the treatment of behavioral disturbances associated with dementia and related disorders. The ITI-007-200 trial results indicate that lumateperone has a positive safety profile and is well-tolerated across a range of low doses, has linear- and dose-related pharmacokinetics and may improve cognition in the elderly. The most frequent adverse event was mild sedation at the higher doses. We believe these results further position lumateperone as a development candidate for the treatment of behavioral disturbances in patients with dementia and other neuropsychiatric and neurological conditions.

In the second quarter of 2016, we initiated Phase 3 development of lumateperone for the treatment of agitation in patients with dementia, including AD. Our ITI-007-201 trial was a Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trial in patients with a clinical diagnosis of probable AD and clinically significant symptoms of agitation. In this trial, approximately 360 patients were planned to be randomized to receive 9 mg ITI-007 or placebo in a 1:1 ratio orally once daily for four weeks. The primary efficacy measure was the Cohen-Mansfield Agitation Inventory Community version, or CMAI-C. The CMAI-C is a well-validated 37-item scale that measures the ability of a drug to reduce overall frequency of agitation symptoms, including aggressive behaviors. Individual items were to be rated by an expert clinician on a scale of 1 to 7 in which a score of 7 represents the most frequent for each item assessed. The key secondary efficacy measure was the CGI-S. Other exploratory secondary endpoints included measures of other behavioral disturbances associated with dementia. Safety and tolerability were also to be assessed in the trial. In the fourth quarter of 2018, an independent data monitoring committee, or DMC, completed a pre-specified interim analysis of the ITI-007-201 trial, concluded that the trial is not likely to meet its primary endpoint upon completion and therefore recommended the study should be stopped for futility. As a result, we determined to discontinue the ITI-007-201 trial. Lumateperone was generally well tolerated in the ITI-007-201 trial and the decision to discontinue the study was not related to safety. We are analyzing the data set from this trial and will determine the next steps in our program following completion of this analysis.

Lumateperone for the treatment of sleep disturbances associated with neurologic and psychiatric disorders

A Phase 2 double-blind, placebo controlled cross-over clinical trial conducted in 19 patients with primary insomnia with disturbed sleep maintenance at low doses of lumateperone was completed in 2008 in Europe. The primary outcome measure was slow wave sleep as determined by polysomnography. Lumateperone demonstrated a dose-related statistically significant increase in slow wave sleep. Secondary measures were consistent with improvement of sleep maintenance in patients with primary insomnia, indicated by decreased waking after sleep onset, increased total sleep time, and no increase in latency to sleep onset. At these low doses, lumateperone did not induce sleep, but rather helped maintain sleep once sleep had been initiated. In addition, lumateperone was not associated with next day cognitive impairment, or hang-over effects. We believe that lumateperone may be particularly useful in the treatment of sleep disorders that accompany neuropsychiatric and neurologic disorders, including schizophrenia, autism spectrum disorder, or ASD, Parkinson s disease and dementia. Previous work has suggested that selective 5-HT2A receptor antagonists increase deep, slow wave sleep in both humans and animals. We believe, however, that other neuropharmacological mechanisms, in addition to 5-HT2A receptor antagonism, such as engaging some dopamine modulation, may be beneficial for the successful treatment of sleep maintenance insomnia, or SMI, in humans. We believe that lumateperone represents a new approach to the treatment of sleep maintenance insomnia because of its unique pharmacology and neuropharmacological interactions beyond selective 5-HT2A receptor antagonism. We believe that lumateperone offers a potentially new approach to the treatment of sleep

maintenance disorders, particularly in those disorders that accompany neuropsychiatric and neurologic disorders. Many of these disorders are accompanied by profound sleep deficits,

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which impair daytime functioning including cognition, exacerbate disease symptoms and increase the cost of care. We are presently exploring clinical designs to incorporate the examination of sleep disturbances in one or more of these indications. There is no assurance that any such design would be sufficient for an FDA approval for this indication.

Lumateperone for the treatment of sleep and behavioral disturbances associated with autism spectrum disorder

Sleep problems are common in patients with ASD and are not adequately treated by currently available interventions. Approximately two thirds of children and adolescents with ASD experience sleep problems, higher than the rate of sleep problems in age-matched developmentally typical children. Moreover, individuals with ASD suffer from behavioral disturbances, including aggression, irritability, anxiety and depression. With its multiple pathway mechanism of action, we believe that lumateperone could address the multi-faceted behavioral symptoms associated with ASD. 5-HT2A receptor antagonism is predicted to increase slow wave sleep, improve sleep maintenance and reduce aggression. D2 receptor modulation is predicted to improve sleep maintenance and reduce irritability and aggression. Serotonin reuptake inhibition is predicted to reduce anxiety and depression. Accordingly, we believe that lumateperone could improve sleep maintenance, reduce behavioral disturbances and enhance social interaction in patients with ASD. We believe that our completed Phase 1 studies support advancing lumateperone into Phase 2 trials in this patient population, and we are presently exploring the feasibility of such trials.

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 selective serotonin reuptake inhibitors, or SSRIs. Dopamine modulation by lumateperone may 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. Lumateperone also activates key proteins in the mTOR pathway similar to ketamine which has shown rapid antidepressant effects, yet lumateperone has not been associated with ketamine-like safety concerns. As such, lumateperone may be effective for the treatment of mood disorders including MDD, posttraumatic stress disorder and intermittent explosive disorder. We have commenced our program of lumateperone in MDD. In previous studies, schizophrenia patients with co-morbid depression experienced improvements in depressive symptoms. Additionally, recent preclinical data support the potential for rapid-acting antidepressant effects. In order to explore the effect of different modes of drug administration and the potential for rapid-onset antidepressant activity, our program includes the assessment of novel formulations of lumateperone. Pharmacokinetic studies evaluating these novel formulations are currently ongoing.

ITI-002 (PDE1) Program

We have a second major program called ITI-002 that has yielded a portfolio of compounds that selectively inhibits the enzyme phosphodiesterase type 1, or PDE1. In addition, PDE1 inhibitors may have utility in treating non-CNS disorders. On February 25, 2011, we (through our wholly owned operating subsidiary, ITI) and Takeda Pharmaceutical Company Limited, or Takeda, entered into a license and collaboration agreement, or the Takeda License Agreement, under which we agreed to collaborate to research, develop and commercialize our proprietary compound ITI-214 and other selected compounds that selectively inhibit PDE1 for use in the prevention and treatment of human diseases. Takeda conducted four Phase 1 studies. A single rising dose study was conducted in the U.S. in healthy male and female, Japanese and non-Japanese volunteers. In a second U.S. study, ITI-214 was administered once daily over 14 days to healthy volunteers and patients with stable schizophrenia. In a third study, conducted in Japan, ITI-214 was administered for seven days at multiple rising oral doses in both male and female healthy volunteers. A fourth study compared the relative bioavailability of

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oral formulations of ITI-214 used in all previous studies to an immediate-release tablet, either with or without food in healthy volunteers. In these studies, ITI-214 demonstrated a favorable safety profile and was generally well-tolerated across a broad range of doses both in healthy volunteers and in patients with schizophrenia with a pharmacokinetic profile that supports once daily dosing. We believe ITI-214 is the first compound in its class to successfully advance through Phase 1 clinical trials. On October 31, 2014, we entered into an agreement with Takeda terminating the Takeda License Agreement, or the Termination Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. On September 15, 2015, Takeda completed the transfer of the IND for ITI-214 to us. We intend to pursue the development of our PDE program, including ITI-214, for the treatment of several CNS and non-CNS conditions, including cardiovascular disease. Following the positive safety and tolerability results in our Phase 1 program, we initiated our development program for ITI-214 for Parkinson s disease and commenced patient enrollment in the third quarter of 2017 in a Phase 1/2 clinical trial of ITI-214 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 the fourth quarter of 2018, we announced that the Phase 1/2 clinical trial of ITI-214 has been completed and topline results demonstrated ITI-214 was generally well-tolerated with a favorable safety profile and clinical signs consistent with improvements in motor symptoms and dyskinesias. In addition, in the first quarter of 2018, the investigational new drug application, or IND, went into effect for ITI-214 for the treatment of heart failure. We have initiated clinical conduct of the first clinical study in this program, a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 to evaluate safety and hemodynamic effects in patients with systolic heart failure.

Additional PDE Programs

There are multiple forms and isoforms of PDE with distinct roles in intracellular signaling. We have developed strong internal expertise in the design and synthesis of inhibitors specific for individual PDE isoforms. Based on our understanding of the expression and functions of these isoforms in the CNS, we have identified PDE2 and PDE9 as compelling targets for drug discovery. We believe that inhibitors of these PDEs may be useful in treating neurodegeneration and bioenergetic failure in a variety of CNS diseases.

ITI-333 Program

ITI-333 is a pre-clinical stage development program. ITI-333 is designed 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. We believe the potential exists for ITI-333 to address these challenges. In preclinical studies, ITI-333 functions as a partial agonist at mu opiate receptors, attenuating the behavioral effects of morphine while displaying full analgesic efficacy that is reversible by the mu opiate antagonist, naloxone. ITI-333 also acts as a 5-HT2A antagonist with interactions at D1 receptors. Preclinical safety studies with ITI-333 are currently ongoing and we expect to initiate a clinical program in 2019. If successfully translated to humans, this unique pharmacological profile may yield clinical utility for the treatment of substance use disorders and pain.

Intellectual Property

Our Patent Portfolio

As of February 1, 2019, we owned or controlled approximately 105 patent families filed in the United States and other major markets worldwide, including approximately 83 issued or allowed U.S. patents, 27 pending U.S. patent applications, 216 issued or allowed foreign patents and 184 pending foreign patent applications, directed to novel compounds, formulations, methods of treatment, synthetic methods, and platform technologies.

Our ITI-007 program on novel compounds for neuropsychiatric and neurodegenerative diseases includes patents exclusively in-licensed from Bristol-Myers Squibb on families of compounds, including the ITI-007 lead molecule. We have extensively characterized this lead and filed additional patent applications on polymorphs,

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pharmaceutical formulations, new indications, improved methods of manufacture, metabolites, derivatives, and structurally related novel compounds. As of February 1, 2019, our ITI-007 program consisted of approximately 30 patent families that we own or control, filed in the United States and other major markets, including 31 issued or allowed U.S. patents, 13 pending U.S. patent applications, 126 issued or allowed foreign patents and 65 pending foreign patent applications. Patent protection for ITI-007 thus includes:

Summary Description of Patent or Patent Application	**United States or Foreign Jurisdiction**	**Expiration Date**
Base ITI-007 Patent	**Granted:** United States, JP, EP (AT, BE, CH, DE, ES, FR, GB, IE, IT, LU, MC)	June 15, 2025 (including regulatory extensions; additional Orange Book-listable protection to 2034; does not include expected 6 month extension in US for pediatric studies)
Supplemental ITI-007 Patent	**Granted:** US, 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); March 12, 2029 (ex-US)
ITI-007 Dosage Patents (including schizophrenia, bipolar depression, sleep disorder indications)	**Granted:** US, AU, CN, JP, MX Pending: US (continuation), CA, (divisional), EP, IN, KR, MX (divisional)	December 28, 2029 (US); May 27, 2029 (ex-US)
Patents for Additional Dosage Forms	Pending: US provisional, US national and/or PCT	2037-2039
Patents for Additional Indications	Granted or pending in US, EP, JP, and other countries	2033-2034

Our program on PDE1 inhibitors for cognition, dopamine-mediated and other disorders, cardiovascular disorders, as well as several others, includes patent protection across 19 families for the lead molecule, ITI-214, as well as a wide range of filings on other proprietary compounds and indications. The ITI-214 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 for up to 11 years from commercial launch. We have obtained patent coverage for ITI-214 in the treatment of cardiovascular disorders, including heart failure, that extends to 2034. We are also evaluating potential follow-on compounds for ITI-214 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. 12 families of patent applications have been filed, including one which has already resulted in a

U.S. patent. 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.

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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 exacerbated schizophrenia. Upon FDA acceptance of an 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 accrued the $2.0 million milestone, which was paid in the first quarter of 2019. Remaining potential milestone payments under the agreement with respect to lumateperone total $10.0 million, including a $5.0 million milestone payable upon an NDA approval. 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 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, active pharmaceutical ingredient, or API, and finished product for our preclinical research and clinical trials, including the Phase 3 trials for lumateperone for the treatment of bipolar depression. We believe that we would be able to contract with other third-party contract manufacturers to obtain 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.

On January 4, 2017, we entered into a supply agreement, or the Siegfried Agreement, with Siegfried Evionnaz SA, or Siegfried. Under the Siegfried Agreement, 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, with the first 12 months of each forecast being binding on us. Under the

agreement, our purchase prices for supply of the API from Siegfried are specified prices based on the volume of API produced. The term of the Siegfried Agreement extends for five years. Either party may terminate the agreement prior to its expiration upon an uncured material breach by the other party, the liquidation or

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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, a continuing force majeure event affecting the other party, or the debarment or certain other events involving the other party s employees, affiliates or agents. Under the Siegfried Agreement, we have the right to and may purchase the API for lumateperone from other suppliers, including if Siegfried cannot fulfill our requirements.

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.

Sales and Marketing

We currently are in the process of building our marketing, sales or distribution capabilities in preparation for the commercial launch of lumateperone for schizophrenia if our NDA is approved by the FDA. In order to commercialize any of our product candidates, we must develop these capabilities internally or through collaboration with third parties. We may choose to commercialize our products in markets outside of the United States by establishing one or more strategic alliances in the future.

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 developing and obtaining approval of our product candidates, the resulting products would compete with a variety of established drugs in the areas of our targeted CNS therapeutic indications. Our potential products for the treatment of schizophrenia and bipolar disorder would compete with, among other branded products including, Latuda®, marketed by Sunovion, Rexulti®, marketed by Otsuka Pharmaceutical, VRAYLAR®, marketed by Allergan, Saphris®, marketed by Allergan, and Fanapt®, marketed by Vanda Pharmaceuticals. In addition, our product candidates, if approved, will compete with, among other generic antipsychotic products, aripiprazole, haloperidol, paliperidone, risperidone, quetiapine/XR, olanzapine and clozapine.

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 we have a product to sell. 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;

preclinical studies and clinical trials of potential pharmaceutical products; and

obtaining FDA and other regulatory clearances.

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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 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, 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, 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 preclinical 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 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 product candidates has been generated in compliance with Good Clinical Practices; and

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FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Preclinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical 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, sponsor or an Institutional Review Board, or IRB, may place a study on hold at any time during development.

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 medical center 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. Study subjects must sign an informed consent form before participating 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 or an IRB may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. 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.

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

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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 preclinical 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, which is waived for the first NDA submitted by a qualifying small business. 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 priority review of those NDAs, 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 and may deem it to be inadequate to support approval, and we cannot be sure that any approval will be granted on a timely basis, if at all. 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. If the FDA evaluates the NDA and the manufacturing facilities are deemed acceptable, the FDA may issue an approval letter, or in some cases 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. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or additional clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. 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 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 effects 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. 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.

If post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. 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/or 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 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 restrictions on a product, manufacturer or holder of an approved NDA, including recall of the product from the market or withdrawal of approval of the NDA for that drug.

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. 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

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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 conditions 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 preclinical studies, adequate and well-controlled 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 U.S.). The exclusivity prohibits the approval of the same drug for the same disease or condition, unless there is a showing of clinical superiority.

Foreign Regulation

In addition to regulations in the United States, we will be 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 products that we market in the future, 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 products that, if successfully developed, we bring to market.

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 in the 115th United States Congress and under the Trump Administration. For instance, the Bipartisan Budget Act of 2018 increased the ACA required manufacturer point-of-sale discount from 50% to 70% off the negotiated price for Medicare Part D beneficiaries during their

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coverage gap period beginning in 2019. 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.

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. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to collect additional data or conduct additional preclinical studies and clinical trials. 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.

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. 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.

Outside the United States, our ability to market a product is contingent upon obtaining marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from country to country.

At such time as we market, sell and distribute any products for which we obtain marketing approval, it is possible that our business activities could be 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 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 health care items or service 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;

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;

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The federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, requires certain pharmaceutical manufacturers to engage in extensive tracking of payments and other transfers of value to physicians and teaching hospitals, and to submit such data to the Centers for Medicare and Medicaid Studies (CMS), which will then make all of this data publicly available on the CMS website; and

Analogous state 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.

Violations of fraud and abuse 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.

Description of the Merger

Pursuant to an Agreement and Plan of Merger dated August 23, 2013, or the Merger Agreement, by and among Oneida Resources Corp., which we refer to as the Company, we, our and us; ITI, Inc., a Delaware corporation and wholly-owned subsidiary of the Company, or Merger Sub; and Intra-Cellular Therapies, Inc., a Delaware corporation, which we refer to as ITI; Merger Sub merged with and into ITI, with ITI remaining as the surviving entity and a wholly-owned operating subsidiary of the Company. This transaction is referred to throughout this report as the Merger. The Merger was effective on August 29, 2013, upon the filing of a Certificate of Merger with the Secretary of State of the State of Delaware. In connection with the Merger, ITI changed its name to ITI, Inc. and Oneida Resources Corp. assumed the name Intra-Cellular Therapies, Inc. The Merger was accounted for as a capital transaction. Upon the effectiveness of the Merger, the Company s business became the operation of ITI and its business.

At the effective time of the Merger, or the Effective Time, the legal existence of Merger Sub ceased and each share of ITI common stock and each share of ITI preferred stock that was issued and outstanding immediately prior to the Effective Time was automatically exchanged for 0.5 shares of our common stock, which we refer to as the Exchange. Immediately following the Effective Time, we completed the closing of a redemption of 5,000,000 shares of our common stock, or the Redemption, from our then-current sole stockholder, which constituted all of the issued and outstanding shares of our capital stock, on a fully-diluted basis, immediately prior to the Merger. Upon completion of the Merger and the Redemption, the former stockholders of ITI held 100% of the outstanding shares of our capital stock. Unless otherwise indicated in this report, all share and per share figures reflect the exchange of each share of

ITI common stock and each share of ITI preferred stock then outstanding for 0.5 shares of our common stock at the Effective Time.

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Employees

As of February 15, 2019, we employed 73 employees all of whom were full-time. We consider our relations with our employees to be good. To successfully develop our drug candidates, we must be able to attract and retain highly skilled personnel. We anticipate hiring a substantial number of additional employees for sales and marketing, research and development, clinical and regulatory affairs, and general and administrative activities over the next few years. In addition, we intend to use clinical research organizations and third parties to perform our clinical studies and manufacturing.

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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 entitled 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.

Risks Related to Our Business

We depend heavily on the success of our product candidate lumateperone for the treatment of schizophrenia, which has not yet been approved by the FDA. If we experience material delays in obtaining or are unable to obtain marketing approval for lumateperone for the treatment of schizophrenia, our business will be materially harmed.

We believe that a significant portion of the value attributed to our company by investors is based on the commercial potential of lumateperone for the treatment of schizophrenia, which has not yet been approved by the FDA. The FDA has substantial discretion in deciding whether or not lumateperone for the treatment of schizophrenia should be granted approval based our clinical trials and nonclinical studies to date. We completed this NDA submission in the third quarter of 2018 and the FDA accepted for review the NDA in the fourth quarter of 2018. The FDA assigned a Prescription Drug User Fee Act, or PDUFA, target action date of September 27, 2019. There is no assurance, however, that the FDA will complete its review within this timeframe and does not ensure that our NDA for lumateperone for the treatment of schizophrenia will be approved.

Obtaining approval to market lumateperone for the treatment of schizophrenia in a timely manner will depend on many factors, including the following:

- whether or not the FDA determines that the evidence gathered in well-controlled clinical trials, other clinical trials and nonclinical studies of lumateperone demonstrates that lumateperone is safe and effective as a treatment for schizophrenia;

- whether or not the FDA is satisfied that the manufacturing facilities, processes and controls for lumateperone are adequate, that the labeling is satisfactory and that plans for post-marketing studies, safety monitoring and risk evaluation and mitigation are sufficient; and

- the timing and nature of the FDA s comments and questions regarding the NDA for lumateperone for the treatment of schizophrenia, the scheduling and recommendations of any advisory committee meeting to consider lumateperone, the time required to respond to the FDA s comments and questions and to obtain the

final labeling for lumateperone and any other delays that may be associated with the NDA review process. If we experience material delays in obtaining marketing approval for lumateperone for the treatment of schizophrenia in the United States, we will not receive product revenues during the delay. Any such delay may materially harm our product revenues and cash flows. If we do not obtain approval to market lumateperone for the treatment of schizophrenia in the United States, our business will be materially harmed.

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In order to execute our business plan and achieve profitability, we need to effectively commercialize lumateperone for the treatment of schizophrenia.

We cannot be sure that lumateperone for the treatment of schizophrenia will be commercially successful in the pharmaceutical market even if we gain marketing approval for lumateperone for the treatment of schizophrenia in a timely manner. We expect that the initial commercial success of lumateperone for the treatment of schizophrenia, if approved, will depend on many factors, including the following:

- the efficacy, cost, approved use, and side-effect profile of lumateperone regimens relative to competitive treatment regimens for the treatment of schizophrenia;
- the timing of potential marketing approval from the FDA for the treatment of lumateperone;
- the effectiveness of our commercial strategy for the launch and marketing of lumateperone, including our pricing strategy and the effectiveness of our efforts to obtain adequate third-party reimbursements;
- maintaining and successfully monitoring commercial manufacturing arrangements for lumateperone 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 lumateperone;
- the acceptance of lumateperone 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 lumateperone for the treatment of schizophrenia will have a commercially competitive profile, we cannot accurately predict the amount of revenue that will be generated if lumateperone receives regulatory approval. If we do not effectively commercialize lumateperone, 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 lumateperone do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

Even if we gain regulatory approval for any of our drug candidates, if the sales and marketing capabilities we are establishing or our third-party relationships for the commercialization of our drug candidates are not effective, our drug candidates may not be successfully commercialized.

We have no experience as a company in marketing drugs or with respect to pricing and obtaining adequate third-party reimbursement for drugs. We are in the process of building our commercial organization and capabilities in the United States in order to prepare to market lumateperone for the treatment of schizophrenia. We will need to successfully complete the expansion of our capabilities and/or enter into arrangements with third parties to sell and market our

other product candidates, including lumateperone for the treatment of schizophrenia, if they are approved for sale. If our sales and marketing capabilities or our third-party relationships for the commercialization of our drug candidates are not effective, our business could be materially harmed.

We have never generated revenue from product sales and do not expect to do so until at least the fourth quarter of 2019, if ever.

Our ability to generate revenue from product sales and achieve profitability depends on our ability to successfully complete the development of and obtain regulatory approvals necessary to commercialize lumateperone and our other product candidates. We have a limited operating history on which to evaluate our business and prospects. To date, we have not generated any product revenues from our product candidates currently in development. We cannot guarantee that any of our product candidates currently in development will ever become marketable products.

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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, preclinical testing and clinical testing is required before we can file applications with the FDA or other regulatory authorities for premarket 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.

Our lead product candidate, lumateperone, is in Phase 3 clinical development as a novel treatment for schizophrenia, bipolar depression and agitation associated with dementia, including AD. In the third quarter of 2018, we completed the rolling submission of our NDA with the FDA for lumateperone for the treatment of schizophrenia. The FDA accepted for review the NDA in the fourth quarter of 2018 and assigned a Prescription Drug User Fee Act, or PDUFA, target action date of September 27, 2019. There can be no assurance that any NDA that we submit to the FDA will approved by the FDA or that, if approved, we will be able to successfully commercialize lumateperone for the treatment of patients with schizophrenia. In addition, in response to questions raised by the FDA relating to certain findings observed in nonclinical toxicology studies of lumateperone in an animal species, based on feedback from the FDA, we incorporated additional monitoring in our long-term safety study for metabolites seen in animal species but not seen to date in humans, and continued to monitor for toxicities in our nonclinical studies. If the FDA determines the results of our long-term safety study and nonclinical studies do not sufficiently demonstrate the safety and tolerability of long-term use of lumateperone, the FDA may not approve an NDA for lumateperone for a chronic condition such as schizophrenia.

Our bipolar depression program consists of three Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials. In the ITI-007-401 and the ITI-007-404 trials, lumateperone is being evaluated as a monotherapy and in the ITI-007-402 trial, lumateperone is being evaluated as an adjunctive therapy with lithium or valproate. All three trials are evaluating lumateperone in patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode. We have also initiated Phase 3 development of lumateperone for the treatment of agitation in patients with dementia, including AD. Our ITI-007-201 trial is a Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trial in patients with a clinical diagnosis of probable AD and clinically significant symptoms of agitation. In the fourth quarter of 2018, an independent data monitoring committee, or DMC, completed a pre-specified interim analysis of the ITI-007-201 trial, concluded that the trial is not likely to meet its primary endpoint upon completion and therefore recommended the study should be stopped for futility. As a result, we determined to discontinue the ITI-007-201 trial. Lumateperone was generally well tolerated in the ITI-007-201 trial and the decision to discontinue the study was not related to safety. We are analyzing the data set from this trial and will determine the next steps in our dementia program following completion of this analysis.

In addition, we intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, including cardiovascular disease. Following the positive safety and tolerability results in our Phase 1 program, we have initiated our development program for ITI-214 for Parkinson s disease. In the fourth quarter of 2018, we announced that the Phase 1/2 clinical trial of ITI-214 has been completed and topline results demonstrated ITI-214 was generally well-tolerated with a favorable safety profile and clinical signs consistent with improvements in motor symptoms and dyskinesias. In addition, in the first quarter of 2018, the investigational new drug application, or IND, went into effect for ITI-214 for the treatment of heart failure. We have initiated clinical conduct of the first clinical study in this program, a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 to evaluate safety and hemodynamic effects in patients with systolic heart failure.

We cannot be certain that the clinical development of these or any other drug candidates in preclinical 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

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suitable for investigation through clinical trials. Our commercial revenues from our product candidates currently in development, if any, will be derived from sales of drugs that will not become marketable until at least the fourth quarter of 2019, if at all.

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 may be required to conduct further clinical trials in patients with schizophrenia, and we plan to conduct further clinical trials in other indications beyond schizophrenia, there is no guarantee that we will have the same level of success in these trials as we have had in certain of our earlier 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, such as behavioral disturbances in dementia, bipolar disorder, 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 2 clinical trials in the patient population for these other indications, except for ITI-007-200, a Phase 1/2 clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of lumateperone in healthy geriatric subjects and in patients with dementia, including AD, for which we announced top-line data in the fourth quarter of 2014.

If we do not successfully complete clinical development of lumateperone, we will be unable to market and sell products derived from it and to generate product revenues. Even though we have successfully completed certain clinical trials for lumateperone in patients with schizophrenia, 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 the initial or other future indications. Of the vast number of drugs in development, only a small percentage result in the submission of an NDA to the FDA, and even less result in the NDA ultimately being approved by the FDA for commercialization.

The FDA may ultimately determine that our Phase 3 clinical trials and non-clinical studies are not sufficient for regulatory approval. If we are required to conduct additional clinical trials and non-clinical studies, our development of lumateperone for schizophrenia will be more time-consuming and costly than we presently anticipate, which would have a material adverse effect on our business, results of operations, financial condition and cash flows.

The FDA may not agree with our belief that the lumateperone late-stage clinical development program, including two large, well-controlled positive studies (a Phase 2 and a Phase 3) and supportive evidence from a second Phase 3 study, collectively provide evidence of the efficacy and safety of lumateperone for the treatment of schizophrenia. In addition, the FDA may not agree with one or more aspects of our clinical trial designs, including the duration of the trials, clinical endpoints, controls, dose ranges, collection of safety data, or adequacy of our non-clinical studies. If the FDA does not agree with our clinical and non-clinical designs, or our interpretations of the data from such studies, our development of lumateperone in schizophrenia and other indications may be delayed, and we may incur additional costs and devote additional resources to address any concerns the FDA may have. In addition, we may be required to conduct additional clinical trials or studies, which could result in additional delays and costs.

Even if we eventually receive approval of lumateperone, the FDA may grant approval contingent on the performance of costly additional post-approval clinical trials. The FDA may also approve lumateperone for a more limited indication or a narrower patient population than we originally requested, and the FDA may not approve the labeling that we believe is necessary or desirable for the successful commercialization of lumateperone or our other product candidates. Any delay in obtaining, or inability to obtain, applicable regulatory approval for lumateperone would delay or prevent commercialization of lumateperone and would materially adversely impact our business, results of

operations, financial condition and cash flows.

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If the results of our long-term safety study do not adequately demonstrate the safety and tolerability of long-term use of lumateperone, the FDA may not approve our NDA for lumateperone for a chronic condition such as schizophrenia.

The FDA had raised questions relating to certain findings observed in nonclinical toxicology studies of lumateperone in an animal species and requested additional information to confirm that the nonclinical findings are not indicative of a safety risk associated with long term exposure in humans. The data we presented supports the position that there are significant species differences in the metabolism of lumateperone. Based on the FDA s agreement that we presented adequate data indicating that the toxicity seen in the animal species is not relevant to humans, we proceeded with our long-term safety study of lumateperone in patients with schizophrenia. In December 2018, we released results from the second part of our open-label safety switching study assessing the effects of long-term administration of lumateperone in patients with stable symptoms of schizophrenia. The data demonstrated that lumateperone, administered for up to one year, was generally well tolerated and exhibited statistically significant improvements from baseline on key safety measures of body weight, cardiometabolic and endocrine parameters, without motor side effects often associated with other antipsychotic medications. The study has been extended to allow patients to stay on lumateperone for more than one year and study conduct is ongoing. If the FDA determines the results of our long-term safety study do not adequately demonstrate the safety and tolerability of long-term use of lumateperone, our NDA for lumateperone for the treatment of schizophrenia may not be approved and we may not be able to file an NDA for lumateperone for another chronic condition. The failure to receive FDA approval of our NDA for lumateperone for the treatment of schizophrenia would have a significant adverse effect on our business.

We expect our net losses to continue for at least several years 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 our inception. As of December 31, 2018, we had an accumulated deficit of approximately $562.4 million. We expect to incur net losses over the next several years as we advance our programs and incur significant clinical development costs. We have not received, and do not expect to receive until at least the fourth quarter of 2019, any revenues from the commercialization of our product candidates. Substantially all of our revenues to date 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. In October 2014, we entered into the Takeda Termination Agreement, which terminated our license and collaboration agreement with Takeda, pursuant to which all rights with respect to ITI-214 that we previously granted to Takeda were returned to us. We will not, therefore, receive any further milestone payments from Takeda and we cannot be certain that we will enter into additional collaboration agreements. 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 will require substantial 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 and investment securities totaled $347.5 million at December 31, 2018. While we believe that our existing cash, cash equivalents and investment securities, together with interest on cash balances, will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2020, the amount and timing of our actual expenditures will depend upon numerous factors, including the ongoing status of our NDA submission for lumateperone in patients with schizophrenia; the ongoing status of our Phase 3 clinical trials of lumateperone in patients with bipolar depression; the continued development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS

conditions; and our other planned clinical and non-clinical trials. We anticipate that we will need to secure additional funding for further development of lumateperone in patients with dementia, including AD and in other programs including in patients with depressive disorders and other

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indications, and for development of our other product candidates. If the FDA requires that we perform additional preclinical studies or clinical trials, or we experience delays or other setbacks in our clinical trials, our expenses would further increase beyond what we currently expect and the anticipated timing of any potential future NDA submission would likely be delayed.

With the remaining proceeds from our public offerings in September 2015 and October 2017, we intend to fund the following: pre-launch activities for lumateperone for the treatment of schizophrenia and, if it receives regulatory approval, to fund our initial commercialization efforts; the completion of our clinical trials of lumateperone in bipolar disorder as a monotherapy and as an adjunctive therapy with lithium or valproate; clinical trials of lumateperone for the treatment of depressive disorders; clinical trials of lumateperone for the treatment of behavioral disturbances in dementia, including AD; preclinical and clinical development of our ITI-007 long acting injectable development program; other clinical trials of lumateperone; the continued clinical development of our PDE1 program, including ITI-214; and research and preclinical development of our other product candidates and the continuation of manufacturing activities in connection with the development of lumateperone. The remaining proceeds, if any, will be used to fund new and ongoing research and development activities, new business opportunities, general corporate purposes, including general and administrative expenses, capital expenditures and working capital. Accordingly, we will continue to require substantial additional capital beyond the net proceeds from these offerings 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:

- whether the FDA ultimately determines that our Phase 3 clinical trials and non-clinical studies of lumateperone are or are not sufficient for regulatory approval of lumateperone for the treatment of schizophrenia;
- the progress in, and the costs of, our preclinical studies and clinical trials and other research and development programs;
- the scope, prioritization and number of our research and development programs;
- 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;
- our ability to enter into new, and to maintain any existing, collaboration and license 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 securing manufacturing arrangements for clinical or commercial production;

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 clearances to market our product candidates;

the costs involved in expanding the accounting and data management systems to support commercial operations, including but not limited to an Enterprise Resource Planning system (ERP); and

the costs associated with litigation.

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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 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 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, including the net proceeds from our public offerings completed in September 2015 and October 2017, 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.

We may encounter substantial delays in our clinical trials for lumateperone or we may fail to demonstrate safety and efficacy to the satisfaction of the FDA.

Before obtaining marketing approval from the FDA for the sale of lumateperone, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the drug candidate for its proposed indications. Clinical trials are time-consuming, expensive and unpredictable processes that can be subject to delays. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a drug, and delays or failure can occur at any stage. Interim results of clinical trials do not necessarily predict final results, and success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials.

In connection with clinical trials, we face risks that a product candidate may not prove to be efficacious; patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested; the results may not confirm the positive results of our earlier preclinical studies and clinical trials; and the results may not meet the level of statistical significance required by the FDA or other regulatory agencies. If we do not successfully complete preclinical and clinical development, we will be unable to market and sell products derived from our product candidates and to generate product revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before an NDA may be submitted to the FDA or the FDA may approve the NDA.

Additionally, the FDA may not agree with our belief that the lumateperone late-stage clinical development program collectively provides evidence of the efficacy and safety of lumateperone for the treatment of schizophrenia, which

may require us to conduct additional trials, which would be expensive and time-consuming, would delay our ability to file an NDA with the FDA, and may have a material adverse effect on our business, results of operations, financial condition and cash flows.

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Delays, suspensions and terminations in our clinical trials 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 efficacy to obtain regulatory approval 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. In the fourth quarter of 2018, a DMC completed a pre-specified interim analysis of our ITI-007-201 Phase 3 trial in patients with a clinical diagnosis of probable AD and clinically significant symptoms of agitation, concluded that the trial is not likely to meet its primary endpoint upon completion and therefore recommended the study should be stopped for futility. As a result, we determined to discontinue the ITI-007-201 trial.

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, 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.

Safety issues with our product candidates, 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 could adversely affect the development, regulatory approval and commercialization of our product candidates. 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, there can be no assurance that our product candidates 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. If we or others later identify undesirable side effects caused by the mechanisms of action or classes of our product

candidates or specific product candidates:

- we may be required to conduct additional clinical trials or implement a Risk Evaluation and Mitigation Strategies program prior to or following approval;

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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 that the drug be scheduled under the Controlled Substances Act. Any failure or delay in commencing or completing clinical trials or obtaining regulatory approvals for our product candidates would delay commercialization of our product candidates, and severely harm our business, results of operations, financial condition 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;

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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 studies 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 studies. Preliminary and interim results of a clinical trial are not necessarily predictive of final results. 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 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 preclinical studies and clinical trials, we do not now 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 preclinical studies, including studies regarding biological activity, safety, absorption, metabolism, and excretion of product candidates.

Our preclinical 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 preclinical 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.

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;

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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.

Following regulatory approval of any of our drug candidates, we will be subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our potential products.

With regard to our drug 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 drug 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 drug 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 drug 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.

Our product candidates 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.

Even if our product candidates are approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product candidate by physicians, health care professionals and third-party payors, and our profitability and growth will depend on a number of factors, including:

our ability to provide acceptable evidence of safety and efficacy;

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;

prevalence and severity of any adverse side effects; and

availability of alternative treatments.

If any product candidate 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.

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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, 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, scientific or technical staff may significantly delay or prevent the achievement of drug development 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 will 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 will 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, 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 and managerial personnel, due to intense competition and our limited resources, would limit or delay our product development efforts, which would adversely affect the development of our drug candidates and commercialization of our potential drugs 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 product candidates.

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale. In particular, we will need to develop a larger scale manufacturing process that is more efficient and cost-effective to commercialize lumateperone and other product candidates, which may not be successful.

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of raw materials. On January 4, 2017, we entered into a supply agreement with Siegfried. Under the Siegfried Agreement, Siegfried has agreed to manufacture and supply the API for lumateperone in commercial quantities. There is no assurance that Siegfried or other manufacturers will be successful in establishing a larger-scale commercial manufacturing process for lumateperone which achieves our objectives for manufacturing capacity and cost of goods. Even if we could otherwise obtain regulatory approval for any product candidate, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities of the approved product for commercialization, our commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

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We rely on third-party manufacturers to manufacture and supply our 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. For example, on January 4, 2017, we entered into a supply agreement with Siegfried 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, with the first 12 months of each forecast being binding on us. Under the Siegfried Agreement, we have the right to and may purchase the API for lumateperone from other suppliers, including if Siegfried cannot fulfill our requirements. In addition, we expect to have an additional third party source of supply of the API for lumateperone in commercial quantities. 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 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 candidates in our clinical trials would be jeopardized. 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 that are being conducted following our request for regulatory approval for lumateperone 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 and to document their adherence to such practices may lead to significant delays in clinical trials or in obtaining regulatory approval of product candidates or the ultimate launch of products based on our product candidates 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 pre-market approval of drugs,

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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 not be able to obtain regulatory approval for or successfully commercialize our products and 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, 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 and ITI-214), 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 may have to develop information technology systems and internal sales, marketing, and distribution capabilities if we decide to market any drug that we may successfully develop. 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 our products do not receive coverage from payors or sell 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 is 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 any approved 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 any products we may market unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of those products.

In addition, the market for any products 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.

Third-party payors, whether foreign or domestic, governmental or commercial, are developing increasingly sophisticated methods of controlling health care costs. 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 can 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 product candidates to each payor separately, with no assurance that coverage will be obtained. If we are unable to obtain 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.

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In the future, if we have products that are approved, health care legislation may make it more difficult to receive revenues from those 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. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, or collectively, ACA, became law in the United States. The ACA substantially changed the way health care is financed by both governmental and private insurers and significantly affects the health care industry. Among the provisions of ACA of importance to our potential product candidates are the following:

- imposition of an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government health care programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively;

- expansion of health care fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a Medicare Part D coverage gap discount program, in which manufacturers agreed to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting any payments or transfers of value made or distributed to prescribers, teaching hospitals and other health care providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year;

a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Some of the details regarding the implementation of the ACA are yet to be determined and, at this time, it remains unclear what the full effect that the ACA will have on our business. Moreover, certain legislative changes to and regulatory changes under the ACA have occurred in the 115th United States Congress and under the Trump Administration. For instance, the Bipartisan Budget Act of 2018 increased the ACA required manufacturer point-of-sale discount from 50% to 70% off the negotiated price for Medicare Part D beneficiaries during their coverage gap period beginning in 2019. 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.

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

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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 expect that the ACA, in its current form or as it may be amended, as well as other health care reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other health care reforms may prevent us from being able to generate revenue, attain profitability, or commercialize any products for which we receive regulatory approval.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any products we may develop, we may not be able to generate product revenue.

In order to market any products that may be approved by the FDA, we must build our sales, marketing, managerial, and related capabilities or make arrangements with third parties to perform these critical commercial services. While we have begun the process of building an organization for the sales, marketing or distribution of pharmaceutical products, there are risks involved with both establishing our own sales, marketing, managerial and related capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We also may not be successful entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively, which could damage our reputation. If we do not establish adequate sales, marketing, and distribution capabilities, whether independently or in collaboration with third parties, we will not be successful in commercializing our product candidates, may not be able to generate product revenue and may not become profitable.

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

As of December 31, 2018, we had net operating loss carryforwards, or NOLs, of approximately $145 million, which are available to reduce any future federal and state taxable income and will begin to expire in the year 2034. 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, substantial changes in our ownership 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, 2018 and 2017, 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

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public offering in 2017. Our previous ownership analysis, through December 31, 2015, reflected an ownership change occurred as a result of our 2015 public offerings. Based on the analysis performed, however, we do not believe that the Section 382 annual limitation will impact our ability to utilize the tax attributes that existed as of the date of the ownership change in a material manner. If we experience an ownership change in the future, the tax benefits related to the NOLs and tax credit carryforwards may be further limited or lost.

In September 2016, we licensed certain intellectual property rights to our wholly-owned subsidiary, ITI Limited, which was formed in the third quarter of 2016. The costs to develop, test, manufacture and perform other activities related to the ITI-007 program will be the responsibility of ITI Limited and will be incurred outside of the United States. Therefore, the majority of expected losses that we incur during the next several years will not result in additional NOLs in the U.S. to be carried forward and used against future net income of the U.S. operations.

The comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act, or TCJA, that significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a worldwide system of taxation to a territorial system. In addition, the TCJA repealed the alternative minimum tax (AMT) and provides for a refund of taxes paid between 2018 and 2021. With the passing of the TCJA, the Company will receive a refund in future periods for AMT paid in prior years. The Company has recognized a benefit of approximately $1.1 million for these taxes on its December 31, 2017 consolidated statement of operations. 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.

In the ordinary course of our business, we, our clinical research organizations and other third parties on which we rely collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems. These applications and data encompass a wide variety of business critical information, including research and development information and business and financial information.

The secure processing, storage, maintenance and transmission of this critical information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure may be vulnerable to attacks by hackers, viruses, breaches, interruptions due to employee error, malfeasance or other disruptions, lapses in compliance with privacy and security mandates, or damage from natural disasters, terrorism, war and telecommunication and electrical failures. Any such event could compromise our networks and the information stored there could be accessed by unauthorized parties, publicly disclosed, lost or stolen. We have measures in place that are designed to detect and respond to such security incidents and breaches of privacy and security mandates. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as HIPPA, government enforcement actions and regulatory

penalties. Unauthorized access, loss or dissemination could also disrupt our operations, including our ability to conduct research and

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development activities, process and prepare company financial information, manage various general and administrative aspects of our business and damage our reputation, any of which could adversely affect our business. 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 further development of our product candidates could be delayed.

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 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 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 and ITI-002 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 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 product candidates or technologies, we may still be barred from making, using and selling our 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

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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 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 of our patents. 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 product candidates, technologies or activities infringe the intellectual property rights of others. If our drug development 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

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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 U.S. Patent and Trademark Office s, or USPTO s, standards 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 and products 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. The product candidates that we are developing are protected by intellectual property rights, including patents and patent applications. If any of our product candidates becomes a marketable product, 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 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 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 recently signed into law 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 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.

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Risks Related to the Transfer of Certain Intellectual Property Rights to our Foreign Subsidiary

We may need to utilize all of our available net operating losses, and we may be subject to additional income taxes in connection with our transfer of certain intellectual property rights to our foreign subsidiary.

In September 2016, we licensed certain intellectual property rights to our wholly-owned Bermuda subsidiary, ITI Limited for $125 million and other consideration. The fair value of the intellectual property rights were determined by an independent third party. The proceeds from this license represented a prior year gain for U.S. tax purposes which was offset partially by prior year losses. However, the Internal Revenue Service, or the IRS, could challenge the valuation of the intellectual property rights and assess a greater valuation, which would require us to utilize a portion, or all, of our available NOLs at such time. If an IRS valuation exceeds our available NOLs, we could incur additional income taxes in the future. Our ability to use our NOLs is generally subject to the limitations of IRS Section 382, as well as expiration of federal and state net operating loss carryforwards.

Risks Related to Our Industry

We will be subject to stringent regulation in connection with the marketing of any 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 it has completed rigorous preclinical 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. These limitations may limit 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 our 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, our potential products for the treatment of schizophrenia and bipolar disorder would compete with, among other branded products including, Latuda®, marketed by Sunovion, Rexulti® marketed by Otsuka Pharmaceutical, VRAYLAR®, marketed by Allergan, Saphris® marketed by Allergan and Fanapt®, marketed by

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Vanda Pharmaceuticals. In addition, our product candidates, if approved, will compete with, among other generic antipsychotic products, aripiprazole, haloperidol, paliperidone, risperidone, quetiapine/XR, olanzapine and clozapine.

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;
- preclinical studies and clinical trials of potential pharmaceutical products; and
- obtaining FDA and other regulatory approvals.

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 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 his or her 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.

Consumers may sue us for product liability, which could result in substantial liabilities that exceed our available resources and damage our reputation.

Researching, developing, and commercializing drug products entail significant product liability risks. Liability claims may arise from our and our collaborators use of products in clinical trials and the commercial sale of those products. Consumers may make these claims directly and our collaborators or others selling these products may seek contribution from us if they receive claims from consumers. We have obtained limited product liability insurance coverage for our clinical trials. Our product liability insurance coverage for clinical

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trials is currently limited to an aggregate of $30 million. As such, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Although we currently have product liability insurance that covers our clinical trials, we will need to increase and expand this coverage if our 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. Product liability claims could have a material adverse effect on our business and results of operations. Our liability could exceed our total assets if we do not prevail in a lawsuit from any injury caused by our drug products.

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, 2018, the price per share of our common stock on the Nasdaq Global Select Market has ranged from a high of $25.82 to a low of $10.21. We have several stockholders, including affiliated 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:

- 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 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.

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

We will 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 product candidates and technology and, to a lesser extent, grant funding, although there can be no assurances such financing can be obtained. We filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on September 14, 2016, on which we registered for sale up to $350 million of any combination of our common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. On October 2, 2017 and October 5, 2017, we completed our public offering of approximately $172 million of shares of our common stock registered on the universal shelf registration statement and received net proceeds of approximately $162 million, after deducting underwriting discounts and commissions and estimated offering expenses. After the public offering in October 2017, approximately $178 million of securities remain available for issuance under this shelf registration statement. This registration statement will remain in effect for up to three years from the date it was declared effective. 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 will incur increased 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

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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 evaluated frequently. We currently do not have an internal audit group, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we fail to maintain the effectiveness of our internal controls or fail to comply in a timely manner with the requirements of the Sarbanes-Oxley Act, 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

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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 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.

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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, co 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, future revenues, uses of cash, cash equivalents and investment securities, capital requirements and the need for additional financing;
- the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials;
- the timing of and our ability to obtain and maintain regulatory approval, or submit an application for regulatory approval, of our 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 our current and future product candidates;
- our collaborators election 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 our product candidates;

the size and growth of the markets for our product candidates and our ability to serve those markets;

the rate and degree of market acceptance of any 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 and capital market risk; and

our ability to attract and retain key scientific or management personnel.

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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

We are not currently a party to any material legal proceedings.

Item 4. MINE SAFETY DISCLOSURES

Not applicable.

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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 25, 2019, we had 55,116,739 outstanding shares of common stock and no outstanding shares of preferred stock. As of February 25, 2019, there were approximately 106 holders of record of our outstanding shares of common stock.

Unregistered Sales of Securities

Not applicable.

Issuer Purchases of Equity Securities

Not applicable.

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Item 6. SELECTED FINANCIAL DATA

The following table sets forth consolidated financial data with respect to the Company for each of the five years in the period ended December 31, 2018. The selected financial data for each of the five years in the period ended December 31, 2018 have been derived from our audited consolidated financial statements. The consolidated balance sheets as of December 31, 2018 and 2017 and 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, 2018, and the report thereon, are included elsewhere in this Annual Report on Form 10-K. The information below should be read in conjunction with the consolidated financial statements (and notes thereon) and Management s Discussion and Analysis of Financial Condition and Results of Operations, included in Item 7.

	2018	2017	2016	2015	2014
Statements of Operations:					
Revenues:					
License and collaboration revenue	$	$	$	$ 30,659	$ 547,546
Grant revenue		245,837	330,702	60,705	29,755
Total Revenues		245,837	330,702	91,364	577,301
Costs and expenses:					
Research and development	132,166,913	79,419,009	93,831,530	87,718,074	21,226,345
General and administrative	30,099,855	23,666,957	24,758,063	18,187,286	10,337,679
Total costs and expenses	162,266,768	103,085,966	118,589,593	105,905,360	31,564,024
Loss from operations	(162,266,768)	(102,840,129)	(118,258,891)	(105,813,996)	(30,986,723)
Interest income	(7,140,957)	(4,005,864)	(2,935,077)	(1,022,455)	(303,936)
Interest expense			36,781		7,073
Income tax expense (benefit)	1,600	(1,060,851)	1,065,673	1,600	1,600
Net Loss	$ (155,127,411)	$ (97,773,414)	$ (116,426,268)	$ (104,793,141)	$ (30,691,460)
Net Loss per common share	$ (2.84)	$ (2.12)	$ (2.69)	$ (2.91)	$ (1.07)
Weighted average number of common shares:	54,707,865	46,181,926	43,240,188	36,069,237	28,650,067

	2018	2017	December 31, 2016	2015	2014
Balance Sheet data:					
Cash and cash equivalents	$ 54,947,502	$ 37,790,114	$ 48,642,225	$ 47,159,303	$ 61,325,044
Investments	292,583,046	426,540,921	428,041,021	428,041,021	68,320,672
Total assets	357,206,498	471,486,699	388,903,495	484,103,528	131,111,769
Total liabilities	39,491,617	17,049,738	13,400,956	7,860,617	10,557,064
Accumulated deficit	(562,376,191)	(407,248,780)	(309,475,366)	(193,049,098)	(88,255,957)
Total stockholders equity	317,714,881	454,436,961	375,502,539	476,242,911	120,554,705

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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. 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 and clinical development 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. Lumateperone (also known as ITI-007) is our lead product candidate with mechanisms of action that, we believe, may represent an effective treatment across multiple therapeutic indications. In our preclinical and clinical trials to date, lumateperone combines potent serotonin 5-HT2A receptor antagonism, dopamine receptor phosphoprotein modulation, or DPPM, glutamatergic modulation, and serotonin reuptake inhibition into a single drug candidate for the treatment of acute and residual schizophrenia and for the treatment of bipolar disorder, including bipolar depression. At dopamine D2 receptors, lumateperone has been demonstrated to have dual properties and to act as both a pre-synaptic partial agonist and a post-synaptic antagonist. Lumateperone has also been demonstrated to have affinity for dopamine D1 receptors and indirectly stimulate phosphorylation of glutamatergic NMDA GluN2B receptors in a mesolimbic specific manner. We believe that this regional selectivity in brain areas thought to mediate the efficacy of antipsychotic drugs, together with serotonergic, glutamatergic, and dopaminergic interactions, may result in efficacy for a broad array of symptoms associated with schizophrenia and bipolar disorder with improved psychosocial function. The serotonin reuptake inhibition potentially allows for antidepressant activity in the treatment of schizoaffective disorder, other disorders with co-morbid depression, and/or as a stand-alone treatment for MDD. We believe lumateperone may also be useful for the treatment of other psychiatric and neurodegenerative disorders, particularly behavioral disturbances associated with dementia, autism, and other CNS diseases. Lumateperone is in Phase 3 clinical development as a novel treatment for schizophrenia, bipolar depression and agitation associated with dementia, including AD.

We had a pre-NDA meeting with the FDA in the first quarter of 2018 and reached agreement on the timing and content of a rolling NDA submission for lumateperone for the treatment of schizophrenia. We initiated the rolling submission of our NDA with the FDA for lumateperone for the treatment of schizophrenia in the second quarter of 2018, we completed this NDA submission in the third quarter of 2018 and the FDA accepted the NDA for review in the fourth quarter of 2018.

Our lumateperone bipolar depression Phase 3 clinical program consists of two monotherapy studies and one adjunctive study. We have completed patient enrollment in our first monotherapy study (Study 401) conducted in the U.S. and in the second monotherapy study (Study 404) conducted globally. Given the relative timing of these two events and to avoid introducing potential expectation bias in the ongoing Study 404, we anticipate reporting topline results from Study 401 and Study 404 simultaneously in the second quarter of 2019. The Study 401 dataset will remain locked and blinded until the Study 404 dataset is available and then both datasets will be analyzed concurrently. Subject to the outcome of these trials, we expect to submit in the second half of 2019 for FDA regulatory approval for bipolar depression. Our global study evaluating adjunctive lumateperone in bipolar depression (Study 402) is ongoing.

In the second quarter of 2016, we initiated Phase 3 development of lumateperone for the treatment of agitation in patients with dementia, including AD. Our ITI-007-201 trial is a Phase 3 multi-center, randomized,

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double-blind, placebo-controlled clinical trial in patients with a clinical diagnosis of probable AD and clinically significant symptoms of agitation. In the fourth quarter of 2018, an independent data monitoring committee, or DMC, completed a pre-specified interim analysis of the ITI-007-201 trial, concluded that the trial is not likely to meet its primary endpoint upon completion and therefore recommended the study should be stopped for futility. As a result, we determined to discontinue the ITI-007-201 trial. Lumateperone was generally well tolerated in the ITI-007-201 trial and the decision to discontinue the study was not related to safety. We are analyzing the data set from this trial and will determine the next steps in our program following completion of this analysis.

We are also pursuing clinical development of lumateperone for the treatment of additional CNS diseases and disorders. At the lowest doses, lumateperone has been demonstrated to act primarily as a potent 5-HT2A serotonin receptor antagonist. As the dose is increased, additional benefits are derived from the engagement of additional drug targets, including modest dopamine receptor modulation and modest inhibition of serotonin transporters. We believe that combined interactions at these receptors may provide additional benefits above and beyond selective 5-HT2A antagonism for treating agitation, aggression and sleep disturbances in diseases that include dementia, AD, Huntington s disease and autism spectrum disorders, while avoiding many of the side effects associated with more robust dopamine receptor antagonism. As the dose of lumateperone is further increased, leading to moderate dopamine receptor modulation, inhibition of serotonin transporters, and indirect glutamate modulation, these actions complement the complete blockade of 5-HT2A serotonin receptors. At a dose of 60 mg, ITI-007 has been shown effective in treating the symptoms associated with schizophrenia, and we believe this higher dose range will be useful for the treatment of bipolar disorder, depressive disorders and other neuropsychiatric diseases. Within the ITI-007 portfolio, we are also developing a long-acting injectable formulation to provide more treatment options to patients suffering from mental illness. Given the encouraging tolerability data to date with oral lumateperone, we believe that a long-acting injectable option, in particular, may lend itself to being an important formulation choice for patients.

Given the potential utility for lumateperone and follow-on compounds to treat these additional indications, we may investigate, either on our own or with a partner, agitation, aggression and sleep disturbances in additional diseases that include autism spectrum disorders, depressive disorder, intermittent explosive disorder, non-motor symptoms and motor complications associated with Parkinson s disease, and post-traumatic stress disorder. We hold exclusive, worldwide commercialization rights to lumateperone and a family of compounds from Bristol-Myers Squibb Company pursuant to an exclusive license.

We have a second major program called ITI-002 that has yielded a portfolio of compounds that selectively inhibits the enzyme phosphodiesterase type 1, or PDE1. ITI-214 is our lead compound in this program. We believe ITI-214 is the first compound in its class to successfully advance into Phase 1 clinical trials. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, including cardiovascular disease. Following the positive safety and tolerability results in our Phase 1 program, we initiated our development program for ITI-214 for Parkinson s disease and commenced patient enrollment in the third quarter of 2017 in a Phase 1/2 clinical trial of ITI-214 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 the fourth quarter of 2018, we announced that the Phase 1/2 clinical trial of ITI-214 has been completed and topline results demonstrated ITI-214 was generally well-tolerated with a favorable safety profile and clinical signs consistent with improvements in motor symptoms and dyskinesias. In addition, in the first quarter of 2018, the investigational new drug application, or IND, went into effect for ITI-214 for the treatment of heart failure. We have initiated clinical conduct of the first clinical study in this program, a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 to evaluate safety and hemodynamic effects in patients with systolic heart failure.

Our pipeline also includes preclinical programs that are focused on advancing drugs for the treatment of schizophrenia, Parkinson s disease, AD and other neuropsychiatric and neurodegenerative disorders. We are also

investigating the development of treatments for disease modification of neurodegenerative disorders and non-CNS diseases, including our ITI-333 development program. ITI-333 is designed as a potential treatment for

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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. We believe the potential exists for ITI-333 to address these challenges. Preclinical safety studies with ITI-333 are currently ongoing and we expect to initiate a clinical program in 2019.

Results of Operations

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

Revenues

We have not generated any revenue from product sales to date and we do not expect to generate revenues from product sales until at least the fourth quarter of 2019, if ever. We had no revenues for the year ended December 31, 2018, and our revenues for the year ended December 31, 2017 were from a government grant. We have received and may continue to receive grants from U.S. government agencies and foundations.

We do not expect any revenues that we may generate in the next several years to be significant enough to fund our operations.

Expenses

The process of researching and developing 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 clinical development of lumateperone for the treatment of schizophrenia and for the treatment of bipolar depression consumes and, together with our anticipated clinical development programs for depressive disorders and ITI-214, 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 ITI-002 program has a compound, ITI-214, in Phase 1/2 development. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, including cardiovascular disease. We have initiated our development program for ITI-214 for Parkinson s disease. In addition, in the first quarter of 2018, the IND went into effect for ITI-214 for the treatment of heart failure. We have initiated clinical conduct of the first clinical study in this program, a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 to evaluate safety and hemodynamic effects in patients with systolic heart failure. Our other projects are still in the preclinical stages, and will require extensive funding not only to complete preclinical testing, but to commence and complete clinical trials. Expenditures that we incur on these projects 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 projects to the advancement of lumateperone, which could have a material adverse impact on the advancement of these other projects and on our results of operations. Our operating expenses are comprised of (i) research and development expenses and (ii) general and administrative expenses. Our research and development costs are comprised of:

- internal recurring costs, such as costs relating to labor and fringe benefits, materials, supplies, facilities and maintenance; and

fees paid to external parties who provide us with contract services, such as pre-clinical testing, manufacturing and related testing, clinical trial activities and license milestone payments.

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General and administrative expenses are incurred in three major categories:

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

We expect that research and development expenses will increase moderately as we proceed with our Phase 3 clinical trials of lumateperone for the treatment of bipolar disorder and depressive disorders and as we proceed with increased manufacturing of drug product for clinical trials and pre-commercialization testing. We also expect that our general and administrative costs will increase from prior periods primarily due to costs to perform pre-product commercialization activities and the increased costs associated with building infrastructure to support the anticipated commercial sales of lumateperone if it is approved for sale in the United States, which could include hiring additional personnel and the cost of additional facility space. On September 28, 2018, we signed a lease with a related party to acquire 15,534 square feet of additional office space in our current headquarters facility. We granted options to purchase 1,175,187 shares of our common stock in 2018 and have granted options to purchase an additional 1,218,494 shares of our common stock on January 8, 2019. We also granted time based restricted stock units, or RSUs, for 544,542 of our common stock in 2018 and time based RSUs for 886,802 shares of our common stock on January 8, 2019. We will recognize expense associated with these RSUs and options over the next three years in both research and development expenses and general and administrative expenses. In the first quarter of 2017, we also granted performance based RSUs, which vest based on the achievement of certain milestones that include (i) the submission of an NDA with the FDA, (ii) the approval of the NDA by the FDA, or the Milestone RSUs, and (iii) the achievement of certain comparative shareholder returns against our peers, or the TSR RSUs. The Milestone RSUs were valued at the closing price on March 8, 2017. The RSUs related to the NDA submission were amortized through December 31, 2018 based on the probable vesting date. The NDA submission milestone was achieved in the third quarter of 2018. The Milestone RSUs related to the NDA submission vested on December 31, 2018. The amortization of the expenses of the Milestone RSUs related to the approval of the NDA will commence if and when the filing has been approved through the last day of the calendar year in which the milestone is achieved and expires on December 31, 2019 if not achieved. The TSR RSUs were valued using the Monte Carlo simulation method and will be amortized over the life of the RSU agreements which ends December 31, 2019. The Milestone RSUs and the TSR RSUs are target based and the ultimate awards, if attained, could be the target amount or higher or lower than the target amount, depending on the timing or achievement of the goal. We expect this non-cash expense to be substantial and affect quarter to quarter and year to date comparisons in the upcoming year. We expect to continue to grant stock options and other stock-based awards in the future, which with our growing employee base will increase our stock-based compensation expense in future periods.

The following table sets forth our revenues, operating expenses, interest income, net and income tax (benefit) expenses for the years ended December 31, 2018, 2017 and 2016 (in thousands):

	For the Year Ended December 31,		
	2018	2017	2016
Revenues	**$**	$ 246	$ 330

Expenses			
Research and Development	**132,167**	79,419	93,831
General and Administrative	**30,099**	23,667	24,758
Total costs & expenses	**162,266**	103,086	118,589
Loss from operations	**(162,266)**	(102,840)	(118,259)
Interest income, net	**(7,141)**	(4,006)	(2,898)
Income tax expense (benefit)	**2**	(1,061)	1,065
Net Loss	**$ (155,127)**	$ (97,773)	$ (116,426)

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Comparison of Years Ended December 31, 2018 and December 31, 2017

Revenues

Revenues for the year ended December 31, 2018 were zero as compared to $246 thousand for the year ended December 31, 2017, due to a government grant that was completed in the fourth quarter of 2017. We expect to have a moderate amount of grant revenue in the future.

Research and Development Expenses

	2018	2017	2016
External Costs	**$ 110,700**	$ 64,404	$ 81,230
Internal Costs	**21,467**	15,015	12,601
Total Research and Development Expenses	**$ 132,167**	$ 79,419	$ 93,831

	2018	2017	2016
Lumateperone costs	**$ 82,288**	$ 53,124	$ 69,771
Manufacturing costs	**22,741**	12,282	15,441
Stock based compensation	**7,381**	5,083	4,473
Other projects and overhead	**19,757**	8,930	4,146
Total Research and Development Expenses	**$ 132,167**	$ 79,419	$ 93,831

Research and development expenses increased to $132.2 million for the year ended December 31, 2018 as compared to $79.4 million for the year ended December 31, 2017, representing an increase of approximately $52.8 million, or 66%. This increase is due primarily to an increase of approximately $23.2 million of costs associated with lumateperone clinical costs, a $6.0 million increase in costs for lumateperone non-clinical efforts, approximately $10.5 million increase in manufacturing expense, approximately $2.3 million increase in stock compensation expense and an increase of approximately $10.8 million of non ITI-007 projects and overhead expenses. Expenses for other projects and overhead increased as we expanded our preclinical development of ITI-333 and ITI-214, among others. Internal costs increased by $6.5 million for the period as we hired additional staff and increased our stock based compensation expense.

As development of lumateperone progresses, we anticipate costs for lumateperone to increase due primarily to ongoing and planned clinical trials relating to our lumateperone programs in the next several years as we conduct Phase 3 and other clinical trials. We are also required to complete non-clinical testing to obtain FDA approval and manufacture material needed for clinical trial use, which includes non-clinical testing of the drug product and the creation of an inventory of drug product in anticipation of possible FDA approval.

As of December 31, 2018, we employed 49 full time personnel in our research and development group as compared to 32 full time personnel in our research and development group at December 31,2017. We expect to hire additional staff as we increase our development efforts and grow our business in the upcoming years.

We currently have several projects, in addition to lumateperone, that are in the research and development stages, including in the areas of cognitive dysfunction and the treatment of neurodegenerative diseases, including AD, among others. We have used internal resources and incurred expenses not only in relation to the development of lumateperone, but also in connection with these additional projects as well, including our PDE program. We have not, however, reported these costs on a project by project basis, as these costs are broadly spread among these projects. The external costs for these projects have been modest and are reflected in the amounts discussed in this section Research and Development Expenses.

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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 pre-clinical 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 pre-clinical 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 entitled Risk Factors in this Annual Report on Form 10-K.

General and Administrative Expenses

General and administrative expenses increased for the year ended December 31, 2018 as compared to the year ended December 31, 2017 by approximately $6.4 million, or 27.2%. The increase is primarily the result of an increase

pre-commercialization costs of approximately $4.0 million, labor costs of approximately $1.8 million, stock compensation expense of approximately $457,000, rent expense of approximately $405,000 and is offset partially by lower professional fees of approximately $443,000. Salaries, bonuses and related benefit costs for our executive, finance and administrative functions for the years ended 2018 and 2017 constituted approximately 56% and 62%, respectively, of our total general and administrative costs. The next major categories of expenses were patent costs and, to a lesser extent, general office-related overhead.

We expect general and administrative costs to increase significantly as we hire additional staff and expand our operations, in particular, the addition of a sales force and related commercial and other infrastructure as we prepare for potential commercial activities.

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Interest Income

Interest income has increased to approximately $7.1 million from $4.0 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017. This increase is primarily a result of slightly higher than average cash balances and rising interest rates in 2018 as compared to 2017. The higher balances in 2018 were primarily due to the net offering proceeds of $162.1 million that we received in October 2017 and is offset partially by the $118.2 million of cash and investments utilized in 2018.

Income Taxes

In September 2016, the Company licensed certain intellectual property rights to its wholly-owned subsidiary, ITI Limited, which was formed in the third quarter of 2016. Although the license of intellectual property rights did not result in any gain or loss in the consolidated statements of operations, the transaction generated taxable net income in the U.S in 2016. We utilized a portion of our available federal and state net operating loss carryforwards to offset the majority of this net income but incurred approximately $1.1 million of alternative minimum tax related to intercompany transactions that were treated as tax expense in our consolidated statement of operations in 2016. In December 2017 the Tax Cuts and Jobs Act law was passed which will allow the Company to receive a refund in future periods for these taxes paid. The Company has therefore recognized a benefit of approximately $1.1 million for these taxes in 2017. The Company expects to receive approximately half of this amount in the next year.

Comparison of Years Ended December 31, 2017 and December 31, 2016

Revenues

Revenues decreased for the year ended December 31, 2017 as compared to the year ended December 31, 2016 by approximately $84 thousand, or 26%, due to a government grant that was completed in the fourth quarter of 2017. We do not expect to have any significant grants in the future.

Research and Development Expenses

Research and development expenses decreased for the year ended December 31, 2017 as compared to the year ended December 31, 2016 by approximately $14.4 million, or 15%. This change is due primarily to a decrease of approximately $11.4 million in clinical trials related costs, a decrease of approximately $4.6 million in non-clinical costs, and a decrease of approximately $3.2 million of costs associated with manufacturing. These decreases in 2017 are offset in part by an increase of approximately $2.3 million of labor related costs. For the year ended December 31, 2016, the majority of the $93.8 million in research and development costs was related to the second Phase 3 trial of lumateperone in patients with schizophrenia and to a lesser extent the Phase 3 trials of lumateperone in patients with bipolar depression and the Phase 3 trial of lumateperone for the treatment of agitation in patients with dementia, including AD, other supporting trials for lumateperone and costs for manufacturing lumateperone. For the year ended December 31, 2017, the majority of the $79.4 million in research and development costs was related to clinical trial costs of lumateperone in patients with schizophrenia and to a lesser extent the Phase 3 trials of lumateperone in patients with bipolar depression, the Phase 3 trial of lumateperone for the treatment of agitation in patients with dementia, including AD, and costs for manufacturing lumateperone. Amounts paid to external parties comprised most of our research and development costs. For the year ended December 31, 2017, we incurred approximately $64.3 million of costs to external parties who manufactured, tested and performed clinical trial related activities as compared to $81.1 million for the year ended December 31, 2016. Of these external costs, approximately $60.1 million for the year ended December 31, 2017 and approximately $80.6 million in the year ended December 31, 2016 were for lumateperone related projects. The remaining external costs for each of these periods were spent on

other projects. Internal costs are comprised primarily of labor, fringe benefits, materials, stock-based compensation, supplies and facilities and maintenance costs and were approximately $15.1 million and $12.7 million for the years ended December 31, 2017 and 2016, respectively.

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General and Administrative Expenses

General and administrative expenses decreased for the year ended December 31, 2017 as compared to the year ended December 31, 2016 by approximately $1.1 million, or 4.4%, primarily due to a decrease of approximately $1.5 million of marketing and consulting costs in 2017 compared to 2016, offset by higher capital tax expense in 2017. Salaries, bonuses, share based compensation and related benefit costs for our executive, finance and administrative functions for the years ended December 31, 2017 and 2016 were approximately 62% and 61%, respectively, of our total general and administrative costs. Our other general and administrative expenses include patent costs and other professional fees and, to a lesser extent, general office-related overhead.

Interest Income

Interest income has increased to approximately $4.0 million from $2.9 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. This increase is primarily a result of higher than average cash balances and rising interest rates in 2017 as compared to 2016. The higher balances in 2017 were primarily due to the net offering proceeds of $162.1 million that we received in October 2017 and is offset partially by the $80.5 million of cash and investments utilized in 2017.

Income Taxes

In September 2016, we licensed certain intellectual property rights to its wholly-owned subsidiary, ITI Limited, which was formed in the third quarter of 2016. Although the license of intellectual property rights did not result in any gain or loss in the consolidated statements of operations, the transaction generated taxable net income in the U.S in 2016. We utilized a portion of our available federal and state net operating loss carryforwards to offset the majority of this net income but incurred approximately $1.1 million of alternative minimum tax related to intercompany transactions that were treated as tax expense in our consolidated statement of operations in 2016. In December 2017 the Tax Cuts and Jobs Act law was passed which will allow the Company to receive a refund in future periods for these taxes paid. The Company therefore recognized a benefit of approximately $1.1 million for these taxes in December 2017.

Liquidity and Capital Resources

Through December 31, 2018, we provided funds for our operations by obtaining approximately $880.3 million of cash primarily through public and private offerings of our common stock and other securities, grants from government agencies and foundations and payments received under the terminated Takeda License Agreement. We do not believe that grant revenue will be a significant source of funding in the near future.

On October 2, 2017, we completed a public offering of 9,677,419 shares of our common stock for aggregate gross proceeds of approximately $150 million and net proceeds of approximately $140.6 million. On October 5, 2017, the underwriters exercised in full their option to purchase an additional 1,451,613 shares. All of the shares in the offering were sold by the Company, with gross proceeds to the Company of approximately $172 million from the offering of an aggregate of 11,129,032 shares and net proceeds of approximately $162 million, after deducting underwriting discounts, commissions and estimated offering expenses.

As of December 31, 2018, we had a total of approximately $347.5 million in cash and cash equivalents and available-for-sale investment securities, and approximately $36.3 million of short-term liabilities consisting entirely of liabilities from operations. In the year ended December 31, 2018, we spent approximately $125.7 million in cash for operations and equipment, not including $7.1 million of interest income. We reduced working capital by approximately $135.9 million for the year ended December 31, 2018. This use of cash was primarily for conducting

clinical trials and non-clinical testing, including manufacturing related activities and funding recurring operating expenses.

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For the year 2019, subject to the timing of NDA approval, clinical trial conduct, regulatory activities, precommercial, manufacturing, and other development activities, we expect to spend between $225 million and $240 million. We expect these expenditures to be due primarily to the pre-commercialization activities, initial commercialization activities and related infrastructure expansion in connection with the commercialization of lumateperone for the treatment of schizophrenia; the development of lumateperone in our late stage clinical programs; the development of our other product candidates, including ITI-214; the continuation of manufacturing activities in connection with the development of lumateperone; and general operations. We expect our existing cash and cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2020.

We will require significant additional financing in the future to continue to fund our operations. We believe that we have the funding in place to complete the additional clinical and non-clinical trials, manufacturing and pre-commercialization activities needed for potential regulatory approval and initial commercialization of lumateperone in patients with schizophrenia. With our existing cash, cash equivalents and available-for-sale investment securities, we believe that we have the funds to complete our ongoing clinical trials of lumateperone in bipolar disorder as a monotherapy and as an adjunctive therapy with lithium or valproate. We also plan to fund additional clinical trials of lumateperone for the treatment of behavioral disturbances in dementia and depressive disorders; preclinical and clinical development of ITI-007 long acting injectable development program; additional clinical trials of lumateperone; continued clinical development of our PDE program, including ITI-214; research and preclinical development of our other product candidates; and the continuation of manufacturing activities in connection with the development of lumateperone. We anticipate requiring additional funds for further development of lumateperone in patients with dementia, including AD, for further development of lumateperone in patients with bipolar disorder, depressive disorders and other indications, and for development of our other product candidates. We have incurred losses in every year since inception with the exception of 2011, when we received an up-front fee and a milestone payment related to the Takeda License Agreement. These losses have resulted in significant cash used in operations. For the year ended December 31, 2018, we used net cash in operating activities and purchases of equipment of approximately $125.7 million. This total does not include an offset for $7.1 million of interest income received. While we have several research and development programs underway, the lumateperone program has advanced the furthest and will continue to consume increasing amounts of cash for conducting clinical trials and the testing and manufacturing of product material. As we continue to conduct the activities necessary to pursue FDA approval of lumateperone and our other product candidates, as well as commercialization efforts, we expect the amount of cash to be used to fund operations to increase over the next several years.

With the termination of the Takeda License Agreement in October 2014, we are responsible for the costs of developing ITI-214. On September 15, 2015, Takeda completed the transfer of the IND for ITI-214 to us. We intend to pursue the development of our PDE1 program, including ITI-214 for the treatment of several CNS and non-CNS conditions. We anticipate a moderate increase in our operating expenses related to our PDE development programs. Following the positive safety and tolerability results in our Phase 1 program, we have initiated our development program for ITI-214 for Parkinson s disease and commenced patient enrollment in the third quarter of 2017 in a Phase 1/2 clinical trial of ITI-214 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 addition, in the first quarter of 2018, the IND went into effect for ITI-214 for the treatment of heart failure. We have initiated clinical conduct of the first clinical study in this program, a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 to evaluate safety and hemodynamic effects in patients with systolic heart failure. We expect these expenses to increase for 2019 and beyond.

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. Until we can generate

significant revenues from operations, we will 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

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lesser extent, grant funding. On September 2, 2016, we filed a universal shelf registration statement on Form S-3, which was declared effective by the SEC on September 14, 2016, on which we registered for sale up to $350 million of any combination of our common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. After the public offering in October 2017, approximately $178 million of securities remain available for issuance under this shelf registration statement. This registration statement will remain in effect for up to three years from the date it was declared effective.

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 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. In addition, any 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 pre-clinical studies, clinical trials or other clinical development activities for one or more of our product candidates, including our lead product candidate lumateperone, ITI-214, and our other pre-clinical stage product candidates; (2) delay, limit, reduce or terminate our discovery research or pre-clinical development activities; or (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.

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 current low interest rates available for these instruments, we are earning limited interest income. We do not expect interest income to be a significant source of funding over the next several quarters. Our investment portfolio has not been adversely impacted by the problems in the credit markets that have existed over the last several years, but there can be no assurance that our investment portfolio will not be adversely affected in the future.

In 2014, we entered into a long-term lease, which was amended in December 2015, for 16,753 square feet of useable laboratory and office space located at 430 East 29th Street, New York, New York 10016. Due to the amortization of total lease payments, we have recognized $3.2 million of deferred rent through the end of 2018. In September 2018, we further 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 14.2 years ending in March 2029. We expect that our facility related costs will increase significantly from year to year as a result of leasing this additional space.

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Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Contractual Obligations and Commitments

Total contractual obligations as of December 31, 2018 are summarized in the following table (in thousands):

		Payments Due By Period			
	Total	2019	2020-2021	2022-2024	After 2024
Operating Lease Obligations for existing space	$ 17,704	$ 1,501	$ 3,137	$ 5,069	$ 7,997
Operating Lease Obligations for additional office space beginning October 1, 2018	$ 15,702	$ 1,022	$ 2,843	$ 4,592	$ 7,245
	$ 33,406	$ 2,523	$ 5,980	$ 9,661	$ 15,242

The table of Contractual Obligations and Commitments does not reflect that, under the License Agreement with BMS, we may be obligated to make future milestone payments to BMS totaling $12 million, including the $2.0 million paid in January 2019; to make other future milestone payments to BMS for each licensed product of up to an aggregate of approximately $14.75 million; to make tiered single digit percentage royalty payments on sales of licensed products; and to pay BMS a percentage of non-royalty payments made in consideration of any sublicense.

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 revenue recognition, stock-based compensation and clinical trial accruals. Actual results may differ from those estimates and under different assumptions or conditions.

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

Research and Development

Except for payments made in advance of services, we expense our research and development costs as incurred. For payments made in advance, we recognize research and development expense as the services are rendered. 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 preclinical analytical testing, manufacturing of drug product, 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 its vendors 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.

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As part of the process of preparing its financial statements, we are 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. Our 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. 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 outside 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 its clinical expense recognition if actual results differ from its estimates. We make estimates of our accrued expenses as of each balance sheet date based on the facts and circumstances known to it 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 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. For the years ended December 31, 2018 and 2017, there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Stock-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 is estimated, on the date of grant, using the Black-Scholes-Merton 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, 2018, 2017 and 2016 is based on share-based awards ultimately expected to vest.

We utilize 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.

Expected volatility rates are based on a combination of the historical volatility of the common stock of comparable publicly traded entities and the limited historical information about our 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. We have not paid dividends to its stockholders since its inception and does not plan to pay cash dividends in the foreseeable future. Therefore, we have assumed an expected dividend rate of zero.

Prior to January 1, 2014, at which time there was no active market for our common stock, the exercise price of the stock options on the date of grant was determined and approved by the board of directors using several factors, including progress and milestones achieved in our business development and performance, the price per share of its

convertible preferred stock offerings, and general industry and economic trends. In establishing the estimated fair value of the common stock, we considered the guidance set forth in American Institute of Certified

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Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. For stock options granted on or after January 1, 2014, the exercise price was determined by using the closing market price of our common stock on the date of grant.

An RSU is a stock award that entitles the holder to receive shares of our common stock as the award vests. The fair value of each RSU is based on the fair market value of our common stock on the date of grant. We have granted RSUs that vest in three equal annual installments provided that the employee remains employed with us.

Beginning in the first quarter of 2016, and in the first quarter of 2017 and 2018, we granted time based RSUs that vest in three equal annual installments. In the first quarter of 2017, we granted additional time-based RSUs as well as performance-based RSUs, which vest based on the achievement of certain milestones that include (i) the submission of an NDA with the FDA, (ii) the approval of the NDA by the FDA (collectively, the Milestone RSU grants) and (iii) the achievement of certain comparative shareholder returns against the Company s peers (the TSR RSU grants) . The Milestone RSU grants were valued at the closing price on March 8, 2017. The Milestone RSU grants that vest upon the NDA submission were amortized through December 31, 2018 based on the probable vesting date. The NDA submission milestone was achieved in the third quarter of 2018, so the Milestone RSUs related to the NDA submission vested on December 31, 2018. The amortization of the expenses for Milestone RSU grants related to the approval of the NDA will commence if and when the NDA filing has been approved through the last day of the calendar year in which the milestone is achieved. The TSR RSU grants were valued using the Monte Carlo Simulation method and will be amortized over the life of the RSU agreements which ends December 31, 2019. The Milestone RSU grants and TSR RSU grants are target based and the ultimate awards, if attained, could be the target amount or higher or lower than the target amount, depending on the timing or achievement of the goal.

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 shall be 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 us, as all the deferred tax assets have a full valuation allowance.

Since we have net operating loss carryforwards as of December 31, 2018, 2017 and 2016, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations. In March 2016, the FASB issued ASU 2016-09. ASU 2016-09 simplifies several areas of accounting for stock compensation, including simplification of the accounting for income taxes, classification of excess tax benefits on the Statement of Cash Flows and forfeitures. As of January 1, 2017, the Company adopted ASU 2016-09 for the quarter ended March 31, 2017. Accordingly, the Company recognized previously unrecognized excess tax benefits of $9.7 million recorded as deferred tax assets with a corresponding offsetting full valuation allowance at the beginning of 2017, which yielded no tax impact.

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.

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.

In May 2014, the FASB issued ASC Update No. 2014-09, Revenue from Contracts with Customers (Topic 606), which has been subsequently updated (as updated, ASC Topic 606). The purpose of ASC Topic 606 is to provide enhancements to the quality and consistency of how revenue is reported while also

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improving comparability in the financial statements of companies using U.S. GAAP and International Financial Reporting Standards. The core principle requires entities to recognize revenue in a manner that depicts the transfer of goods or services to customers in amounts that reflect the consideration to which an entity expects to be entitled in exchange for those goods or services. ASC Topic 606 became effective for annual periods beginning after December 15, 2017.

We adopted this standard using the modified retrospective method which did not result in an impact to its financial statements as we have not had product sales to date. Upon commercializing a product or executing any revenue generating contracts, we will provide additional disclosures in the notes to the consolidated financial statements related to the relevant aspects of any revenue generating contracts that we have or into which we expect to enter.

In January 2016, the FASB issued ASU No. 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities (ASU 2016-01). ASU 2016-01 eliminates the requirement to disclose the methods and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet. The standard also clarifies the need to evaluate a valuation allowance on a deferred tax asset related to available-for-sale securities in combination with the Company s other deferred tax assets. ASU 2016-01 is effective for annual reporting periods beginning after December 15, 2017. The Company adopted ASU 2016-01 as of January 1, 2018 but the adoption did not have any material impact on the Company s consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, Leases (ASU 2016-02). ASU 2016-02 requires the recognition of lease assets and lease liabilities by lessees for those leases classified as operating leases under previous GAAP. The classification criteria for distinguishing between finance leases and operating leases are substantially similar to the classification criteria for distinguishing between capital leases and operating leases in the previous leases guidance. ASU 2016-02 is effective for annual reporting periods beginning after December 15, 2018 and early adoption is permitted. The Company elected not to early adopt the standard, and therefore, will adopt the standard on January 1, 2019. We will elect the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allows us to carryforward the historical lease classification. We are not electing the hindsight practical expedient. We will make an accounting policy election to keep leases with an initial term of 12 months or less off of the balance sheet. We will recognize those lease payments in the consolidated statements of operations on a straight-line basis over the lease term.

We estimate adoption of the standard will result in recognition of additional net lease assets and lease liabilities of approximately $18 million and $21 million, respectively, as of January 1, 2019. The difference between these amounts represents the net deferred rent as of January 1, 2019 with no impact to the accumulated deficit. We do not believe the new standard will have a notable impact on our liquidity.

In February 2018, the FASB issued ASU No. 2018-02, Income Statement-Reporting Comprehensive Income (Topic 220) Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income, to address a specific consequence of the TCJA by allowing a reclassification from accumulated other comprehensive income to retained earnings for stranded tax effects resulting from the TCJA s reduction of the U.S. federal corporate income tax rate. The ASU is effective for all entities for fiscal years beginning after December 15, 2018, with early adoption permitted, and is to be applied either in the period of adoption or retrospectively to each period in which the effect of the change in the U.S. federal corporate income tax rate in the TCJA is recognized. The Company does not have any stranded tax effects to which this ASU would apply. Therefore, there is no impact to the Company s consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07, Compensation-Stock Compensation (Topic 718) Improvements to Nonemployee Share-Based Payment Accounting (ASU 2018-07). The standard allows for the entity to only remeasure equity-classified awards for which a measurement date has not been established through a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year of adoption. After

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adoption, the nonemployee share-based payment awards would be treated similar to employee share-based payment awards going forward. The ASU is effective for all entities for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. We are currently analyzing the impact of ASU 2018-07. As our nonemployee share-based awards are not significant, we do not expect the adoption will have a material impact on the consolidated accumulated deficit.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity. As of December 31, 2018, we had cash, cash equivalents and marketable securities of approximately $347.5 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 rise in interest rates has resulted in our unrealized loss on investments as of December 31, 2018 and 2017 totaling approximately $0.7 million and $0.8 million, respectively. Since we plan on holding those investments to maturity, no recognition of impairment is required. Declines in interest rates, however, would reduce future investment income.

Capital Market Risk. We currently have no product revenues and 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

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the period covered by this Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were effective 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, 2018. 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, 2018, 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 our assessment 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, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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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 subsidiaries internal control over financial reporting as of December 31, 2018, 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, Intra-Cellular Therapies, Inc. and subsidiaries (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, 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 of the Company as of December 31, 2018 and 2017, 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, 2018, and the related notes and our report dated February 27, 2019 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 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

February 27, 2019

Item 9B. OTHER INFORMATION

Not applicable.

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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, Section 16(a) Beneficial Ownership Reporting Compliance, and Code of Conduct and Ethics in the Company s Proxy Statement for the 2019 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 2019 Annual Meeting of Stockholders.

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 2019 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 2019 Annual Meeting of Stockholders.

Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The response to this item is incorporated by reference from the discussion responsive thereto under the caption Proposal [2]: Ratification of Selection of Independent Registered Public Accounting Firm in the Company s Proxy Statement for the 2019 Annual Meeting of Stockholders.

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PART IV

Item 15. EXHIBITS, 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 Consolidated 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, filed with the Secretary of State of the State of Delaware on November 7, 2013.		S-1/A (Exhibit 3.1)	11/26/13	333-191238
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		8-K (Exhibit 3.4)	9/5/2013	000-54896

	Registrant.			
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

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Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
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/A (Exhibit 10.1.1)	10/31/2013	000-54896
	.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 4, 2017 by and between Siegfried Evionnaz SA and ITI Limited.**		10-K (Exhibit 10.3)	3/1/2017	001-36274
10.3		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
10.4	.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
10.5		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
10.6	.1	Employment Agreement effective as of November 4, 2015 by and between Robert Davis, Ph.D. and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.6)	2/25/2016	001-36274
	.2	Amendment No.1 to Employment Agreement dated as of November 9, 2016 by and between Robert Davis, Ph.D. and Intra-Cellular Therapies, Inc.*		10-Q (Exhibit 10.2)	11/9/2016	001-36274
10.7	.1	Employment Agreement effective as of November 5, 2015 by and between Kimberly Vanover, Ph.D. and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.7)	2/25/2016	000-54896

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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 Employment Agreement dated as of November 9, 2016 by and between Kimberly Vanover, Ph.D. and Intra-Cellular Therapies, Inc.*		10-Q (Exhibit 10.3)	11/9/2016	001-36274
10.8	Employment Agreement effective as of November 13, 2017 by and between Andrew Satlin, M.D. and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.8)	3/1/2018	001-36274
10.9	Employment Agreement effective as of October 15, 2018 by and between Mark Neumann and Intra-Cellular Therapies, Inc.	X			
10.10	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
10.11	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
10.12	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
10.13	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of November 4, 2015 by and between Robert Davis, Ph.D. and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.11)	2/25/2016	001-36274
10.14	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of March 5, 2007 by and between Kimberly E. Vanover, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.12)	9/5/2013	000-54896

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Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.15	Employee Proprietary Information, Inventions, Inventions, and Non-Competition Agreement effective as of November 13, 2017 by and between Andrew Satlin, M.D. and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.14)	3/1/2018	001-36274
10.16	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.	X			
10.17	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
10.18	2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.14)	9/5/2013	000-54896
10.19	Form of Stock Option Agreement under the 2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.15)	9/5/2013	000-54896
10.20	Amended and Restated 2013 Equity Incentive Plan.*		8-K (Exhibit 10.1)	6/18/2015	001-36274
10.21	Form of Stock Option Agreement under the 2013 Equity Incentive Plan.*		10-K (Exhibit 10.19)	3/25/2014	001-36274
10.22	Intra-Cellular Therapies, Inc. 2018 Equity Incentive Plan.*		8-K (Exhibit 10.1)	6/21/2018	001-36274
10.23	Form of Stock Option Agreement under the 2018 Equity Incentive Plan.*		8-K (Exhibit 10.2)	6/21/2018	001-36274
10.24	Form of Director Stock Option Agreement under the 2018 Equity Incentive Plan.*		8-K (Exhibit 10.3)	6/21/2018	001-36274
10.25	Form of Restricted Stock Unit Agreement under the 2018 Equity Incentive Plan.*		8-K (Exhibit 10.4)	6/21/2018	001-36274

10.26	Form of Director Restricted Stock Unit Agreement under the 2018 Equity Incentive Plan.*	8-K (Exhibit 10.5)	6/21/2018	001-36274
10.27	Non-Employee Director Compensation Policy, as amended.*	10-Q (Exhibit 10.6)	8/2/2018	001-36274
10.28	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

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Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.29		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
10.30		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
14.1		Corporate Code of Conduct and Ethics and Whistleblower Policy.		10-K (Exhibit 14.1)	2/25/2016	001-36274
21.1		Subsidiaries.		10-K (Exhibit 21.1)	3/1/2017	001-36274
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	XBRL Instance Document.	X			
	.SCH	XBRL Taxonomy Extension Schema Document.	X			
	.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.	X			
	.DEF	XBRL Taxonomy Extension Definition.	X			
	.LAB	XBRL Taxonomy Extension Label Linkbase Document.	X			
	.PRE	XBRL Taxonomy Presentation Linkbase Document.	X			

* Management contract or compensatory plan or arrangement.

** Confidential treatment has been granted for portions of this Exhibit. Redacted portions filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

Not Applicable.

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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: February 27, 2019

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)	February 27, 2019
By: /s/ Lawrence J. Hineline Lawrence J. Hineline	Senior Vice President of Finance and Chief Financial Officer (principal financial officer and principal accounting officer)	February 27, 2019
By: /s/ Christopher Alafi, Ph.D. Christopher Alafi, Ph.D.	Director	February 27, 2019
By: /s/ Richard Lerner, M.D. Richard Lerner, M.D.	Director	February 27, 2019
By: /s/ Joel S. Marcus Joel S. Marcus	Director	February 27, 2019
By: /s/ Rory B. Riggs Rory B. Riggs	Director	February 27, 2019
By: /s/ Robert L. Van Nostrand Robert L. Van Nostrand	Director	February 27, 2019

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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 subsidiaries (the Company) as of December 31, 2018 and 2017, 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, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, 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, 2018, 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 February 27, 2019 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.

/s/ Ernst & Young LLP

We have served as the Company s auditor since 2002.

Baltimore, MD

February 27, 2019

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Intra-Cellular Therapies, Inc. and Subsidiaries

Consolidated Balance Sheets

	December 31, 2018	2017
Assets		
Current assets:		
Cash and cash equivalents	**$ 54,947,502**	$ 37,790,114
Investment securities, available-for-sale	**292,583,046**	426,540,921
Prepaid expenses and other current assets	**7,908,133**	4,884,293
Total current assets	**355,438,681**	469,215,328
Property and equipment, net	**1,159,766**	1,137,171
Long term deferred tax asset, net	**529,218**	1,058,435
Other assets	**78,833**	75,765
Total assets	**$ 357,206,498**	$ 471,486,699
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	**$ 13,961,060**	$ 6,173,539
Accrued and other current liabilities	**20,044,866**	6,424,221
Accrued employee benefits	**2,293,259**	1,611,846
Total current liabilities	**36,299,185**	14,209,606
Long-term deferred rent	**3,192,432**	2,840,132
Total liabilities	**39,491,617**	17,049,738
Stockholders equity:		
Common stock, $.0001 par value: 100,000,000 shares authorized; 54,895,295 and 54,597,679 shares issued and outstanding at December 31, 2018 and 2017, respectively	**5,490**	5,460
Additional paid-in capital	**880,753,339**	862,479,505
Accumulated deficit	**(562,376,191)**	(407,248,780)
Accumulated comprehensive loss	**(667,757)**	(799,224)
Total stockholders equity	**317,714,881**	454,436,961
Total liabilities and stockholders equity	**$ 357,206,498**	$ 471,486,699

See accompanying notes to consolidated financial statements.

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Intra-Cellular Therapies, Inc. and Subsidiaries

Consolidated Statements of Operations

	Years Ended December 31,		
	2018	**2017**	**2016**
Grant revenue	**$**	$ 245,837	$ 330,702
Costs and expenses:			
Research and development	**132,166,913**	79,419,009	93,831,530
General and administrative	**30,099,855**	23,666,957	24,758,063
Total costs and expenses	**162,266,768**	103,085,966	118,589,593
Loss from operations	**(162,266,768)**	(102,840,129)	(118,258,891)
Interest income	**(7,140,957)**	(4,005,864)	(2,935,077)
Interest expense			36,781
Loss before provision (benefit) for income taxes	**(155,125,811)**	(98,834,265)	(115,360,595)
Income tax expense (benefit)	**1,600**	(1,060,851)	1,065,673
Net loss	**$ (155,127,411)**	$ (97,773,414)	$ (116,426,268)
Net loss per common share:			
Basic & Diluted	**$ (2.84)**	$ (2.12)	$ (2.69)
Weighted average number of common shares:			
Basic & Diluted	**54,707,865**	46,181,926	43,240,188

See accompanying notes to consolidated financial statements.

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Intra-Cellular Therapies, Inc. and Subsidiaries

Consolidated Statements of Comprehensive Loss

	Years Ended December 31,		
	2018	**2017**	**2016**
Net loss	**$ (155,127,411)**	$ (97,773,414)	$ (116,426,268)
Other comprehensive loss:			
Unrealized gain (loss) on investment securities	**131,467**	(481,985)	273,171
Comprehensive loss	**$ (154,995,944)**	$ (98,255,399)	$ (116,153,097)

See accompanying notes to consolidated financial statements.

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Intra-Cellular Therapies, Inc. and Subsidiaries

Consolidated Statements of Stockholders Equity

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Comprehensive Loss	Total Stockholders Equity
	Shares	Amount				
Balance at December 31, 2015	43,155,875	$ 4,316	$ 669,878,103	$ (193,049,098)	$ (590,410)	$ 476,242,911
Exercise of stock options	123,745	12	477,722			477,734
Restricted Stock issued to employee	1,757					
Stock issued for services	11,529	1	233,771			233,772
Share-based compensation			14,701,219			14,701,219
Net loss				(116,426,268)		(116,426,268)
Other comprehensive gain					273,171	273,171
Balance at December 31, 2016	43,292,906	$ 4,329	$ 685,290,815	$ (309,475,366)	$ (317,239)	$ 375,502,539
Common shares issued October 2017	11,129,032	1,113	162,071,143			162,072,256
Exercise of stock options and issuances of restricted stock	162,642	17	285,143			285,160
Stock issued for services	13,099	1	190,884			190,885
Share-based compensation			14,641,520			14,641,520
Net loss				(97,773,414)		(97,773,414)
Other comprehensive loss					(481,985)	(481,985)
Balance at December 31, 2017	**54,597,679**	**$ 5,460**	**$ 862,479,505**	**$ (407,248,780)**	**$ (799,224)**	**$ 454,436,961**
Exercise of stock options and issuances of restricted stock	**284,326**	**29**	**674,177**			**674,206**
Stock issued for services	**11,468**	**1**	**192,529**			**192,530**
Share-based compensation			**17,396,146**			**17,396,146**
Stock warrant	**1,822**		**10,982**			**10,982**
Net loss				**(155,127,411)**		**(155,127,411)**
Other comprehensive gain					**131,467**	**131,467**

Balance at December 31, 2018	**54,895,295**	**$ 5,490**	**$ 880,753,339**	**$ (562,376,191)**	**$ (667,757)**	**$ 317,714,881**

See accompanying notes to consolidated financial statements.

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Intra-Cellular Therapies, Inc. and Subsidiaries

Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2018	**2017**	**2016**
Operating activities			
Net loss	**$ (155,127,411)**	$ (97,773,414)	$ (116,426,268)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation expense	**368,673**	213,872	196,872
Share-based compensation	**17,396,146**	14,641,520	14,701,219
Stock issued for services	**192,530**	190,885	233,772
Amortization of premiums and discounts on investment activities	**(943,239)**	429,839	544,354
Changes in operating assets and liabilities:			
Accounts receivable		94,339	(63,679)
Prepaid expenses and other assets	**(3,026,908)**	(879,200)	4,016,164
Long term deferred tax asset, net	**529,217**	(1,058,435)	
Accounts payable	**7,787,521**	2,418,892	2,121,742
Accrued liabilities and employee benefits	**14,386,774**	1,211,103	2,147,080
Deferred rent	**267,584**	18,787	1,271,517
Net cash used in operating activities	**(118,169,113)**	(80,491,812)	(91,257,227)
Investing activities			
Purchases of investments	**(271,156,707)**	(520,926,824)	(395,757,168)
Maturities of investments	**406,189,288**	428,932,538	488,068,547
Purchases of property and equipment	**(391,268)**	(723,429)	(48,964)
Net cash provided by (used in) investing activities	**134,641,313**	(92,717,715)	92,262,415
Financing activities			
Proceeds from line of credit			125,000,000
Repayment of line of credit			(125,000,000)
Proceeds from stock option exercises	**674,206**	285,160	477,734
Proceeds of public offerings, net		162,072,256	
Proceeds from stock warrant	**10,982**		
Net cash provided by financing activities	**685,188**	162,357,416	477,734
Net increase (decrease) in cash and cash equivalents	**17,157,388**	(10,852,111)	1,482,922
Cash and cash equivalents at beginning of period	**37,790,114**	48,642,225	47,159,303
Cash and cash equivalents at end of period	**$ 54,947,502**	$ 37,790,114	$ 48,642,225
Cash paid for interest	**$**	$	$ 36,781

Cash paid for taxes	**$ 1,600**	$ 1,600	$ 1,001,600	

See accompanying notes to consolidated financial statements.

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Intra-Cellular Therapies, Inc. and Subsidiaries

Notes to Consolidated Financial Statements

December 31, 2018

1. Organization

Intra-Cellular Therapies, Inc. (the Company), through its wholly-owned operating subsidiaries, ITI, Inc. (ITI) and ITI Limited, is a biopharmaceutical company focused on the discovery and clinical development of innovative, small molecule drugs that address underserved medical needs in neuropsychiatric and neurological disorders by targeting intracellular signaling mechanisms within the central nervous system (CNS). The Company s lead product candidate, lumateperone, is in Phase 3 clinical development as a novel treatment for schizophrenia, bipolar depression and agitation associated with dementia, including Alzheimer s disease.

The Company was originally incorporated in the State of Delaware in August 2012 under the name Oneida Resources Corp. Prior to a reverse merger that occurred on August 29, 2013 (the Merger), Oneida Resources Corp. was a shell company registered under the Securities Exchange Act of 1934, as amended (the Exchange Act), with no specific business plan or purpose until it began operating the business of ITI, through the Merger transaction on August 29, 2013. 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 CNS. Effective upon the Merger, a wholly-owned subsidiary of the Company merged with and into ITI, and ITI continues as the operating subsidiary of the Company.

In September 2016, the Company licensed certain intellectual property rights to its wholly-owned subsidiary, ITI Limited, which was formed in the third quarter of 2016. Although the license of intellectual property rights did not result in any gain or loss in the consolidated statements of operations, the $125 million of gain related to the transaction helped generate net taxable income for tax purposes in the U.S. and the Company utilized a portion of its available federal and state net operating loss carryforwards to offset the majority of this gain. Any taxes incurred related to intercompany transactions were treated as tax expense in the Company s consolidated statement of operations. In addition to the license, the Company also entered into a research and development agreement with ITI Limited pursuant to which the Company will conduct research and development services related to the license agreement and charge ITI Limited for these services.

On October 2, 2017 and October 5, 2017, the Company completed a public offering of common stock in which the Company sold 11,129,032 shares of common stock, which included the exercise of the underwriters option to purchase an additional 1,451,613 shares, at an offering price of $15.50 per share for aggregate gross proceeds of approximately $172 million. After deducting underwriting discounts, commissions and offering expenses, the net proceeds to the Company were approximately $162 million.

In order to further its research projects and support its collaborations, the Company will 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 into the second half of 2020, at which time the Company will require additional financing. Possible sources of funds include public or private sales of the Company s equity securities, sales of debt securities, the incurrence of debt from commercial lenders, strategic collaborations, licensing a portion or all of the Company s product candidates and technology and, to a lesser extent, grant funding. On September 2, 2016, the Company filed a universal shelf registration statement on Form S-3, which was declared effective by the Securities

and Exchange Commission (the SEC) on September 14, 2016, on which the Company registered for sale up to $350 million of any combination of its common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that the Company may determine. After the public offering in October 2017, approximately $178 million of securities remain available for issuance under this shelf registration statement. This registration statement will remain in effect for up to three years from the initial effective date.

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1. Organization (continued)

In the third quarter of 2018, the Company completed the rolling submission of its New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for lumateperone, a once-daily, oral investigational medicine with a novel mechanism of action for the treatment of schizophrenia and in the fourth quarter of 2018 the FDA accepted the NDA for review. The NDA submission is supported by data from 20 clinical trials and more than 1,900 subjects exposed to lumateperone. Lumateperone received Fast Track designation from the FDA in November 2017 for the treatment of schizophrenia.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements of Intra-Cellular Therapies, Inc. and its wholly own subsidiaries 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 generally accepted accounting principles 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 and developing drugs 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.

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 balance sheet.

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 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 income, 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 is recognized as interest income when earned. The cost of securities sold is calculated using the specific identification method.

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2. Summary of Significant Accounting Policies (continued)

Investment securities consisted of the following (in thousands):

	December 31, 2018			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
U.S. government agency securities	$ 124,691	$ 24	$ (289)	$ 124,426
FDIC certificates of deposit (1)	245			245
Certificates of deposit	1,000			1,000
Commercial paper	41,317		(45)	41,272
Corporate notes/bonds	125,998	7	(365)	125,640
	$ 293,251	$ 31	$ (699)	$ 292,583

	December 31, 2017			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
U.S. government agency securities	$ 126,330	$	$ (348)	$ 125,982
FDIC certificates of deposit (1)	8,306			8,306
Certificates of deposit	103,500			103,500
Commercial paper	51,414		(61)	51,353
Corporate notes/bonds	137,790		(390)	137,400
	$ 427,340	$	$ (799)	$ 426,541

(1) FDIC Certificates of Deposit consist of deposits that are $250,000 or less.

The Company has classified all of its investment securities 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, 2018 and 2017, the Company held $64.6 million and $93.3 million, respectively, of available-for-sale investment securities with contractual maturity dates more than one year and less than two years.

The Company monitors its investment portfolio for impairment quarterly or more frequently if circumstances warrant. In the event that the carrying value of an investment exceeds its fair value and the decline in value is determined to be other-than-temporary, the Company records an impairment charge within earnings attributable to the estimated credit loss. In determining whether a decline in the value of an investment is other-than-temporary, the Company evaluates currently available factors that may include, among others: (1) general market conditions; (2) the duration and extent

to which fair value has been less than the carrying value; (3) the investment issuer s financial condition and business outlook; and (4) the Company s assessment as to whether it is more likely than not that the Company will be required to sell a security prior to recovery of its amortized cost basis. As of December 31, 2018, the aggregate related fair value of investments with unrealized losses was $272.5 million and the aggregate amount of unrealized losses was $0.7 million. Of the $272.5 million, $180.4 million have been held in a continuous unrealized loss position for less than 12 months and $92.1 million have been held in a continuous loss position for 12 months or longer. The total continuous unrealized loss for investments held for 12 months or longer is approximately $345,000 as of December 31, 2018. As of December 31, 2017, the Company had approximately $37.3 million of investments with a continuous unrealized loss for 12 months or longer of approximately $42,000.

The Company attributes the unrealized losses on the available-for-sale securities as of December 31, 2018 and 2017 to the rise in related market interest rates. The Company does not intend to sell these securities, nor is it

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2. Summary of Significant Accounting Policies (continued)

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. As such, the Company does not consider these securities to be other-than-temporarily impaired.

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.

The Company has no assets or liabilities that were measured using quoted prices for significant unobservable inputs (Level 3 assets and liabilities) as of December 31, 2018 and December 31, 2017. The carrying value of cash held in money market funds of approximately $39.6 million as of December 31, 2018 and $26.2 million as of December 31, 2017 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 certificates of deposit of approximately $7.5 million as of December 31, 2018 is included in cash and cash equivalents and approximates market value based on quoted market price or Level 1 inputs.

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2. Summary of Significant Accounting Policies (continued)

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

	December 31, 2018	Fair Value Measurements at Reporting Date Using: Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds	$ 39,591	$ 39,591	$	$
U.S. government agency securities	124,426		124,426	
FDIC certificates of deposit	245		245	
Certificates of deposit	8,500		8,500	
Commercial paper	41,272		41,272	
Corporate bonds/notes	125,640		125,640	
	$ 339,674	$ 39,591	$ 300,083	$

	December 31, 2017	Fair Value Measurements at Reporting Date Using: Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds	$ 26,181	$ 26,181	$	$
U.S. government agency securities	125,982		125,982	
FDIC certificates of deposit	8,306		8,306	
Certificates of deposit	103,500		103,500	
Commercial paper	51,353		51,353	
Corporate bonds/notes	137,400		137,400	

	$ 452,722	$ 26,181	$ 426,541	$

Financial Instruments

The Company considers the recorded costs of its financial assets and liabilities, which consist of cash equivalents, prepaid expenses, accounts payable and accrued liabilities, to approximate their fair value because of their relatively short maturities at December 31, 2018 and December 31, 2017. At December 31, 2018, the Company has approximately $2.4 million as a prepaid expense related to a regulatory filing fee that is expected to be refunded within the next year. Management believes that the risks associated with its financial instruments are minimal as the counterparties are various corporations, financial institutions and government agencies of high credit standing.

Concentration of Credit Risk

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.

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2. Summary of Significant Accounting Policies (continued)

Accounts Receivable

Accounts receivable that management has the intent and ability to collect are reported in the balance sheets at outstanding amounts, less an allowance for doubtful accounts. The Company writes off uncollectible receivables when the likelihood of collection is not probable.

The Company evaluates the collectability of accounts receivable on a regular basis. The allowance, if any, is based upon various factors including the financial condition and payment history of customers, an overall review of collections experience on other accounts and economic factors or events expected to affect future collections experience. No allowance was recorded as of December 31, 2018 and 2017, as the Company has a history of collecting on all its accounts including government agencies and collaborations funding its research and there were no balances in accounts receivable as of these dates.

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.

Research and Development

Except for payments made in advance of services, the Company expenses its research and development costs as incurred. For payments made in advance, the Company recognizes research and development expense as the services are rendered. 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 preclinical analytical testing, manufacturing of drug product, 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

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2. Summary of Significant Accounting Policies (continued)

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. For the years ended December 31, 2018 and 2017, there were no material adjustments to the Company s prior period estimates of accrued expenses for clinical trials.

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 (previously included in FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes an Interpretation of FASB Statement No. 109*). 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.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act (TCJA) that significantly reforms the Internal Revenue Code of 1986, as amended (the Code). The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a worldwide system of taxation to a territorial system. In addition, the TCJA repealed the alternative minimum tax (AMT) and provides for a refund of taxes paid between 2018 and 2021. With the passing of the TCJA, the Company will receive a refund in future periods for AMT paid in prior years. The Company therefore has recognized a benefit of approximately $1.1 million for these taxes for the year ended December 31, 2017.

During December 2017, the SEC staff issued Staff Accounting Bulletin No. 118 (SAB 118) to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed

(including computations) in reasonable detail to complete the accounting for certain income tax effects of the TCJA. The Company has recognized the provisional tax impacts related to the release of the valuation allowance with respect to AMT credits and the revaluation of deferred tax assets and liabilities

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2. Summary of Significant Accounting Policies (continued)

and included these amounts in its consolidated financial statements for the year ended December 31, 2017. The Company completed its evaluation of the effects of the TCJA during the 4th quarter 2018 and the provisional amounts the Company accounted for in its December 31, 2017 provision were finalized in 2018 with no adjustments.

The Company recorded income tax expense of $1,600, a benefit of $1.1 million, and a tax expense of $1,065,673 for the years ended December 31, 2018, 2017, and 2016, respectively. The Company s effective tax rate for the years ended December 31, 2018 and 2017 was approximately 0% and 1.1% respectively. The Company s annual effective tax rate of approximately 0% 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.

Comprehensive Income (Loss)

All components of comprehensive income (loss), including net income (loss), are reported in the financial statements in the period in which they are incurred. Comprehensive income (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 income (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 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, 2018, 2017 and 2016 is based on share-based awards ultimately expected to vest.

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.

Expected volatility rates are based on a combination of the historical volatility of the common stock of comparable publicly traded entities and the limited historical information about 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.

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2. Summary of Significant Accounting Policies (continued)

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. The Company has granted RSUs that vest in three equal annual installments provided that the employee remains employed with the Company.

Beginning in the first quarter of 2016 and in 2017 and 2018, the Company granted time-based RSUs that vest in three equal annual installments. In the first quarter of 2017, the Company granted performance-based RSUs, which vest based on the achievement of certain milestones that include (i) the submission of a NDA with the FDA, (ii) the approval of the NDA by the FDA (collectively, the Milestone RSUs) and (iii) the achievement of certain comparative shareholder returns against the Company s peers (the TSR RSUs). The Milestone RSUs were valued at the closing price on March 8, 2017. The Milestone RSUs related to the NDA submission has been fully amortized through December 31, 2018. The NDA submission milestone was achieved in the third quarter of 2018, so the Milestone RSUs related to the NDA submission vested on December 31, 2018. The amortization of the expenses for Milestone RSUs related to the approval of the NDA will commence if and when the NDA submission has been approved through the last day of the calendar year in which the milestone is achieved. The TSR RSUs were valued using the Monte Carlo Simulation method and will be amortized over the life of the RSU agreements which ends December 31, 2019. The Milestone RSUs and TSR RSUs are target based and the ultimate awards, if attained, could be the target amount or higher or lower than the target amount, depending on the timing or achievement of the goal. The expense recognition related to these equity grants is based on the Company s best estimate.

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 shall be 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.

Since the Company had net operating loss carryforwards as of December 31, 2018, 2017 and 2016, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations. In March 2016, the FASB issued ASU No. 2016-09, Compensation Stock Compensation (ASU 2016-09). ASU 2016-09 simplifies several areas of accounting for stock compensation, including simplification of the accounting for income taxes, classification of excess tax benefits on the Statement of Cash Flows and forfeitures. As of January 1, 2017, the Company adopted ASU 2016-09 for the quarter ended March 31, 2017. Accordingly, the Company recognized previously unrecognized excess tax benefits of $9.7 million recorded as deferred tax assets with a corresponding offsetting full valuation allowance at the beginning of 2017, which yielded no tax impact.

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 June 2018, the Company s stockholders approved the Company s 2018 Equity Incentive Plan pursuant to which 4,750,000 additional shares of common stock were reserved for future equity grants.

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.

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2. Summary of Significant Accounting Policies (continued)

The following common stock equivalents were excluded in the calculation of diluted loss per share because their effect would be anti-dilutive as applied to the net loss for the years ended December 31, 2018, 2017 and 2016:

	Year Ended December 31,		
	2018	2017	2016
Common Stock Equivalents	610,429	476,252	1,225,614
RSUs	386,678	87,988	32,781
TSR RSUs	48,500	65,852	

Recently Issued Accounting Standards

In May 2014, the FASB issued ASC Update No. 2014-09, Revenue from Contracts with Customers (Topic 606), which has been subsequently updated (as updated, ASC Topic 606). The purpose of ASC Topic 606 is to provide enhancements to the quality and consistency of how revenue is reported while also improving comparability in the financial statements of companies using U.S. GAAP and International Financial Reporting Standards. The core principle requires entities to recognize revenue in a manner that depicts the transfer of goods or services to customers in amounts that reflect the consideration to which an entity expects to be entitled in exchange for those goods or services. ASC Topic 606 became effective for annual periods beginning after December 15, 2017.

The Company adopted this standard using the modified retrospective method which did not result in an impact to its financial statements as the Company has not had product sales to date. Upon commercializing a product or executing any revenue generating contracts, the Company will provide additional disclosures in the notes to the consolidated financial statements related to the relevant aspects of any revenue generating contracts that the Company has or into which the Company expects to enter.

In January 2016, the FASB issued ASU No. 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities (ASU 2016-01). ASU 2016-01 eliminates the requirement to disclose the methods and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet. The standard also clarifies the need to evaluate a valuation allowance on a deferred tax asset related to available-for-sale securities in combination with the Company s other deferred tax assets. ASU 2016-01 is effective for annual reporting periods beginning after December 15, 2017. The adoption of this standard on January 1, 2018 did not have a material impact on the Company s consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, Leases (ASU 2016-02). ASU 2016-02 requires the recognition of lease assets and lease liabilities by lessees for those leases classified as operating leases under previous GAAP. The classification criteria for distinguishing between finance leases and operating leases are substantially similar to the classification criteria for distinguishing between capital leases and operating leases in the previous leases guidance. ASU 2016-02 is effective for annual reporting periods beginning after December 15, 2018 and early adoption is permitted. The Company elected not to early adopt the standard, and therefore, will adopt the standard on January 1, 2019. We will elect the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allows us to carryforward the historical lease classification. We are not electing the hindsight practical expedient. We will make an accounting policy election to keep leases with an initial term of 12 months or less off of the balance sheet. We will recognize those lease payments in the consolidated statements of

operations on a straight-line basis over the lease term.

We estimate adoption of the standard will result in recognition of additional net lease assets and lease liabilities of approximately $18 million and $21 million, respectively, as of January 1, 2019. The difference between these amounts represents the net deferred rent as of January 1, 2019 with no impact on the accumulated deficit. We do not believe the new standard will have a notable impact on our liquidity.

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2. Summary of Significant Accounting Policies (continued)

In February 2018, the FASB issued ASU No. 2018-02, Income Statement-Reporting Comprehensive Income (Topic 220) Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income, to address a specific consequence of the TCJA by allowing a reclassification from accumulated other comprehensive income to retained earnings for stranded tax effects resulting from the TCJA s reduction of the U.S. federal corporate income tax rate. The ASU is effective for all entities for fiscal years beginning after December 15, 2018, with early adoption permitted, and is to be applied either in the period of adoption or retrospectively to each period in which the effect of the change in the U.S. federal corporate income tax rate in the TCJA is recognized. The Company does not have any stranded tax effects to which this ASU would apply. Therefore, there is no impact to the Company s consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07, Compensation-Stock Compensation (Topic 718) Improvements to Nonemployee Share-Based Payment Accounting (ASU 2018-07). The standard allows for the entity to only remeasure equity-classified awards for which a measurement date has not been established through a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year of adoption. After adoption, the nonemployee share-based payment awards would be treated similar to employee share-based payment awards going forward. The ASU is effective for all entities for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. The Company is currently analyzing the impact of ASU 2018-07. As the Company s nonemployee share-based awards are not significant, the Company does not expect the adoption will have a material impact on the consolidated accumulated deficit.

3. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2018	**2017**
Computer equipment	$ 44,427	$ 33,584
Furniture and fixtures	341,582	301,509
Scientific equipment	3,658,209	3,494,866
Leasehold improvements	149,470	
	4,193,688	3,829,959
Less accumulated depreciation	(3,033,922)	(2,692,788)
	$ 1,159,766	$ 1,137,171

Depreciation expense for the years ended December 31, 2018, 2017 and 2016 was $368,673, $213,872 and $196,872, respectively.

4. Share-Based Compensation

On June 18, 2018, the Company s stockholders approved the 2018 Equity Incentive Plan (the 2018 Plan). The 2018 Plan provides for the granting of stock-based awards, such as stock options, restricted common stock, RSUs and stock appreciation rights to employees, directors and consultants as determined by the Board of Directors. The 2018 Plan replaced the Company s Amended and Restated 2013 Equity Incentive Plan (the 2013 Plan). The Company will grant no further stock options or other awards under the 2013 Plan. Any options or other awards outstanding under the 2013 Plan remain outstanding in accordance with their terms and the terms of the 2013 Plan. As of December 31, 2018, the total number of shares reserved under all equity plans is 10,287,390 and the Company had 4,807,323 shares available for future issuance under the 2018 Plan. Stock options granted under the Plan may be either incentive stock options (ISOs) as defined by the Code, or non-qualified stock options. 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

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4. Share-Based Compensation (continued)

exercise price of ISOs granted under the Plan must be at least equal to the fair market value of the common stock on the date of grant.

Total stock-based compensation expense related to all of the Company s share-based awards, including stock options and RSUs granted to employees, directors and consultants recognized during the years ended December 31, 2018, 2017 and 2016, was comprised of the following:

	Years Ended December 31,		
	2018	**2017**	**2016**
Research and development	**$ 7,380,814**	$ 5,082,823	$ 4,472,658
General and administrative	**10,015,332**	9,558,697	10,228,561
Total share-based compensation expense	**$ 17,396,146**	$ 14,641,520	$ 14,701,219

The following table describes the assumptions used for calculating the value of options granted during the years ended December 31, 2018, 2017 and 2016:

	2018	**2017**	**2016**
Dividend yield	**0%**	0%	0%
Expected volatility	**85.2%-85.8%**	87.4%-90.4%	80.0%-90.0%
Weighted-average risk-free interest rate	**2.48%**	2.1%	1.7%
Expected term (in years)	**6.0**	6.0	5.9

Information regarding the stock options activity, including with respect to grants to employees, directors and consultants as of December 31, 2018, and changes during the period then ended, are summarized as follows:

	Number of Shares	**Weighted-Average Exercise Price**	**Aggregate Intrinsic Value**	**Weighted-Average Contractual Life**
Outstanding at December 31, 2017	3,755,736	$ 18.75	$ 7,450,293	7.04 years
Options granted	1,175,187	$ 15.22		9.37 years
Options exercised	(143,056)	$ 4.71		1.55 years
Options canceled or expired	(39,476)	$ 23.25		8.33 years
Outstanding at December 31, 2018	4,748,391	$ 18.26	$ 4,074,116	6.98 years
Vested or expected to vest at December 31, 2018	4,748,391	$ 18.26		

Exercisable at December 31, 2018	2,936,552	$ 18.70	$ 4,074,116	5.89 years

The weighted-average grant date fair value for awards granted during the years ended December 31, 2018, 2017 and 2016 was $15.22, $15.08 and $48.85 per share, respectively. Total intrinsic value of the options exercised during the years ended December 31, 2018, 2017 and 2016 was approximately $1,683,679, $1,609,268 and $2,984,283, respectively. The total fair value of shares vested in the years ended December 31, 2018, 2017 and 2016 was approximately $11,348,595, $7,212,195 and $9,310,898, respectively.

During 2018, 2017 and 2016, the Company granted options to certain scientific advisory board members of the Company to purchase 12,000, 0 and 5,000 shares of common stock, respectively, at an average exercise price per share of $15.47, $0 and $53.63, respectively. The options vest ratably over a period of 2 years. Stock compensation related to these grants will fluctuate with any changes in the underlying value of the Company s common stock.

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4. Share-Based Compensation (continued)

As of December 31, 2018 and 2017, there were $6,493,399 and $2,866,164, respectively, of unrecognized compensation costs related to unvested time based RSUs which will be recognized over a weighted-average period 1.9 years. The unrecognized share-based compensation expense related to stock option awards at December 31, 2018 is $13,669,451 and will be recognized over a weighted-average period of 2.0 years.

The fair value of an RSU is based on the closing price of the Company s common stock on the date of grant. Information regarding RSU activity, including with respect to grants to employees as of December 31, 2018, and changes during the year then ended, is summarized as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value
Outstanding at December 31, 2017	190,933	$ 25.48
RSU s granted	544,542	$ 17.02
RSU s vested	(72,663)	$ 29.03
RSU s cancelled	(15,401)	$ 17.13
Outstanding at December 31, 2018	647,411	$ 18.16

The Company recognized non-cash stock-based compensation expense related to RSU s for the years ended December 31, 2018, 2017 and 2016 of approximately $4.8 million, $2.1 million and $1.5 million, respectively.

Information related to the Company s Milestone RSUs and the TSR RSUs during the year ended December 31, 2018 are summarized as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value Per Share
Outstanding at December 31, 2017	347,199	$ 15.35
RSU s granted		$
RSU s vested	(68,607)	$ 15.35
RSU s cancelled		$
Outstanding at December 31, 2018	278,592	$ 15.35

The weighted average estimated fair value per share of the TSR RSUs granted in March 31, 2017 was $17.08, which was derived from a Monte Carlo simulation. Significant assumptions utilized in estimating the value of the awards

granted include an expected dividend yield of 0%, a risk free rate of 1.6%, and expected volatility of 95.4%. The TSR RSUs granted in 2017 will entitle the grantee to receive a number of shares of the Company s common stock determined over a three-year performance period ending and vesting on December 31, 2019, provided the grantee remains in the service of the Company on the settlement date. The Company expenses the cost of these awards ratably over the requisite service period. The number of shares for which the TSR RSUs will be settled will be a percentage of shares for which the award is targeted and will depend on the Company s total shareholder return (as defined below), expressed as a percentile ranking of the Company s total shareholder return as compared to the Company s peer group (as defined below). The number of shares for which the TSR RSUs will be settled vary depending on the level of achievement of the goal. Total shareholder return is determined by dividing the average share value of the Company s common stock over the 30 trading days preceding January 1, 2020 by the average share value of the Company s common stock over the 30 trading days beginning on January 1, 2017, with a deemed reinvestment of any dividends declared during the performance period. The Company s peer group includes 223 companies at December 31, 2018 which comprise the Nasdaq

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4. Share-Based Compensation (continued)

Biotechnology Index, which was selected by the Compensation Committee of the Company s Board of Directors and includes a range of biotechnology companies operating in several business segments.

As of December 31, 2018 and 2017 there were $2,795,202 and $4,177,362 respectively of unrecognized compensation costs related to unvested Milestone RSU grants and TSR RSU grants which will be recognized over a weighted average period of 1.0 years.

5. Line of Credit

On September 30, 2016, the Company entered into a secured line of credit with a lender for an amount not to exceed $150.8 million. This line of credit was secured by approximately $150.8 million of collateral held by the lender. The interest on advances under this line of credit was fixed at LIBOR plus 2.991% on the date of advance. The Company borrowed $125.0 million on September 30, 2016 and repaid the entire amount on October 3, 2016. Interest expense under this secured line of credit was $36,781 for the year ended December 31, 2016. On October 6, 2016, the line of credit was terminated by the Company.

6. Income Taxes

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act (TCJA) that significantly reforms the Internal Revenue Code of 1986, as amended (the Code). The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a worldwide system of taxation to a territorial system. In addition, the TCJA repealed the alternative minimum tax (AMT) and provides for a refund of taxes paid between 2018 and 2021. With the passing of the TCJA, the Company will receive a refund in future periods for AMT paid in prior years. The Company therefore has recognized a benefit of approximately $1.1 million for these taxes in December 2017.

While the TCJA provide for a territorial tax system, beginning in 2018, it includes two new U.S. tax base erosion provisions, the global intangible low-taxed income (GILTI) provisions and the base-erosion and anti-abuse tax (BEAT) provisions.

The GILTI provisions require the Company to include in its U.S. income tax return foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary s tangible assets. As of year ended December 31, 2018, the Company s foreign operations do not generate income and the Company is not currently subject to the GILTI provisions. The Company has not made an accounting policy election for GILTI and will analyze and formulate its GILTI accounting policy in the period which the Company becomes subject to the GILTI provisions.

The BEAT provisions eliminates the deduction of certain base-erosion payments made to related foreign corporations, and impose a minimum tax if greater than regular tax. The Company has not made any qualifying payments and the BEAT tax is not applicable in 2018. Therefore, the Company has not included any tax impacts of BEAT in its consolidated financial statements for the year ended December 31, 2018.

During December 2017, the SEC staff issued Staff Accounting Bulletin No. 118 (SAB 118) to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed

(including computations) in reasonable detail to complete the accounting for certain income tax effects of the TCJA. The Company has recognized the provisional tax impacts related to the release of the valuation allowance with respect to AMT credits and the revaluation of deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2017. The Company completed its evaluation of the effects of the TCJA during the 4th quarter 2018 and the provisional amounts the Company accounted for in its December 31, 2017 provision were finalized in 2018 with no adjustments.

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6. Income Taxes (continued)

Income (loss) before income taxes is as follows:

	2018	2017	2016
U.S.	**$ (30,299,751)**	$ (20,486,935)	$ (86,965,860)
Non-U.S.	**(124,826,060)**	(78,347,330)	(28,394,735)
Total loss before taxes	**$ (155,125,811)**	$ (98,834,265)	$ (115,360,595)

Total income tax (benefit) expense for the years ended December 31, 2018, 2017 and 2016 is allocated as follows:

	2018	2017	2016
Current	**$ 1,600**	$ (2,416)	$ 1,065,673
Deferred	**(5,054,468)**	13,713,987	19,605,520
Valuation allowance	**5,054,468**	(14,772,422)	(19,605,520)
Provision (benefit) for income taxes	**$ 1,600**	$ (1,060,851)	$ 1,065,673

A reconciliation of the difference between the statutory federal income tax rate and the effective income tax rate for the years ended December 31, 2018, 2017 and 2016 is as follows:

	December 31,		
	2018	2017	2016
Income tax benefit at statutory federal rate	**21.00%**	35.00%	35.00%
Royalty Income	**0.00**	0.00	(37.93)
Other Permanent differences	**(0.58)**	(0.43)	(0.78)
Foreign rate differential	**(16.90)**	(27.75)	(8.61)
2017 US Tax Reform impact	**0.00**	(21.89)	0.00
R&D Credit	**0.00**	(0.05)	2.08
Change in effective state tax rates	**(0.38)**	0.84	(6.98)
State income tax expense	**0.12**	0.40	(0.70)
Change in valuation allowance	**(3.26)**	14.95	16.99
Benefit (provision) for income taxes	**0.00%**	1.07%	(0.93)%

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, 2018, the Company had $145.3 million of federal net operating loss carryforwards, which expire at various dates through 2037. 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, 2018, 2017 and 2015, 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, 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.

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6. Income Taxes (continued)

In September 2016, the Company licensed certain intellectual property rights to its wholly-owned subsidiary, ITI Limited, which was formed in the third quarter of 2016. The costs to develop, test, manufacture and perform other activities related to the lumateperone (also known as ITI-007) program will be the responsibility of ITI Limited and will be incurred outside of the United States. Therefore, the majority of expected losses incurred by the Company during the next several years will not result in additional NOLs to be carried forward and used against future net income in the U.S. The following summarizes the significant components of the Company s deferred tax assets and liabilities as of December 31, 2018 and 2017, respectively:

	December 31,	
	2018	**2017**
Deferred tax assets:		
Net operating loss carryforwards	$ 43,872,566	$ 40,746,589
Accrued employee benefits	441,780	378,058
Research and development credit	9,321,214	9,321,214
Stock compensation	10,530,859	8,711,721
Federal AMT credit	529,218	1,058,435
Deferred rent	712,314	699,560
Unrealized comprehensive loss	146,531	187,714
Depreciation	1,082	
Deferred tax liabilities:		
Depreciation		(31,796)
Net deferred tax asset	65,555,564	61,071,495
Valuation allowance	(65,026,346)	(60,013,060)
Net deferred tax asset	$ 529,218	$ 1,058,435

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, excluding the refundable alternative minimum tax credit in 2017 and 2018, for financial reporting purposes because it is not more likely than not that these deferred tax assets will be realized. In 2018, the Company reclassified $529,218 (50%) Federal AMT to Other Current Assets.

The total amount of unrecognized tax benefits was $1.7 million as of December 31, 2018 and December 31, 2017. If recognized none of these tax benefits would affect the effective tax rate due to valuation allowances.

The following summarizes the significant components of gross unrecognized tax benefits as of December 31, 2018 and 2017, respectively:

	December 31,	
	2018	**2017**
Balance at January 1,	**$ 1,738,815**	$ 1,738,815
Current Year Uncertain Tax Positions:		
Gross Increases		
Balance at December 31,	**$ 1,738,815**	$ 1,738,815

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7. Collaborations and License Agreements

The Bristol-Myers Squibb License Agreement

On May 31, 2005, the Company entered into a worldwide, exclusive License Agreement with Bristol-Myers Squibb Company (BMS), 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, 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. The Company achieved the acceptance in the third quarter of 2018 and has therefore accrued the $2.0 million which was paid in January 2019. Possible milestone payments remaining total $10.0 million, including a $5.0 million milestone payable upon an NDA approval. 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 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, 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. In connection with the transfer, the Company guaranteed ITI Limited s performance of its obligations under the BMS Agreement.

8. Commitments and Contingencies

The Company currently has an operating lease agreement with a commitment for $33,406,432 for laboratory and office facilities through 2029.

At December 31, 2018, future minimum lease payments under leases having an initial or remaining non-cancellable lease term in excess of one year are set forth in the table below:

Year	
2019	$ 2,522,918
2020	2,946,086
2021	3,034,469
2022	3,125,503
2023	3,219,268
Thereafter	18,558,188
	$ 33,406,432

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8. Commitments and Contingencies (continued)

Rent expense for the years ended December 31, 2018, 2017 and 2016 was $1,847,392, $1,427,716 and $1,419,940, respectively.

9. Employee Benefit Plan

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, 2018 and 2017 and a matching contribution of 50% on the first 6% of contributions in the year ended 2016. Participant and Company contributions vest immediately. During the years ended December 31, 2018, 2017 and 2016, the Company recorded matching contribution expense of $429,318, $378,233 and $157,244, respectively.

10. Related Parties

In the first quarter of 2015, the Company moved its headquarters to 430 East 29th Street, New York, New York 10016. The Company has entered into a long-term lease with a related party for approximately 16,753 square feet of useable laboratory and office space**.** On September 28, 2018, we signed a lease with the same related party to acquire an additional 15,534 square feet of additional office space in our current headquarters facility. The amended lease has a term of 14.2 years. The amendment includes provisions for yearly rent escalation, a limited rent abatement for the additional space, and an amount provided for leasehold improvements. A member of the Company s board of directors is the Chairman of the board of directors, Chief Executive Officer and President of the parent company to the landlord under this lease.

11. Unaudited Quarterly Financial Information

The tables herein set forth the Company s unaudited condensed consolidated 2018 and 2017 quarterly statements of operations.

The following table sets for the Company s unaudited condensed consolidated statements of operations for the 2018 quarters ended:

2018 Quarter Ended	**December 31,**	**September 30,**	**June 30,**	**March 31,**
Net loss	(40,748,036)	(41,522,914)	(37,376,383)	(35,480,078)
Basic and diluted net loss per share	$ (0.75)	$ (0.76)	$ (0.68)	$ (0.65)

The following table sets for the Company s unaudited condensed consolidated statements of operations for the 2017 quarters ended:

2017 Quarter Ended	**December 31,**	**September 30,**	**June 30,**	**March 31,**
Revenue	$ 5,055	$ 30,754	$ 114,741	$ 95,287

Net loss	(30,208,712)	(22,870,416)	(17,760,704)	(26,933,582)
Basic and diluted net loss per share	$ (0.56)	$ (0.53)	$ (0.41)	$ (0.62)