INTRA-CELLULAR THERAPIES, INC.

FORM 10-K
(Annual Report)

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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, 2016

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post 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, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐ [Do not check if a smaller reporting company]	Smaller reporting company	☐

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 $1.4 billion.

As of February 15, 2017, the registrant had 43,410,277 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 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission.

PART I

All brand names or trademarks appearing in this report are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this report is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners. Unless the context requires otherwise, references in this report to the "Company," "we," "us," and "our" refer to Intra-Cellular Therapies, Inc. and its wholly-owned 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 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 pre-clinical 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. 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 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 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 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 2015, we also announced top-line data from an open-label positron emission tomography, or 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.

The top-line results from our first Phase 3 clinical trial of lumateperone confirm 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 Phase 2 trial (ITI-007-005), 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, orally once daily for 28 days. The primary endpoint for this clinical trial was change from baseline to Day 28 on the PANSS total score. In this study, lumateperone 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. 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.

We have a meeting scheduled with the Division of Psychiatry Products of the U.S. Food and Drug Administration, or FDA, in late March 2017 to discuss the submission of a new drug application, or NDA, for lumateperone in schizophrenia. We expect to provide an update on the status of our discussions with the FDA following this meeting.

We will need to complete other development, manufacturing and pre-commercialization activities necessary to support the submission of a planned NDA for lumateperone in schizophrenia.

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

Our bipolar depression program consists of two Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials: one to evaluate lumateperone as a monotherapy and the other to evaluate lumateperone as an adjunctive therapy with lithium or valproate. In each trial, patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode 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-007-401 trial, 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 both 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. Patient enrollment in the ITI-007-401 trial, is expected to complete in the first half of 2018. Patient enrollment in the ITI-007-402 trial, is expected to complete in the second half of 2018. One of our strategies to optimize potential success in this program is to initiate a third trial in bipolar depression conducted globally. We anticipate completing patient enrollment in our global study by the end of 2018.

The primary endpoint for both clinical trials is change from baseline at Day 42 on the Montgomery-Åsberg Depression Rating Scale, or 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 both clinical trials.

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 marks 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 improves 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 this trial, approximately 360 patients are planned to be randomized to receive 9 mg ITI-007 or placebo in a 1:1 ratio orally once daily for four weeks. This study includes a single interim analysis reviewed by an independent data monitoring committee, which will be used to assess the assumptions of variability and effect size. The primary efficacy measure is 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 are 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 is a Clinical Global Impression scale for Severity, or CGI-S, of illness. Other exploratory secondary endpoints include measures of other behavioral disturbances associated with dementia. Safety and tolerability are also assessed in the trial.

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. 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 posttraumatic 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. We believe PDE1 helps regulate brain activity related to cognition, memory processes and movement/coordination. 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. 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, in the first half of 2017 we expect to initiate a Phase 1/2 clinical trial with 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.

Our pipeline also includes pre-clinical 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.

We have assembled a management team with significant industry experience to lead the discovery and development 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.

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 Investor Relations 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 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 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 disease which are not 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 and residual symptoms in schizophrenia;
- 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 and major depressive disorder;
- 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.

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 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.

During the years ended December 31, 2016 and 2015, we incurred approximately $93.8 million and $87.7 million in research and development expenses, respectively.

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 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 CNS 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 National Institute of Mental Health, over 1% of the world’s population suffers from schizophrenia, and more than 2.5 million Americans suffer from the illness in any given year. Worldwide sales of antipsychotic drugs exceeded $20 billion in 2015. 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 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 5.7 million adults in the United States in any given year, or about 2.6 percent of the adult U.S. population. In 2012, therapeutics used to treat bipolar disorder had global sales of approximately $6 billion.

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 44.4 million people worldwide were living with dementia in 2013, including over 5.2 million patients with AD in the United States. This number is expected to increase to 75.6 million by 2030 and to increase to 135.5 million by 2050. 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.

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 Aricept ® , Namenda ® , Exelon ® and Ebixa ® . These two segments had total sales of $4.9 billion in 2013.

According to the Alzheimer's Association, 5.2 million people in the United States are living with AD, and it is currently the fifth leading cause of death for people age 65 and older. It has been estimated that 44.4 million people worldwide were living with dementia in 2013. This number is expected to increase to 75.6 million by 2030 and to increase to 135.5 million by 2050. 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 51% 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 from approximately 4 to

6 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. Sales of therapeutics such as L-DOPA and dopamine agonists used to treat the motor symptoms of the disease reached $2.3 billion in 2013.

Non-motor symptoms can be particularly distressing and even more troublesome to patients with Parkinson's disease than the primary motor disturbances. Non-motor symptoms substantially contribute to the burden of Parkinson's disease and deeply affect the quality of life of patients and their caregivers. Non-motor symptoms of Parkinson's disease are associated with increased caregiver stress and burden, nursing home placement, and increased morbidity and mortality.

Treatment of non-motor symptoms associated with Parkinson's disease poses a challenge to physicians. Current dopamine replacement drugs used to treat the motor symptoms of Parkinson's disease do not help, and sometimes worsen, the non-motor symptoms. 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.

Depression

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 3% of teenagers and approximately 7% of adults experience MDD each year. Worldwide sales of antidepressant drugs reached $9.3 billion in 2013. The antidepressant market is primarily composed of selective serotonin reuptake inhibitors such as Lexapro ® (marketed by Forest Laboratories and Lundbeck) and selective norepinephrine reuptake inhibitors, or SNRIs, such as Cymbalta ® (marketed by Eli Lilly). Antipsychotics such as Seroquel ® (marketed by Astrazeneca) and Abilify ® (marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical) 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.

Our Clinical Programs

Our pipeline includes two product candidates in clinical development and two product candidates in advanced pre-clinical 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. In the third quarter of 2016, we completed the second Phase 3 trial for the treatment of schizophrenia. In our pre-clinical and clinical trials to date, we have demonstrated that 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. 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 antipsychotic efficacy for positive, negative, affective and cognitive symptoms associated with schizophrenia. The serotonin reuptake inhibition could allow for antidepressant activity for the treatment of schizoaffective disorder, other disorders with co-morbid depression, and/or as a stand-alone treatment for major depressive disorder. 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.

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 been shown to be safe and 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 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.

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

Lumateperone for the treatment of schizophrenia is currently in Phase 3 development. 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 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 since it did not separate on the primary 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. 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 ITI-007 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.

We have a meeting scheduled with the FDA in late March of 2017 to discuss the submission of an NDA for lumateperone in schizophrenia. We expect to provide an update on the status of our discussions with the FDA following this meeting.

We will need to complete other development, manufacturing and pre-commercialization activities necessary to support the submission of a planned NDA for lumateperone in schizophrenia. In addition to the meeting we have scheduled in late March of 2017 with the FDA, additional 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 pre-clinical stage development program and we expect to commence clinical development in 2018.

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 D_2 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.

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 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 two Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials: one to evaluate lumateperone as a monotherapy and the other to evaluate lumateperone as an adjunctive therapy with lithium or valproate. In each trial, patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode 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-007-401 trial, 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 both 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. Patient enrollment in the ITI-007-401 trial, is expected to complete in the first half of 2018. Patient enrollment in the ITI-007-402 trial, is expected to complete in the second half of 2018. One of our strategies to optimize potential success in this program is to initiate a third trial in bipolar depression conducted globally. We anticipate completing patient enrollment in our global study by the end of 2018.

The primary endpoint for both 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 both 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 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 marks 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 improves 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 this trial, approximately 360 patients are planned to be randomized to receive 9 mg ITI-007 or placebo in a 1:1 ratio orally once daily for four weeks. This study includes a single interim analysis reviewed by an independent data monitoring committee, which will be used to assess the assumptions of variability and effect size. The primary efficacy measure is 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 are 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 is a Clinical Global Impression scale for Severity, or CGI-S, of illness. Other exploratory secondary endpoints include measures of other behavioral disturbances associated with dementia. Safety and tolerability are also assessed in the trial.

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, 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 depression 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. As such, lumateperone may be effective for the treatment of mood disorders including MDD, posttraumatic stress disorder and intermittent explosive disorder. We are presently exploring the feasibility of clinical studies in these indications.

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. We believe PDE1 helps regulate brain activity related to cognition, memory processes and movement/coordination. 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 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. ITI-214 is the first compound in its class to successfully advance into 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, in the first half of 2017 we expect to initiate a Phase 1/2 clinical trial with 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. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

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.

Intellectual Property

Our Patent Portfolio

As of February 1, 2017, we owned or controlled approximately 80 patent families filed in the United States and other major markets worldwide, including approximately 67 issued or allowed U.S. patents, 33 pending U.S. patent applications, 271 issued or allowed foreign patents and 207 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, pharmaceutical formulations, new indications, improved methods of manufacture, metabolites, derivatives, and structurally related novel compounds. As of February 1, 2017, our ITI-007 program consisted of approximately 26 patent families that we own or control, filed in the United States and other major markets, including 21 issued or allowed U.S. patents, 19 pending U.S. patent applications, 100 issued foreign patents and 93 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, CN, JP and MX; Pending in CA, IL, IN	June 24, 2029 (US); March 12, 2029 (ex-US)

Summary Description of Patent or Patent Application	United States or Foreign Jurisdiction	Expiration Date
ITI-007 Dosage Patents	**Granted:** US, AU, CN, MX Pending: US (continuation, allowed), AU, CA, EP, IN, JP, KR, MX (divisional)	December 28, 2029 (US); May 27, 2029 (ex-US)
Patents for Additional Indications	Pending in US, EP, JP, and other countries	2033-2034

Our program on PDE1 inhibitors for cognition and dopamine-mediated disorders, such as Parkinson's disease, includes patent protection 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 are also evaluating potential follow-on compounds for ITI-214 which would have patent protection beyond 2030.

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

License Agreement

The Bristol-Myers Squibb License Agreement

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

Under the agreement, we made an upfront payment of $1.0 million to BMS, a milestone payment of $1.25 million in December 2013, and a milestone payment of $1.5 million in December 2014 following the initiation of our first Phase 3 clinical trial for lumateperone for patients with exacerbated schizophrenia. Possible milestone payments remaining total $12.0 million. Under the agreement, we may be obliged to make other milestone payments to BMS for each licensed product of up to an aggregate of approximately $14.75 million. We are also obliged to make tiered single digit percentage royalty payments 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.

Collaboration Agreement

The Takeda Pharmaceutical License and Collaboration Agreement and Termination Agreement

On February 25, 2011, we entered into a license and collaboration agreement with Takeda Pharmaceutical Company Limited 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. As part of the agreement, we assigned to Takeda certain patents owned by us that claim ITI-214 and granted Takeda an exclusive license to develop and commercialize compounds identified in the conduct of the research program that satisfy specified criteria. However, we retained rights to all compounds that do not meet the specified criteria and we continue to develop PDE1 inhibitors outside the scope of the agreement. Upon execution of the agreement, Takeda made a nonrefundable payment to us.

Under the terms of the agreement, we conducted a research program with an initial term of three years to identify and characterize compounds that meet certain specified criteria sufficient for further development by Takeda. This research program ended in February 2014. We were responsible for our expenses incurred in the conduct of certain research activities specified in the research plan. Takeda agreed to reimburse us for expenses we incurred in conducting additional research activities.

On October 31, 2014, we entered into an agreement with Takeda terminating the Takeda License 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. 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, in the first half of 2017 we expect to initiate a Phase 1/2 clinical trial with 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. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

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 schizophrenia and 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 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 have no marketing, sales or distribution capabilities. In order to commercialize any of our product candidates, we must develop these capabilities internally or through collaboration with third parties. In selected therapeutic areas where we feel that our product candidates can be commercialized by a specialty sales force that calls on a limited and focused group of physicians, we may plan to participate in the commercialization of our product candidates in the United States. In therapeutic areas that require a large sales force selling to a large and diverse prescribing population, we may elect to commercialize through, or in collaboration with, strategic partners. 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 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, Abilify ® , marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical; Fanapt ® , marketed by Novartis Pharmaceuticals; Seroquel XR ® , marketed by AstraZeneca; Invega ® , marketed by Janssen; VRAYLAR ® , marketed by Allergan, Rexulti ® marketed by Otsuka Pharmaceutical and Latuda ® , marketed by Sunovion. In addition, our product candidates, if approved, will compete with, among other generic antipsychotic products, haloperidol, risperidone, quetiapine, olanzapine and clozapine.

In addition, the companies described above and other competitors may have a variety of drugs in development or 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 and clinical trials of potential pharmaceutical products; and
- obtaining FDA and other regulatory clearances.

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

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

Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved by the FDA or are in advanced development. We face competition from other companies, academic institutions, governmental agencies and other public and private research organizations for collaborative arrangements with pharmaceutical and biotechnology companies, in recruiting and retaining highly qualified 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 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 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
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Pre-clinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The conduct of the pre-clinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the pre-clinical 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 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 pre-clinical 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 FDA at the end of that period. For NDAs assigned a standard review designation, the FDA's goal is to complete its review 12 months from submission and for priority review NDAs, 8 months from submission. 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, pre-clinical 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 studies. 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 a new NDA. Obtaining approval for a new indication generally requires that additional clinical studies 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. 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 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 pre-clinical studies, adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

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, or collectively, the ACA, enacted in March 2010, substantially changed the way health care is financed by both governmental and private insurers. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the ACA that are repealed. 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 regulates all advertising and promotion activities for products under its 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 pre-clinical 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.

We may also be subject to various federal and state laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. Due to the breadth of the statutory provisions, the absence of guidance in the form of regulations, and very few court decisions addressing industry practices, it is possible that our practices might be challenged under anti-kickback or similar laws. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented, for payment to third-party payors (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

Violations of fraud and abuse laws may be punishable by 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 of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing attention being given to 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.

Employees

As of February 15, 2017, we employed 42 employees, 41 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 additional employees for research and development, clinical and regulatory affairs, general and administrative and commercial related 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.

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 currently do not have, and may never have, any products that generate significant revenues.

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.

We must demonstrate that our drug 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 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, but 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. We have a meeting scheduled with the FDA in late March of 2017 to discuss the submission of an NDA for lumateperone in schizophrenia. We expect to provide an update on the status of our discussions with the FDA following this meeting. In addition, we initiated Phase 3 development for the treatment of bipolar depression in the third quarter of 2015 and Phase 3 development for the treatment of agitation in patients with dementia, including AD, in the second quarter of 2016. In addition, all rights with respect to ITI-214, which has advanced into Phase 1 clinical trials, that we previously granted to Takeda were returned to us in connection with the termination of the Takeda License Agreement. 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. 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 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 2018, if at all.

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

In our Phase 1 and Phase 2 clinical trials, our lead product candidate, lumateperone, has demonstrated improved sleep maintenance, antipsychotic efficacy, and clinical signals consistent with reduction in negative symptoms associated with schizophrenia, depression and anxiety, and other symptoms associated with impaired social function. In September 2015, we announced top-line clinical results from our first randomized, double-blind, placebo-controlled Phase 3 clinical trial in patients with an acutely exacerbated episode of schizophrenia. In this trial, a once-daily 60 mg dose of ITI-007 met the primary endpoint and demonstrated antipsychotic efficacy with statistically significant superiority over placebo at week 4 (study endpoint). In addition, the 60 mg dose of ITI-007 met the key secondary endpoint of statistically significant improvement on the CGI-S. In September 2016, we announced top-line results from the second Phase 3 clinical trial 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 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 magnitude of change from baseline in the primary endpoint, the PANSS total score.

We have a meeting scheduled with the FDA in late March of 2017 to discuss the submission of an NDA for ITI-007 in schizophrenia. We expect to provide an update on the status of our discussions with the FDA following this meeting. In addition, we initiated Phase 3 development for the treatment of bipolar depression in the third quarter of 2015 and Phase 3 development for the treatment of agitation in patients with dementia, including AD, in the second quarter of 2016.

The historical rate of failures for product candidates in clinical development and late-stage clinical trials is high. While we may be required to conduct further clinical trials in patients with schizophrenia and we plan to conduct further clinical trials in other indications, 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 pivotal 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.

We recently completed our second Phase 3 clinical trial of lumateperone for the treatment of schizophrenia. Although we previously discussed our clinical development plans with the FDA, the agency may ultimately determine that our Phase 3 clinical trials and non-clinical studies, even if certain of the trials are successfully completed, 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 and financial condition.

In June 2014, we held our end-of-Phase 2 meeting with the FDA to discuss our plans for initiating Phase 3 clinical trials of lumateperone in schizophrenia. Following this meeting, we proceeded with our Phase 3 development program, in which we recently completed the second of two randomized, double-blind, placebo-controlled Phase 3 clinical trials of lumateperone in patients with acutely exacerbated schizophrenia, with 450 patients enrolled in the first Phase 3 clinical trial and 696 patients enrolled in the second Phase 3 clinical trial. We completed enrollment of the first Phase 3 clinical trial in schizophrenia in the second quarter of 2015 and completed enrollment of the second Phase 3 clinical trial in schizophrenia in the second quarter of 2016. In the first Phase 3 trial, we randomized patients to two doses of ITI-007 (60mg or 40mg) or placebo over a 4-week treatment duration, and the primary outcome measure is change from baseline to Day 28 on the PANSS total score. In the second Phase 3 trial, we randomized patients to receive one of four treatments: 60 mg ITI-007, 20 mg ITI-007, 4 mg risperidone (active control) or placebo in a 1:1:1:1 ratio. The second Phase 3 trial was conducted for a 6-week treatment duration. We announced top-line results of the first Phase 3 clinical trial of lumateperone in patients with schizophrenia in September 2015 and top-line results of the second Phase 3 clinical trial in September 2016. In the second Phase 3 clinical trial, neither dose of ITI-007 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 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. Even though we believe that our recently completed Phase 3 trials and ongoing and planned clinical and non-clinical studies for lumateperone in schizophrenia, if successful, will be sufficient to support our NDA, the FDA may not agree with our belief that 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. 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 we submit an NDA and the FDA does not agree with our clinical and non-clinical designs, 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 with our trial designs. In addition, we may be required to conduct additional clinical trials or studies, which could result in additional delays and costs. There is no assurance that we will complete the other clinical and non-clinical studies within the timeframes and the costs that we currently expect, or at all, or in a manner that is acceptable to the FDA. Any delays or unplanned costs resulting from our Phase 3 clinical trials of lumateperone in schizophrenia may have a material adverse effect on our business, results of operations and financial condition. Even if we eventually submit an NDA and 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 and financial condition.

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, 2016, we had an accumulated deficit of approximately $309.5 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 for until at least 2018, 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 $384.1 million at December 31, 2016, which includes net proceeds of approximately $121.8 million from the public offering of shares of our common stock in March 2015 and approximately $327.4 million from the public offering of shares of our common stock in September 2015. 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 through the end of 2018 , the amount and timing of our actual expenditures will depend upon numerous factors, including the ongoing status of our planned NDA submission for lumateperone in patients with schizophrenia and the meeting that we have scheduled with the FDA in late March 2017 regarding the submission of This NDA; the ongoing status of our Phase 3 clinical trials of lumateperone in patients with bipolar depression and dementia, including AD; 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 may require additional funds to obtain regulatory approval for lumateperone for patients with bipolar disorder. Furthermore, we anticipate that we will need to secure additional funding to obtain regulatory approval for lumateperone in patients with dementia, including AD, for further development of lumateperone in other programs including in patients with depressive disorders and other 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 NDA would likely be delayed.

With the remaining proceeds from our public offerings in February 2014, March 2015 and September 2015, we intend to fund the following: the initiation of other planned clinical and non-clinical trials, including manufacturing, needed for anticipated regulatory approval of lumateperone in patients with acute exacerbated schizophrenia and other potential additional indications; 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, a program we initiated in the third quarter of 2015; clinical trials of lumateperone for the treatment of behavioral disturbances in dementia, including AD, a program we initiated in the second quarter of 2016; pre-clinical 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:

- the results of the meeting in late March of 2017 that we have with the FDA regarding the submission of an NDA for lumateperone in 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; and
- the costs associated with litigation.

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 February 2014, March 2015 and September 2015, 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.

Our lead product candidate, lumateperone, is only part way through the clinical trials we anticipate needing to complete before we may be able to submit an NDA to the FDA. Clinical trials are long, expensive and unpredictable, and there is a high risk of failure.

Preclinical testing and clinical trials are long, 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.

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. Even though we believe that our recently completed Phase 3 trials and ongoing and planned clinical and non-clinical studies for lumateperone in schizophrenia, if successful, will be sufficient to support our NDA, the FDA may not agree with our belief that 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, 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 and financial condition.

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.

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. To date, none of our product candidates have experienced any serious and unexpected suspected adverse reactions that resulted in the submission of an IND safety report to the FDA; however, some approved products marketed by third parties for psychiatric indications that utilize different therapeutic targets or are in a different therapeutic class have experienced significant safety issues. 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;

- 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 and financial condition.

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

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

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

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

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

- we may not be able to control the amount and timing of resources that our collaborators may devote to the drug candidates;
- our collaborators may experience financial difficulties;

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

Preliminary and interim data from our clinical 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;

- 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, 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.

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, and we plan to transfer our production to one or more other third-party manufacturers in addition to our current third-party manufacturer, potentially delaying regulatory approval and commercialization.***

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.

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 will be conducted after we request regulatory approval 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, 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 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.

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, 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 new Medicare Part D coverage gap discount program, in which manufacturers must agree 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.

Many 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. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the ACA that are repealed. 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 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, 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.

We do not currently have an organization for the sales, marketing or distribution of pharmaceutical products. 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. 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, 2016, we had net operating loss carryforwards, or NOLs, of approximately $121.0 million to reduce any future federal and state taxable income through 2035. Since we had NOLs as of December 31, 2016, 2015 and 2014, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations. The NOLs of approximately $121.0 million as of December 31, 2016 will begin to expire in the year 2033 if unused. The use of our NOLs may be restricted due to changes in our ownership, including as a result of our public offerings in March 2015 and September 2015.

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 year ended December 31, 2015 we performed a Section 382 ownership analysis and determined that an ownership change occurred (within the meaning of Section 382 of the Code) in 2015. 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.

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 the Health Insurance Portability and Accountability Act of 1996, government enforcement actions and regulatory penalties. Unauthorized access, loss or dissemination could also disrupt our operations, including our ability to conduct research and 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 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 central nervous system disorders and the other fields in which we are developing products. 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 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.

Risks Relating 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 or an alternative minimum tax, in connection with our transfer of certain intellectual property rights to our foreign subsidiary.

In September 2016, the Company licensed certain intellectual property rights to our wholly-owned 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 represent a current year gain for U.S. tax purposes and will be offset partially by current 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 in the future. If an IRS valuation exceeds our available NOLs, we could incur additional income taxes in the future. Our ability to use our NOLs is subject to the limitations of IRS Section 382, as well as expiration of federal and state net operating loss carryforwards. Additionally, in the event our NOLs were sufficient to offset the regular income taxes associated with an IRS revaluation of the intellectual property transferred to our Bermuda subsidiary, we may be subject to alternative minimum tax.

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 would compete with, among other branded products, Abilify ® , marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical, Fanapt ® , marketed by Novartis Pharmaceuticals, Seroquel XR ® , marketed by AstraZeneca, Invega ® , marketed by Janssen, VRAYLAR ® , marketed by Allergan, Rexulti ® marketed by Otsuka Pharmaceutical and Latuda ® , marketed by Sunovion. In addition, our product candidates, if approved, will compete with, among other generic antipsychotic drugs, haloperidol, risperidone, quetiapine, 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 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, 2016, the price per share of our common stock on the NASDAQ Global Select Market has ranged from a high of $55.35 to a low of $10.80. 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 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 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, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

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

We 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. 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. 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 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 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.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

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

- the accuracy of our estimates regarding expenses, future revenues, uses of cash, 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 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;
- the results of the meeting scheduled with the FDA to discuss the submission of an NDA for ITI-007 in schizophrenia and the timing of our expected update on such discussions;
- 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.

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 16,753 square feet of useable office and laboratory space. The term of the lease, as amended, expires January 31, 2027. We also lease office space in Towson, Maryland on a month to month basis.

Item 3. LEGAL PROCEEDINGS

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

Item 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is traded on the NASDAQ Global Select Market under the symbol "ITCI." The high and low sales prices per share of our common stock as reported by NASDAQ for each quarter during the fiscal years ended December 31, 2016 and 2015 are set forth below:

Year Ended December 31, 2016	High	Low
First Quarter	$55.35	$22.41
Second Quarter	$42.03	$27.13
Third Quarter	$45.20	$14.44
Fourth Quarter	$17.00	$10.80

Year Ended December 31, 2015	High	Low
First Quarter	$30.72	$16.29
Second Quarter	$35.45	$19.86
Third Quarter	$60.79	$21.19
Fourth Quarter	$59.96	$37.75

Stockholders

As of February 15, 2017, we had 43,410,277 outstanding shares of common stock and no outstanding shares of preferred stock. As of February 15, 2017, there were approximately 125 holders of record of our outstanding shares of common stock.

Dividends

We have never paid cash dividends on any of our capital stock and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

Unregistered Sales of Securities

Not applicable.

Issuer Purchases of Equity Securities

Not applicable.

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, 2016. The selected financial data for each of the five years in the period ended December 31, 2016 have been derived from our audited consolidated financial statements. The consolidated balance sheets as of December 31, 2016 and 2015 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, 2016, 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.

	2016	2015	2014	2013	2012
Statements of Operations:					
Revenues:					
License and collaboration revenue	$ —	$ 30,659	$ 547,546	$ 2,737,002	$ 3,117,991
Grant revenue	330,702	60,705	29,755	—	—
Total Revenues	330,702	91,364	577,301	2,737,002	3,117,991
Costs and expenses:					
Research and development	93,831,530	87,718,074	21,226,345	23,027,578	15,486,476
General and administrative	24,758,063	18,187,286	10,337,679	5,976,276	4,034,925
Total costs and expenses	118,589,593	105,905,360	31,564,024	29,003,854	19,521,401
Loss from operations	(118,258,891)	(105,813,996)	(30,986,723)	(26,266,852)	(16,403,410)
Interest income	(2,935,077)	(1,022,455)	(303,936)	(29,617)	(39,002)
Interest expense	36,781	—	7,073	612,963	193,498
Income tax expense	1,065,673	1,600	1,600	18,000	32,921
Net Loss	$ (116,426,268)	$ (104,793,141)	$ (30,691,460)	$ (26,868,198)	$ (16,590,827)
Net Loss per common share:					
Basic	$ (2.69)	$ (2.91)	$ (1.07)	$ (1.56)	$ (2.96)
Diluted	$ (2.69)	$ (2.91)	$ (1.07)	$ (1.56)	$ (2.96)
Weighted average number of common shares:					
Basic	43,240,188	36,069,237	28,650,067	17,260,768	5,607,539
Diluted	43,240,188	36,069,237	28,650,067	17,260,768	5,607,539

	December 31,				
	2016	2015	2014	2013	2012
Balance Sheet data:					
Cash and cash equivalents	$ 48,642,225	$ 47,159,303	$ 61,325,044	$ 35,150,924	$ 15,645,528
Total assets	388,903,495	484,103,528	131,111,769	38,449,312	19,823,680
Total liabilities	13,400,956	7,860,617	10,557,064	6,834,037	2,839,595
Accumulated deficit	(309,475,366)	(193,049,098)	(88,255,957)	(57,564,497)	(30,696,299)
Total stockholders' equity	375,502,539	476,242,911	120,554,705	31,615,275	16,984,085

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 and our wholly-owned subsidiary 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 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 pre-clinical 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. 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.

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 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 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 2015, we also 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 D_2 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.

The top-line results from our first Phase 3 clinical trial of lumateperone confirm 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 Phase 2 trial (ITI-007-005), 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, orally once daily for 28 days. The primary endpoint for this clinical trial was change from baseline to Day 28 on the PANSS total score. In this study, lumateperone 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. 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.

We have a meeting scheduled with the FDA in late March of 2017 to discuss the submission of an NDA for lumateperone in schizophrenia. We expect to provide an update on the status of our discussions with the FDA following this meeting. We will also need to complete other development, manufacturing and pre-commercialization activities necessary to support the submission of a planned NDA for lumateperone in schizophrenia.

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

Our bipolar depression program consists of two Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials: one to evaluate lumateperone as a monotherapy and the other to evaluate lumateperone as an adjunctive therapy with lithium or valproate. In each trial, patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode 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-007-401 trial, 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 both 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. Patient enrollment in the ITI-007-401 trial, is expected to complete in the first half of 2018. Patient enrollment in the ITI-007-402 trial, is expected to complete in the second half of 2018. One of our strategies to optimize potential success in this program is to initiate a third trial in bipolar depression conducted globally. We anticipate completing patient enrollment in our global study by the end of 2018.

The primary endpoint for both clinical trials is change from baseline at Day 42 on the Montgomery-Åsberg Depression Rating Scale, or 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 both clinical trials.

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 marks 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 improves 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 this trial, approximately 360 patients are planned to be randomized to receive 9 mg ITI-007 or placebo in a 1:1 ratio orally once daily for four weeks. This study includes a single interim analysis reviewed by an independent data monitoring committee, which will be used to assess the assumptions of variability and effect size. The primary efficacy measure is 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 are 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 is a Clinical Global Impression scale for Severity, or CGI-S, of illness. Other exploratory secondary endpoints include measures of other behavioral disturbances associated with dementia. Safety and tolerability are also assessed in the trial.

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. 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.

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. We believe PDE1 helps regulate brain activity related to cognition, memory processes and movement/coordination. 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 IND for ITI-214 to us. 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. We expect to advance ITI-214 into additional clinical development trials in both CNS and non-CNS indications. Following the positive safety and tolerability results in our Phase 1 program, in the first half of 2017 we expect to initiate a Phase 1/2 clinical trial with 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. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

Our pipeline also includes pre-clinical 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.

We have assembled a management team with significant industry experience to lead the discovery and development 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.

Since inception, we have devoted substantially all of our efforts and resources to our research and development activities. We have incurred significant net losses since inception. As of December 31, 2016, our accumulated deficit was $309.5 million. We expect to continue incurring substantial losses for the next several years as we continue to develop our clinical and pre-clinical drug candidates and programs. Our operating expenses are comprised of research and development expenses and general and administrative expenses. Our corporate headquarters and laboratory are located in New York, New York.

Results of Operations

Revenues

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

We have not generated any revenue from product sales to date and we do not expect to generate revenues from product sales for at least the next several years. Our revenues for the year ended December 31, 2016 have been from a government grant. Our revenues for the year ended December 31, 2015 have been from a government grant and the residual reimbursement of expenses from the terminated Takeda License Agreement. We will not receive any further revenue under the Takeda License Agreement, which was terminated on October 31, 2014. 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 any 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 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 development. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's disease, cognition in AD, cognition in schizophrenia and in other non-CNS indications. Our other projects are still in the pre-clinical stages, and will require extensive funding not only to complete pre-clinical testing, but to enter into 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 significant 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 labor and fringe benefits, materials and supplies, facilities and maintenance costs; 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.

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 substantially as we proceed with our Phase 3 clinical trials for lumateperone in patients with bipolar disorder and for the treatment of agitation in patients with dementia, including AD. We also expect that our general and administrative costs will increase substantially from prior periods primarily due to costs to perform pre-product commercialization activities and the increased costs associated with being a public reporting entity, which could include adding additional personnel. We granted options to purchase 487,121 shares of our common stock in 2016 and have granted options to purchase an additional 621,157 shares of our common stock in January 2017. We also granted restricted stock units for 78,806 of our common stock in 2016 and restricted stock units for 154,922 shares of our common stock in January 2017. We will recognize expense associated with these restricted stock units and options over the next three years in both research and development expenses and general and administrative expenses. We expect this non-cash expense to be material 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 will increase our stock-based compensation expense in future periods.

The following table sets forth our revenues, operating expenses, interest income (expense) and income taxes expenses for the years ended December 31, 2016, 2015 and 2014 (in thousands):

	For the Year Ended December 31,		
	2016	**2015**	**2014**
Revenues	**$ 330**	$ 91	$ 577
Expenses			
Research and Development	**93,831**	87,718	21,226
General and Administrative	**24,758**	18,187	10,338
Total costs & expenses	**118,589**	105,905	31,564
Loss from operations	**(118,259)**	(105,814)	(30,987)
Interest income, net	**(2,898)**	(1,022)	(298)
Income tax expense	**1,065**	1	2
Net Loss	**$(116,426)**	$(104,793)	$(30,691)

Comparison of Years Ended December 31, 2016 and December 31, 2015

Revenues

Revenues increased for the year ended December 31, 2016 as compared to the year ended December 31, 2015 by approximately $239 thousand, or 262%, primarily due to a government grant, offset by limited reimbursable costs of $31 thousand paid to us by Takeda in 2015 under the Takeda License Agreement which terminated on October 31, 2014.

Research and Development Expenses

Research and development expenses increased for the year ended December 31, 2016 as compared to the year ended December 31, 2015 by approximately $6.1 million, or 7%. This change is due primarily to an increase of approximately $6.5 million of costs associated with manufacturing and $1.6 million of labor related costs offset in part by $2.8 million less in clinical trials related costs in the year ended December 31, 2016 over the year ended December 31, 2015. For the year ended December 31, 2015, the majority of the $87.7 million of research and development costs was related to the first and second Phase 3 trial of lumateperone in patients with schizophrenia (ITI-007-301 and ITI-007-302). 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 which commenced in the third quarter of 2016 and a significant amount of costs for manufacturing lumateperone. Amounts paid to external parties comprised most of our research and development costs. In the year ended December 31, 2016, we incurred approximately $81.1 million of costs to external parties who manufactured, tested and performed clinical trial related activities as compared to $76.8 million for the year ended December 31, 2015. Of these external costs, approximately $80.6 million in the year ended December 31, 2016 and approximately $76.1 million in the year ended December 31, 2015 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 $12.7 million and $10.9 million in the years ended December 31, 2016 and 2015, respectively.

As development of lumateperone for the treatment of schizophrenia progresses, we anticipate costs for that program to continue in the next several years as we conduct clinical trials and 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. In addition we plan to spend increasing amounts to further our development of lumateperone for other indications, including but not limited to, the treatment of depressive episodes associated with bipolar disorder (bipolar depression), for treatment of behavioral disturbances associated with dementia and related disorders, and for treating agitation, aggression and sleep disturbances in diseases that include dementia, AD, Huntington's disease and autism spectrum disorders, and to further our long acting injectable program among other indications.

As of December 31, 2016, we employed 28 full time personnel in our research and development group as compared to 24 full time personnel at December 31, 2015. 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. 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 minimal and are reflected in the amounts discussed in this section "—Research and Development Expenses."

During previous years, we also incurred costs that were both reimbursable and non-reimbursable under the Takeda License Agreement. For the years ended December 31, 2016 and 2015, we incurred $0 and $30,700, respectively, of costs that were billable to Takeda pursuant to ongoing obligations under the termination agreement. We do not expect to incur material costs going forward under this agreement.

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, 2016 as compared to the year ended December 31, 2015 by approximately $6.6 million, or 36%, primarily due to approximately $4.1 million of higher stock option expense and to a lesser extent to commercial development, rent, accounting, legal, and labor costs. Salaries, bonuses, share based compensation and related benefit costs for our executive, finance and administrative functions for the years ended December 31, 2016 and 2015 were approximately 61% and 59%, 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.

We expect general and administrative costs to increase significantly as we hire additional staff and expand our operations, including preparation for potential commercial activities.

Interest Income

Interest income has increased to approximately $2.9 million from $1.0 million for the year ended December 31, 2016 as compared to the year ended December 31, 2015. This increase is primarily a result of higher than average cash balances and interest rates in 2016 as compared to 2015. The higher balances in 2016 were due to the net offering proceeds of $121.8 million that we received in March 2015 and $327.4 million that we received in September 2015 offset partially by the $91.3 million of cash and investments utilized in 2016.

Income Tax

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. We utilized a portion of our available federal and state net operating loss carryforwards to offset the majority of this net income but incurred $1.1 million of taxes related to intercompany transactions that were treated as tax expense in our consolidated statement of operations.

Comparison of Years Ended December 31, 2015 and December 31, 2014

Revenues

Revenues decreased for the year ended December 31, 2015 as compared to the year ended December 31, 2014 by approximately $485.9 thousand, or 84%, primarily due to reimbursable costs paid to us by Takeda in 2014 under the Takeda License Agreement which terminated on October 31, 2014 with limited reimbursements in 2015, offset by slightly higher revenue in 2015 from a government grant.

Research and Development Expenses

Research and development expenses increased for the year ended December 31, 2015 as compared to the year ended December 31, 2014 by approximately $66.5 million, or 313%. This change is due primarily to an increase of approximately $47.1 million of costs associated with outside clinical testing and an increase of approximately $14.9 million from nonclinical testing in the year ended December 31, 2015 over the year ended December 31, 2014. The vast majority of the increase is due to costs associated with conducting our lumateperone Phase 3 clinical program in schizophrenia. In late 2014, we began a clinical trial of lumateperone in patients with schizophrenia and incurred the majority of the costs for this trial in 2015. In addition, we started our second Phase 3 clinical trial of lumateperone in patients with schizophrenia in June 2015 and incurred significant costs for this trial in the second half of 2015. In December 2015, we commenced our Phase 3 clinical trials in bipolar disorder and have incurred approximately $3.6 million in costs through December 31, 2015. In 2014, we did not incur significant costs related to clinical trials. Amounts paid to external parties comprise a large portion of our research and development costs. In the year ended December 31, 2015, we incurred approximately $76.8 million of costs to external parties who manufactured, tested and performed clinical trial related activities as compared to $16.3 million in the year ended December 31, 2014. Of these external costs, approximately $76.1 million in the year ended December 30, 2015 and $16.0 million in the year ended December 31, 2014 were for lumateperone related projects. The remaining amounts for each of these periods were spent on other projects. Internal costs are comprised primarily of labor, fringe benefits, materials, supplies and facilities and maintenance costs and were approximately $10.9 million and $5.0 million for the years ended December 31, 2015 and 2014, respectively. The increase in these internal costs is due primarily to hiring additional research and development employees in 2015 in addition to increased stock based compensation expense.

General and Administrative Expenses

General and administrative expenses increased for the year ended December 31, 2015 as compared to the year ended December 31, 2014 by approximately $7.8 million, or 76%, primarily due to approximately $4.1 million of higher stock option expense and to a much lesser extent to increased bonus and labor costs and state and local franchise and capital taxes. Salaries, bonuses and related benefit costs for our executive, finance and administrative functions for the years ended December 31, 2015 and 2014 were approximately 59% and 49%, respectively, of our total general and administrative costs. Our other general and administrative expenses include patent costs, legal, accounting and other professional fees and, to a lesser extent, facilities and general office-related overhead.

Interest Income

Interest income has increased to approximately $1.0 million from $304,000 for the year ended December 31, 2015 as compared to the year ended December 31, 2014. This increase is primarily a result of higher than average cash balances in 2015 as compared to 2014 which is due to the net offering proceeds of $121.8 million that we received in March 2015 and $327.4 million that we received in September 2015.

Liquidity and Capital Resources

Through December 31, 2016, we provided funds for our operations by obtaining approximately $717 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, and Takeda has limited ongoing funding obligations following the termination of the Takeda License Agreement on October 31, 2014. On March 11, 2015, we completed a public offering of 5,411,481 shares of our common stock for aggregate gross proceeds of approximately $129.9 million and net proceeds of approximately $121.8 million. On September 28, 2015, we completed an additional public offering of 7,935,000 shares of our common stock for aggregate gross proceeds of approximately $345.2 million and net proceeds of approximately $327.4 million.

As of December 31, 2016, we had a total of approximately $384.1 million in cash and cash equivalents and available-for-sale investment securities, and approximately $10.5 million of short-term liabilities consisting entirely of liabilities from operations. We spent approximately $94.2 million in cash for operations and equipment, not including $2.9 million of net interest income received. We reduced working capital by approximately $99.3 million for the year ended December 31, 2016. The use of cash was primarily for conducting clinical trials and non-clinical testing, including manufacturing related activities and funding recurring operating expenses.

For the year 2017, subject to the timing of clinical trials, manufacturing and other development activities, we expect to spend up to $170 million. We expect these expenditures to be due primarily to the development of lumateperone in patients with schizophrenia, behavioral disturbances in dementia, bipolar disorder and depressive disorders, our ITI-007 long acting injectable development program through pre-clinical and early clinical development, research and preclinical development of our other product candidates, the continuation of manufacturing activities in connection with the development of lumateperone, recurring expenses and costs to produce, develop and validate materials to be used in clinical and non-clinical studies related to lumateperone, and expenses associated with our other development programs, pre-commercialization activities and general operations. We expect that cash expenditures will continue to increase after 2017 as we further expand the lumateperone clinical stage programs, the ITI-007 long acting injectable development program through pre-clinical and early clinical development; research and preclinical development of our other product candidates; the continuation of manufacturing, pre-commercial activities in connection with the development of lumateperone and the early stage pre-commercial launch activities for lumateperone. We believe that our existing cash and cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements through the end of 2018.

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 commercialization of lumateperone in patients with schizophrenia. With the remaining proceeds from our public offerings in March 2015 and September 2015, we believe that we have the funds to complete our proposed clinical trials of lumateperone in bipolar disorder as a monotherapy and as an adjunctive therapy with lithium or valproate. We will also be funding clinical trials of lumateperone for the treatment of behavioral disturbances in dementia; 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 to obtain regulatory approval for 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, 2016, we used net cash in operating activities and purchases of equipment of approximately $94.2 million and expect to use additional cash of up to $180 million during 2017. 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, we expect the amount of cash needed to fund operations to increase significantly 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 in 2017 and increasing for 2018 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 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. 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 $2.9 million of deferred rent through the end of 2016. The deferred rent balance will begin to decrease incrementally in the first quarter of 2017. We occupied these facilities as our headquarters in March 2015, replacing our previous laboratories and offices. The lease, as amended, has a term of 12 years. We expect that our facility related costs will increase moderately as a result of leasing this facility.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Contractual Obligations and Commitments

Total contractual obligations as of December 31, 2016 are summarized in the following table (in thousands):

	Payments Due By Period				
	Total	Less than 1 Year	2-3 Years	4-5 Years	More than 5 Years
Operating Lease Obligations	$16,256	$ 1,300	$2,958	$3,138	$ 8,860

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; 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 and stock-based compensation. 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:

Revenue Recognition

Revenue is recognized when all terms and conditions of the agreements have been met, including that persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable and collectability is reasonably assured. We are reimbursed for certain costs incurred on specified research projects under the terms and conditions of grants, collaboration agreements, and awards. We record the amount of reimbursement as revenues on a gross basis in accordance with ASC Topic 605-45, *Revenue Recognition/Principal Agent Considerations* . We are the primary obligor with respect to purchasing goods and services from third-party suppliers, are obligated to compensate the service provider for the work performed, and have discretion in selecting the supplier. Provisions for estimated losses on research grant projects and any other contracts are made in the period such losses are determined.

We have entered into arrangements involving the delivery of more than one element. Each required deliverable is evaluated to determine whether it qualifies as a separate unit of accounting. For us, this determination is generally based on whether the deliverable has "stand-alone value" to the customer. We adopted this accounting standard on a prospective basis for all Multiple-Deliverable Revenue Arrangements, or MDRAs, entered into on or after January 1, 2011, and for any MDRAs that were entered into prior to January 1, 2011, but materially modified on or after that date.

The adoption of this accounting standard did not have a material impact on our results of operations for the years ended December 31, 2016, 2015 and 2014, or on our financial positions as of those dates.

We have adopted ASC Topic 605-28, *Milestone Method* . Under this guidance, we recognize revenue contingent upon the achievement of a substantive milestone in its entirety in the period the milestone is achieved. Substantive milestone payments are recognized upon achievement of the milestone only if all of the following conditions are met:

- the milestone payments are non-refundable;
- achievement of the milestone involves a degree of risk and was not reasonably assured at the inception of the arrangement;
- substantive effort on our part is involved in achieving the milestone;
- the amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and
- a reasonable amount of time passes between the up-front license payment and the first milestone payment, as well as between each subsequent milestone payment.

Determination as to whether a payment meets the aforementioned conditions involves management's judgment. If any of these conditions are not met, the resulting payment would not be considered a substantive milestone, and therefore, the resulting payment would be considered part of the consideration for the single unit of accounting and be recognized as revenue as such performance obligations are performed under either the proportional performance or straight-line methods, as applicable. In addition, the determination that one such payment was not a substantive milestone could prevent us from concluding that subsequent milestone payments were substantive milestones and, as a result, any additional milestone payments could also be considered part of the consideration for the single unit of accounting and would be recognized as revenue as such performance obligations are performed under either the proportional performance or straight-line methods, as applicable.

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, outside services, providers, materials and consulting fees.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to us by our vendors 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, we are required to estimate our expenses resulting from our obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. Our objective is to reflect the appropriate clinical trial expenses in our financial statements by matching those expenses with the period in which services are performed and efforts are expended. We account for these expenses according to the progress of the clinical trial as measured by subject progression and the timing of various aspects of the trial. We determine accrual estimates through financial models taking into account 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 our clinical expense recognition if actual results differ from our estimates. We make estimates of our accrued expenses as of each balance sheet date based on the facts and circumstances known to us at that time. Our clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2016 and 2015, there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Stock-Based Compensation

Stock-based payments in the form of options 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, or 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. Restricted stock units are valued at the fair market value on the date of grant as determined by the closing stock price. Restricted stock units are valued at the fair market value on the date of grant as determined by the closing stock price.

For all awards granted with time-based vesting conditions, expense is amortized using the straight-line attribution method. For awards that contain a performance vesting condition, expense is amortized using the accelerated attribution method. As share-based compensation expense recognized in the statements of operations for the years ended December 31, 2016, 2015 and 2014 is based on share-based awards ultimately expected to vest, it has been reduced for estimated forfeitures. ASC Topic 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Pre-vesting forfeitures were estimated based on our historical experience for the fiscal years ended December 31, 2016, 2015 and 2014 and have not been material.

We utilize the Black-Scholes model for estimating fair value of our 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 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 is defined 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 our stockholders since our inception and do 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, given that 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 our convertible preferred stock offerings and general industry and economic trends. In establishing the estimated fair value of our common stock, we considered the guidance set forth in American Institute of Certified Public Accountants Practice Guide, "Valuation of Privately-Held-Company Equity Securities Issued as Compensation." For stock options granted in 2016 and 2015, the exercise price was determined by using the closing market price of our common stock on the date of grant.

A restricted stock unit, or 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 closing price 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.

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 had net operating loss carryforwards as of December 31, 2016, 2015 and 2014, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations.

Equity instruments issued to non-employees 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 services required 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 Financial Accounting Standards Board, or FASB, issued Accounting Standards Update No. 2014-09 (ASU 2014-09), Revenue from Contracts with Customers. ASU 2014-09 will eliminate transaction-specific and industry-specific revenue recognition guidance under current GAAP and replace it with a principle-based approach for determining revenue recognition. ASU 2014-09 will require that companies recognize revenue based on the value of transferred goods or services as they occur in the contract. ASU 2014-09 also will require additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. In July 2015, the FASB decided to defer the effective date of the

standard from January 1, 2017, to January 1, 2018, with an option that permits companies to adopt the standard as early as the original effective date. Early adoption of the standard prior to the original effective date is not permitted. The standard permits the use of either the retrospective or cumulative effect transition method.

We started an initial impact assessment of the potential changes from adopting ASU 2014-09. Based on the assessment procedures performed to date, we anticipate that the adoption of ASU 2014-09 will primarily impact the contract revenues recognized by the collaborations and license agreements. We are still completing our initial assessment of the impact of this guidance, including the new disclosure requirements as we have not had product sales to date. We plan to adopt the new standard effective January 1, 2018. We continue to monitor additional changes, modifications, clarifications or interpretations being undertaken by the FASB, which may impact our current conclusions.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity. As of December 31, 2016, we had cash, cash equivalents and marketable securities of $384.1 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, 2016 and 2015 totaling approximately $0.3 million and $0.5 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 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, 2016. 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, 2016, 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, 2016 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

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

We have audited Intra-Cellular Therapies, Inc. and subsidiaries' internal control over financial reporting as of December 31, 2016, 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). Intra-Cellular Therapies, Inc. and subsidiaries' 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 conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). 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.

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.

In our opinion, Intra-Cellular Therapies, Inc. and subsidiaries maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Intra-Cellular Therapies, Inc. and subsidiaries as of December 31, 2016 and 2015, 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, 2016 and our report dated March 1, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Baltimore, MD
March 1, 2017

Item 9B. OTHER INFORMATION

Not applicable.

PART III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management and Corporate Governance," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Code of Conduct and Ethics" in the Company's Proxy Statement for the 2017 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 "Compensation Practices and Policies Relating to Risk Management" in the Company's Proxy Statement for the 2017 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 2017 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 2017 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 2017 Annual Meeting of Stockholders.

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 Registrant.		8-K (Exhibit 3.4)	9/5/2013	000-54896
3.4	Restated Bylaws of the Registrant.		8-K (Exhibit 3.5)	9/5/2013	000-54896
4.1	Form of common stock certificate.		8-K (Exhibit 4.1)	9/5/2013	000-54896

Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
4.2	.1	Warrant to Purchase Common Stock dated April 19, 2013 issued to Alzheimer Drug Discovery Foundation, Inc.		8-K (Exhibit 4.2.1)	9/5/2013	000-54896
	.2	Amendment dated August 29, 2013 to Warrant to Purchase Common Stock dated April 19, 2013 issued to Alzheimer Drug Discovery Foundation, Inc.		8-K (Exhibit 4.2.2)	9/5/2013	000-54896
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	.1	License and Collaboration Agreement dated as of February 25, 2011 by and between Takeda Pharmaceutical Company Limited and Intra-Cellular Therapies, Inc.**		8-K/A (Exhibit 10.2)	10/31/2013	000-54896
	.2	Termination Agreement dated as of October 31, 2014 by and between Takeda Pharmaceutical Company Limited and Intra-Cellular Therapies, Inc.**		10-K (Exhibit 10.2.2)	3/12/2015	001-36274
10.3		Supply Agreement dated as of January 4, 2017 by and between Siegfried Evionnaz SA and ITI Limited. †	X			
10.4		Employment Agreement effective as of February 26, 2008 by and between Sharon Mates, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.3)	9/5/2013	000-54896
10.5	.1	Employment Agreement effective as of August 3, 2015 by and between Michael I. Halstead and Intra-Cellular Therapies, Inc.*		10-Q (Exhibit 10.1)	11/5/2015	001-36274
	.2	Amendment No.1 to Employment Agreement dated as of November 9, 2016 by and between Michael I. Halstead and Intra-Cellular Therapies, Inc.*		10-Q (Exhibit 10.1)	11/9/2016	001-36274

Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.6		Employment Agreement effective as of February 26, 2008 by and between Lawrence J. Hineline and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.4)	9/5/2013	001-36274
10.7	.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
10.8	.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
	.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
10.9		Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of September 1, 2003 by and between Sharon Mates, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.8)	9/5/2013	000-54896
10.10		Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of July 29, 2014 by and between Michael Halstead and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.11)	3/12/2015	001-36274
10.11		Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of December 1, 2003 by and between Lawrence J. Hineline and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.9)	9/5/2013	000-54896
10.12		Employee Proprietary Information, Inventions, 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

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.13	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
10.14	Form of Indemnification Agreement by and between the Company and its directors and executive officers.*		8-K (Exhibit 10.13)	9/5/2013	000-54896
10.15	2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.14)	9/5/2013	000-54896
10.16	Form of Stock Option Agreement under the 2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.15)	9/5/2013	000-54896
10.17	Amended and Restated 2013 Equity Incentive Plan.*		8-K (Exhibit 10.1)	6/18/2015	001-36274
10.18	Form of Stock Option Agreement under the 2013 Equity Incentive Plan.*		10-K (Exhibit 10.19)	3/25/2014	001-36274
10.19	Non-Employee Director Compensation Policy, as amended.*		10-Q (Exhibit 10.1)	4/28/2016	001-36274
10.20	Redemption Agreement dated as of August 29, 2013 by and between the Registrant and NLBDIT 2010 Services, LLC.		8-K (Exhibit 10.17)	9/5/2013	000-54896
10.21	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
10.22	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.	X			
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			

Exhibit Number		Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
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.
† Confidential treatment is being requested for portions of this Exhibit. Redacted portions filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

Not Applicable.

SIGNATURES

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

INTRA-CELLULAR THERAPIES, INC.

Date: March 1, 2017

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 indicated below and on the dates indicated.

Signatures	Title	Date
By: /s/ Sharon Mates, Ph.D. Sharon Mates, Ph.D.	Chairman, President and Chief Executive Officer (principal executive officer)	March 1, 2017
By: /s/ Lawrence J. Hineline Lawrence J. Hineline	Vice President of Finance and Chief Financial Officer (principal financial officer and principal accounting officer)	March 1, 2017
By: /s/ Christopher Alafi, Ph.D. Christopher Alafi, Ph.D.	Director	March 1, 2017
By: /s/ Richard Lerner, M.D. Richard Lerner, M.D.	Director	March 1, 2017
By: /s/ Joel S. Marcus Joel S. Marcus	Director	March 1, 2017
By: /s/ Rory B. Riggs Rory B. Riggs	Director	March 1, 2017
By: /s/ Robert L. Van Nostrand Robert L. Van Nostrand	Director	March 1, 2017

Report of Independent Registered Public Accounting Firm

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

We have audited the accompanying consolidated balance sheets of Intra-Cellular Therapies, Inc. and subsidiaries as of December 31, 2016 and 2015, 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, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Intra-Cellular Therapies, Inc. and subsidiaries at December 31, 2016 and 2015, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2016, 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), Intra-Cellular Therapies, Inc.'s internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 1, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Baltimore, MD
March 1, 2017

Intra-Cellular Therapies, Inc.

Consolidated Balance Sheets

	December 31, 2016	2015
Assets		
Current assets:		
Cash and cash equivalents	**$ 48,642,225**	$ 47,159,303
Investment securities, available-for-sale	**335,458,459**	428,041,021
Accounts receivable	**94,339**	30,660
Prepaid expenses and other current assets	**4,005,093**	8,025,147
Total current assets	**388,200,116**	483,256,131
Property and equipment, net	**627,614**	775,522
Other assets	**75,765**	71,875
Total assets	**$ 388,903,495**	$ 484,103,528
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	**$ 3,754,647**	$ 1,632,905
Accrued and other current liabilities	**5,329,293**	3,423,464
Accrued employee benefits	**1,448,394**	1,207,143
Total current liabilities	**10,532,334**	6,263,512
Long-term deferred rent	**2,868,622**	1,597,105
Total liabilities	**13,400,956**	7,860,617
Stockholders' equity:		
Common stock, $.0001 par value: 100,000,000 shares authorized; 43,292,906 and 43,155,875 shares issued and outstanding at December 31, 2016 and 2015, respectively	**4,329**	4,316
Additional paid-in capital	**685,290,815**	669,878,103
Accumulated deficit	**(309,475,366)**	(193,049,098)
Accumulated comprehensive loss	**(317,239)**	(590,410)
Total stockholders' equity	**375,502,539**	476,242,911
Total liabilities and stockholders' equity	**$ 388,903,495**	$ 484,103,528

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc.

Consolidated Statements of Operations

	Years Ended December 31, 2016	2015	2014
Revenues:			
License and collaboration revenue	**$ —**	$ 30,659	$ 547,546
Grant Revenue	**330,702**	60,705	29,755
Total revenues	**330,702**	91,364	577,301
Costs and expenses:			
Research and development	**93,831,530**	87,718,074	21,226,345
General and administrative	**24,758,063**	18,187,286	10,337,679
Total costs and expenses	**118,589,593**	105,905,360	31,564,024
Loss from operations	**(118,258,891)**	(105,813,996)	(30,986,723)
Interest income	**(2,935,077)**	(1,022,455)	(303,936)
Interest expense	**36,781**	—	7,073
Loss before provision for income taxes	**(115,360,595)**	(104,791,541)	(30,689,860)
Income tax expense	**1,065,673**	1,600	1,600
Net loss	**$ (116,426,268)**	$ (104,793,141)	$ (30,691,460)
Net loss per common share:			
Basic & Diluted	**$ (2.69)**	$ (2.91)	$ (1.07)
Weighted average number of common shares:			
Basic & Diluted	**43,240,188**	36,069,237	28,650,067

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc.

Consolidated Statements of Comprehensive Loss

	Years Ended December 31,		
	2016	**2015**	**2014**
Net loss	**$ (116,426,268)**	$ (104,793,141)	$ (30,691,460)
Other comprehensive loss:			
Unrealized gain (loss) on investment securities	**273,171**	(485,777)	(104,633)
Comprehensive loss	**$ (116,153,097)**	$ (105,278,918)	$ (30,796,093)

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc.

Consolidated Statements of Stockholders' Equity

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2013	22,159,446	$ 2,216	$ 89,177,556	$ (57,564,497)	$ —	$ 31,615,275
Common shares issued February 5, 2014	7,063,300	706	115,442,041	—		115,442,747
Exercise of stock options	247,165	25	162,955	—		162,980
Stock issued for services	10,923	1	176,084			176,085
Stock subscription	18,225	2	109,831			109,833
Share-based compensation	—	—	3,843,878	—		3,843,878
Net loss	—	—	—	(30,691,460)		(30,691,460)
Other comprehensive loss					(104,633)	(104,633)
Balance at December 31, 2014	29,499,059	$ 2,950	$ 208,912,345	$ (88,255,957)	$ (104,633)	$ 120,554,705
Common shares issued March 11, 2015	5,411,481	541	121,803,828	—		121,804,369
Common shares issued September 28, 2015	7,935,000	793	327,435,412	—		327,436,205
Exercise of stock options	305,005	31	653,015	—		653,046
Stock issued for services	5,330	1	182,598			182,599
Share-based compensation	—	—	10,890,905	—		10,890,905
Net loss	—	—	—	(104,793,141)		(104,793,141)
Other comprehensive loss					(485,777)	(485,777)
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**

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc.

Consolidated Statements of Cash Flows

	Years Ended December 31, 2016	2015	2014
Operating activities			
Net loss	**$ (116,426,268)**	$ (104,793,141)	$ (30,691,460)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation expense	**196,872**	139,626	25,481
Share-based compensation expense	**14,701,219**	10,890,905	3,843,878
Issuance of stock for services	**233,772**	182,599	176,085
Amortization of premiums on investment activities	**544,354**	712,675	297,223
Changes in operating assets and liabilities:			
Accounts receivable	**(63,679)**	20,943	284,715
Prepaid expenses and other assets	**4,016,164**	(6,737,125)	(466,099)
Accounts payable	**2,121,742**	(419,860)	(1,342,302)
Accrued liabilities and employee benefits	**2,147,080**	(3,873,692)	5,065,329
Deferred rent	**1,271,517**	1,597,105	—
Net cash used in operating activities	**(91,257,227)**	(102,279,965)	(22,807,150)
Investing activities			
Purchases of investments	**(395,757,168)**	(514,308,249)	(103,601,836)
Maturities of investments	**488,068,547**	153,389,448	36,879,308
Purchase of property and equipment	**(48,964)**	(860,595)	(11,762)
Net cash provided by (used in) investing activities	**92,262,415**	(361,779,396)	(66,734,290)
Financing activities			
Proceeds from line of credit	**125,000,000**	—	—
Repayment of line of credit	**(125,000,000)**	—	—
Proceeds from stock option exercises	**477,734**	653,046	162,980
Proceeds from stock subscription	**—**	—	109,833
Proceeds of public offerings	**—**	449,996,887	116,191,285
Payment of costs of public offerings	**—**	(756,313)	(748,538)
Net cash provided by financing activities	**477,734**	449,893,620	115,715,560
Net increase (decrease) in cash and cash equivalents	**1,482,922**	(14,165,741)	26,174,120
Cash and cash equivalents at beginning of period	**47,159,303**	61,325,044	35,150,924
Cash and cash equivalents at end of period	**$ 48,642,225**	$ 47,159,303	$ 61,325,044
Cash paid for interest	**$ 36,781**	$ —	$ 7,073
Cash paid for taxes	**$ 1,000,000**	$ —	$ —

See accompanying notes to consolidated financial statements.

Intra-Cellular Therapies, Inc.

Notes to Consolidated Financial Statements

December 31, 2016

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, or the Merger, Oneida Resources Corp. was a "shell" company registered under the Securities Exchange Act of 1934 (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.

On March 11, 2015, the Company completed a public offering of common stock in which the Company sold 5,411,481 shares of common stock, which included the exercise of the underwriters' option to purchase an additional 661,481 shares, at an offering price of $24.00 per share for aggregate gross proceeds of approximately $129.9 million. After deducting underwriting discounts, commissions and offering expenses, the net proceeds to the Company were approximately $121.8 million.

On September 28, 2015, the Company completed a public offering of common stock in which the Company sold 7,935,000 shares of common stock, which included the exercise of the underwriters' option to purchase an additional 1,035,000 shares, at an offering price of $43.50 per share for aggregate gross proceeds of approximately $345.2 million. After deducting underwriting discounts, commissions and offering expenses, the net proceeds to the Company were approximately $327.4 million.

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 our 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.

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. 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

1. Organization (continued)

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 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 the Company may determine. This registration statement will remain in effect for up to three years from the initial effective date.

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 as found 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. In conjunction with the capitalization of ITI Limited, the Company entered into a short term line of credit with a lender collateralized by Company investments held by the lender.

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.

2. Summary of Significant Accounting Policies (continued)

Investment securities consisted of the following (in thousands):

	December 31, 2016			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
U.S. government agency securities	$ 67,199	$ 1	$ (74)	$ 67,126
FDIC certificates of deposit (1)	20,740	1	—	20,741
Certificates of deposit	64,500	—	—	64,500
Commercial paper	67,352	11	(52)	67,311
Corporate bonds/notes	115,985	—	(205)	115,780
	$ 335,776	$ 13	$ (331)	$ 335,458

	December 31, 2015			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
U.S. government agency securities	$ 61,510	$ —	$ (271)	$ 61,239
FDIC certificates of deposit (1)	41,343	1	(11)	41,333
Certificates of deposit	219,500	—	—	219,500
Commercial paper	30,122	—	(48)	30,074
Corporate bonds/notes	76,157	—	(262)	75,895
	$ 428,632	$ 1	$ (592)	$ 428,041

(1) "FDIC certificates of deposit" consist of deposits that are less than $250,000.

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, 2016 and 2015 the Company held $47.9 million and $142.4 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, 2016 the Company had $25.5 million of investments that had been held for greater than one year that have a temporary impairment of approximately $25,000. As of December 31, 2015 the Company had approximately $9.2 million of investments that have been held for greater than one year which had a temporary impairment of approximately $19,000.

The Company attributes the unrealized losses on the available-for-sale securities as of December 31, 2016 and 2015, to the variability in related market interest rates. The Company does not intend to sell these securities, nor is it more likely than not that the Company will be required to sell them prior to the end of their contractual

2. Summary of Significant Accounting Policies (continued)

terms. Furthermore, the Company does not believe that these securities expose us 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, 2016 and December 31, 2015. The carrying value of cash held in money market funds of approximately $10.7 million as of December 31, 2016 and $31.1 million as of December 31, 2015, is included in cash and cash equivalents and approximates market value based on quoted market price or Level 1 inputs.

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, 2016	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	$ 10,724	$ 10,724	$ —	$ —
U.S. government agency securities	67,126	—	67,126	—
FDIC certificates of deposit	20,741	—	20,741	—
Certificates of deposit	64,500	—	64,500	—
Commercial paper	67,311	—	67,311	—
Corporate bonds/notes	115,780	—	115,780	—
	$ 346,182	$ 10,724	$ 335,458	$ —

	December 31, 2015	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	$ 31,114	$ 31,114	$ —	$ —
U.S. government agency securities	61,239	—	61,239	—
FDIC certificates of deposit	41,333	—	41,333	—
Certificates of deposit	219,500	—	219,500	—
Commercial paper	30,074	—	30,074	—
Corporate bonds/notes	75,895	—	75,895	—
	$ 459,155	$ 31,114	$ 428,041	$ —

Financial Instruments

The Company considers the recorded costs of its financial assets and liabilities, which consist of cash equivalents, accounts receivable, prepaids, accounts payable and accrued liabilities, to approximate their fair value because of their relatively short maturities at December 31, 2016 and December 31, 2015. 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.

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.

2. Summary of Significant Accounting Policies (continued)

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, 2016 and 2015, as the Company has a history of collecting on all its accounts including government agencies and collaborations funding its research.

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 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.

Revenue Recognition

Revenue is recognized when all terms and conditions of the agreements have been met, including persuasive evidence of an arrangement, delivery has occurred or services have been rendered, price is fixed or determinable and collectability is reasonably assured. The Company is reimbursed for certain costs incurred on specified research projects under the terms and conditions of grants, collaboration agreements, and awards. The Company records the amount of reimbursement as revenues on a gross basis in accordance with ASC Topic 605-45, *Revenue Recognition/Principal Agent Considerations* . The Company is the primary obligor with respect to purchasing goods and services from third-party suppliers, is obligated to compensate the service provider for the work performed, and has discretion in selecting the supplier. Provisions for estimated losses on research grant projects and any other contracts are made in the period such losses are determined.

The Company has entered into arrangements involving the delivery of more than one element. Each required deliverable is evaluated to determine whether it qualifies as a separate unit of accounting. For the Company, this determination is generally based on whether the deliverable has “stand-alone value” to the customer. The Company adopted this accounting standard on a prospective basis for all Multiple-Deliverable Revenue Arrangements (“MDRAs”) entered into on or after January 1, 2011, and for any MDRAs that were entered into prior to January 1, 2011, but materially modified on or after that date.

The Company has adopted ASC Topic 605-28, *Milestone Method* . Under this guidance, the Company recognizes revenue contingent upon the achievement of a substantive milestone in its entirety in the period the milestone is achieved. Substantive milestone payments are recognized upon achievement of the milestone only if all of the following conditions are met:

- The milestone payments are non-refundable;
- Achievement of the milestone involves a degree of risk and was not reasonably assured at the inception of the arrangement;
- Substantive effort on the Company’s part is involved in achieving the milestone;

2. Summary of Significant Accounting Policies (continued)

- The amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and
- A reasonable amount of time passes between the up-front license payment and the first milestone payment, as well as between each subsequent milestone payment.

Determination as to whether a payment meets the aforementioned conditions involves management's judgment. If any of these conditions are not met, the resulting payment would not be considered a substantive milestone, and therefore, the resulting payment would be considered part of the consideration for the single unit of accounting and be recognized as revenue in accordance with the revenue models described above. In addition, the determination that one such payment was not a substantive milestone could prevent the Company from concluding that subsequent milestone payments were substantive milestones and, as a result, any additional milestone payments could also be considered part of the consideration for the single unit of accounting and would be recognized as revenue as such performance obligations are performed under either the proportional performance or straight-line methods, as applicable .

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, 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 with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

As part of the process of preparing its financial statements, the Company is required to estimate its expenses resulting from its obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company's objective is to reflect the appropriate clinical trial expenses in its financial statements by matching those expenses with the period in which services are performed and efforts are expended. The Company accounts for these expenses according to the progress of the clinical trial as measured by subject progression and the timing of various aspects of the trial. The Company determines accrual estimates through financial models taking into account 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, 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 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, 2016 and 2015, there were no material adjustments to the Company's prior period estimates of accrued expenses for clinical trials.

2. Summary of Significant Accounting Policies (continued)

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.

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. For awards that contain a performance vesting condition, expense is amortized using the accelerated attribution method. As share-based compensation expense recognized in the statements of operations for the years ended December 31, 2016, 2015 and 2014 is based on share-based awards ultimately expected to vest, it has been reduced for estimated forfeitures. ASC Topic 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Pre-vesting forfeitures were estimated based on the Company’s historical experience for the years ended December 31, 2016, 2015 and 2014, and have not been material.

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.

2. Summary of Significant Accounting Policies (continued)

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 is defined 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.

Prior to January 1, 2014, given that there was no active market for the Company's 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 the Company's 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, the Company considered the guidance set forth in American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* . For stock options granted in 2016, 2015 and 2014, the exercise price was determined by using the closing market price of the Company's common stock on the date of grant.

A restricted stock unit ("RSU") is a stock award that entitles the holder to receive shares of the Company's common stock as the award vests. The fair value of each RSU is based on the closing price 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.

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, 2016, 2015 and 2014, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations.

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 services required are completed and are marked to market during the service period.

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.

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 loss from operations for the years ended December 31, 2016, 2015 and 2014:

	Years Ended December 31,		
	2016	2015	2014
Common Stock Equivalents	1,225,614	1,322,311	958,712
RSUs	32,781	—	—

2. Summary of Significant Accounting Policies (continued)

Recently Issued Accounting Standards

In August 2014, the FASB issued ASU No. 2014-15, "Presentation of Financial Statements—Going Concern," to provide guidance on management's responsibility in evaluating whether there is substantial doubt about a company's ability to continue as a going concern and about related footnote disclosures. For each reporting period, management will be required to evaluate whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year from the date the financial statements are issued. This guidance is effective for the annual period ending after December 15, 2016, and for annual periods and interim periods thereafter. Early adoption of the guidance was permitted. The Company has adopted ASU No. 2014-15 and the adoption had no impact on the Company's consolidated financial statements.

In May 2014, the FASB issued Accounting Standards Update No. 2014-09 (ASU 2014-09), Revenue from Contracts with Customers. ASU 2014-09 will eliminate transaction-specific and industry-specific revenue recognition guidance under current GAAP and replace it with a principle-based approach for determining revenue recognition. ASU 2014-09 will require that companies recognize revenue based on the value of transferred goods or services as they occur in the contract. ASU 2014-09 also will require additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. In July 2015, the FASB decided to defer the effective date of the standard from January 1, 2017, to January 1, 2018, with an option that permits companies to adopt the standard as early as the original effective date. Early adoption of the standard prior to the original effective date is not permitted. The standard permits the use of either the retrospective or cumulative effect transition method.

The Company started an initial impact assessment of the potential changes from adopting ASU 2014-09. Based on the assessment procedures performed to date the Company anticipates that the adoption of ASU 2014-09 will primarily impact the contract revenues recognized for collaborations and license agreements. The Company is still completing its initial assessment of the impact of this guidance, including the new disclosure requirements, as the Company has not had product sales to date. The Company plans to adopt the new standard effective January 1, 2018. The Company continues to monitor additional changes, modifications, clarifications or interpretations being undertaken by the FASB, which may impact the Company's current conclusions.

In January 2016, the FASB issued Accounting Standards Update 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 is not expected to have a material impact on the Company's consolidated financial statements.

In February 2016, the FASB issued Accounting Standards Update 2016-02, Leases ("ASU 2016-02"). ASU 2016-02 allows 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 is currently analyzing the impact of ASU No. 2016-02 and, at this time, is yet to determine the impact of the new standard, if any, on the Company's consolidated financial statements.

In March 2016, the FASB issued Accounting Standards Update 2016-09, Compensation—Stock Compensation ("ASU 2016-09"). ASU 2016-09 simplifies several areas of accounting for stock compensation, including

2. Summary of Significant Accounting Policies (continued)

simplification of the accounting for income taxes, classification of excess tax benefits on the Statement of Cash Flows and forfeitures. ASU 2016-09 is effective for annual reporting periods beginning after December 15, 2016. An entity that elects early adoption must adopt all of the amendments in the same period. The Company did not early adopt ASU 2016-09 as of and for the period ended December, 2016. The Company intends to adopt this standard for the quarter ending March 31, 2017 and the adoption of this standard is not expected to have a material impact on the Company's consolidated financial statements.

3. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2016	2015
Computer equipment	$ 39,095	$ 42,064
Furniture and fixtures	292,423	266,695
Scientific equipment	2,844,865	2,823,601
	3,176,383	3,132,360
Less accumulated depreciation	(2,548,769)	(2,356,838)
	$ 627,614	$ 775,522

Depreciation expense for the years ended December 31, 2016, 2015 and 2014 was $196,872, $139,626 and $25,481, respectively.

4. Share-Based Compensation

The Company's Amended and Restated 2013 Equity Incentive Plan (the "2013 Plan") to provide 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. In August 2013, in connection with the Merger, the Company assumed the ITI 2003 Equity Incentive Plan, as amended (the "2003 Plan"), which expired by its terms in July 2013. As of December 31, 2016, there were options to purchase 666,909 shares of common stock outstanding under the 2003 Plan and options to purchase 2,434,123 shares of common stock outstanding under the 2013 Plan. Effective in November 2013, the Company adopted the 2013 Plan. The Company initially reserved 2,850,000 shares of common stock for issuance under the 2013 Plan. In both January 2015 and 2014, the number of shares of common stock reserved for issuance under the 2013 Plan automatically increased by 800,000 pursuant to the evergreen provisions of the 2013 Plan. On June 16, 2015, the stockholders of the Company approved, at the Company's 2015 Annual Meeting of Stockholders, an amendment to the 2013 Plan to increase the number of shares of common stock available for issuance under the plan by 3,100,000 shares, to increase by 100,000 shares the maximum number of shares available for the issuance of options, stock appreciation rights and other similar awards to any one participant in any calendar year for purposes of meeting the requirements for qualified performance-based compensation under Section 162(m) of the Internal Revenue Code of 1986, as amended (the "Code"), and to eliminate the evergreen provisions of the 2013 Plan under which 800,000 shares were automatically added to the plan on each of January 1, 2014 and 2015. Stock options granted under the 2013 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 two to three years) and the exercise prices of such options. Options have a maximum term of 10 years. The exercise price of ISOs granted under the 2013 Plan must be at least equal to the fair market value of the common stock on the date of grant.

4. Share-Based Compensation (continued)

Total stock-based compensation expense related to all of the Company's share-based awards, including stock options and RSUs to employees, directors and consultants recognized during the years ended December 31, 2016, 2015 and 2014, was comprised of the following:

	Years Ended December 31,		
	2016	2015	2014
Research and development	**$ 4,472,658**	$ 4,768,131	$ 1,842,828
General and administrative	**10,228,561**	6,122,774	2,001,050
Total share-based compensation expense	**$ 14,701,219**	$ 10,890,905	$ 3,843,878

The following table describes the weighted-average assumptions used for calculating the value of options granted during the years ended December 31, 2016, 2015 and 2014:

	2016	2015	2014
Dividend yield	**0%**	0%	0%
Expected volatility	**80.0%-90.0%**	80.0%	80.0%
Weighted-average risk-free interest rate	**1.7%**	1.8%	2.0%
Expected term (in years)	**5.9**	5.9	6.3

Information regarding the stock options activity, including with respect to grants to employees, directors and consultants as of December 31, 2016, 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, 2015	2,737,657	$ 13.72	$ 109,778,658	7.64 years
Options granted	487,121	$ 48.85		9.15 years
Options exercised	(123,745)	$ 3.86		3.05 years
Options canceled or expired	(1)	$ 1.36		0.00 years
Outstanding at December 31, 2016	3,101,032	$ 19.63	$ 9,351,908	7.18 years
Vested or expected to vest at December 31, 2016	3,101,032	$ 19.63		
Exercisable at December 31, 2016	2,025,757	$ 12.59	$ 9,310,898	6.64 years

The weighted-average grant date fair value for awards granted during the years ended December 31, 2016, 2015, and 2014, was $48.85, $21.00, and $16.50 per share, respectively. Total intrinsic value of the options exercised during the years ended December 31, 2016, 2015, and 2014 was approximately $2,984,283, $10,951,057 and $3,696,775, respectively. The total fair value of shares vested in the years ended December 31, 2016, 2015 and 2014, was approximately $9,310,898, $5,207,073 and $3,703,000, respectively.

During 2016, 2015 and 2014, the Company granted options to certain scientific advisory board members of the Company to purchase 5,000, 45,571 and 95,000 shares of common stock, respectively, at an average exercise price per share of $53.63, $17.57, and $16.86, respectively. The options vest ratably over a period of 12 to 24 months. Stock compensation related to these grants will fluctuate with any changes in the underlying value of the Company's common stock, as the performance period is not fixed.

As of December 31, 2016 and 2015 there was $3,022,843 and $291,644, respectively, of unrecognized compensation costs related to unvested RSUs. The unrecognized share-based compensation expense related to stock option awards at December 31, 2016, is $15,022,101 and will be recognized over a weighted-average period of 1.7 years.

4. Share-Based Compensation (continued)

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, 2016 and changes during the year then ended, is summarized as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value
Outstanding at December 31, 2015	5,272	$ 56.90
RSU's granted in 2016	78,806	$ 53.63
RSU's vested in 2016	(1,757)	$ 56.90
Outstanding at December 31, 2016	82,321	$ 53.77

The Company recognized non-cash stock-based compensation expense related to RSU's for the years ending December 31, 2016 and 2015 of approximately $1.5 million and $8,000, respectively.

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

Total income tax expense for the years ended December 31, 2016, 2015, and 2014 is allocated as follows:

	2016	2015	2014
Current	$ 1,065,673	$ 1,600	$ 1,600
Deferred	(19,605,520)	(51,165,859)	(14,655,320)
Valuation allowance	19,605,520	51,165,859	14,655,320
Provision for income taxes	$ 1,065,673	$ 1,600	$ 1,600

A reconciliation of the difference between the statutory federal income tax rate and the effective income tax rate for the years ended December 31, 2016, 2015, and 2014 is as follows:

	December 31,		
	2016	2015	2014
Income tax benefit at statutory federal rate	35.00%	35.00%	35.00%
Royalty Income	(37.93)	0.00	0.00
Other Permanent differences	(0.78)	(0.56)	0.12
Foreign rate differential	(8.61)	0.00	0.00
Return-to-provision—R&D Credit	(0.03)	0.00	(0.05)
R&D Credit—current year	2.13	4.19	2.32
Reserve for uncertain tax positions	(0.02)	0.00	(0.01)
Change in effective state tax rates	(6.98)	(0.05)	(0.14)
State income tax expense	(.70)	10.24	10.50
Change in valuation allowance	16.99	(48.82)	(47.75)
Provision for income taxes	(0.93)%	(0.00)%	(0.01)%

6. Income Taxes (continued)

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, 2016, the Company had $121.0 million of federal net operating loss carryforwards, which expire at various dates through 2035. 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 year ended December 31, 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. 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.

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. At December 31, 2016, the Company had $1.3 million in excess tax benefits related to stock-based compensation deductions, the benefit of which will be recorded to additional paid-in-capital once the benefit is realized through a reduction of income taxes payable. The following summarizes the significant components of the Company's deferred tax assets and liabilities as of December 31, 2016 and 2015, respectively:

	December 31,	
	2016	2015
Deferred tax assets:		
Net operating loss carryforwards	$ 49,627,652	$ 76,741,198
Accrued employee benefits	535,158	543,466
Research and development credit	9,367,227	6,962,731
Stock compensation	9,360,025	5,641,993
Federal AMT credit	1,062,451	—
Deferred rent	1,095,220	725,195
Deferred tax liabilities:		
Depreciation	(44,732)	(6,062)
Net deferred tax asset	71,003,001	90,608,521
Valuation allowance	(71,003,001)	(90,608,521)
Net deferred tax asset	$ —	$ —

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

The total amount of unrecognized tax benefits as of December 31, 2016 and December 31, 2015 were $1.7 million and $1.7 million respectively. If recognized none of these tax benefits would affect the effective tax rate due to valuation allowances.

6. Income Taxes (continued)

The following summarizes the significant components of gross unrecognized tax benefits as of December 31, 2016 and 2015, respectively:

	December 31, 2016	2015
Balance at January 1,	**$ 1,720,912**	$ 1,717,635
Current Year Uncertain Tax Positions:		
Gross Increases	17,903	3,277
Balance at December 31,	**$ 1,738,815**	$ 1,720,912

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 license 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. Possible milestone payments remaining total $12.0 million. Under the agreement, the Company may be obliged to make other milestone payments to BMS for each licensed product of up to an aggregate of approximately $14.75 million. The Company is also obliged to make tiered single digit percentage royalty payments 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.

The Takeda Pharmaceutical License and Collaboration Agreement and Termination Agreement

On February 25, 2011, the Company entered into a license and collaboration agreement (the "Takeda License Agreement") with Takeda Pharmaceutical Company Limited ("Takeda") under which the Company agreed to collaborate to research, develop and commercialize its proprietary compound ITI-214 and other selected

7. Collaborations and License Agreements (continued)

compounds that selectively inhibit phosphodiesterase type 1 ("PDE1") for use in the prevention and treatment of human diseases. As part of the agreement, the Company assigned to Takeda certain patents owned by the Company that claim ITI-214 and granted Takeda an exclusive license to develop and commercialize compounds identified in the conduct of the research program that satisfy specified criteria. However, the Company retained rights to all compounds that do not meet the specified criteria and the Company continues to develop PDE1 inhibitors outside the scope of the agreement.

On October 31, 2014, the Company entered into an agreement with Takeda terminating the Takeda License Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to the Company. On September 15, 2015, Takeda completed the transfer of the Investigational New Drug Application ("IND") for ITI-214 to the Company. ITI-214 is the first compound in its class to successfully advance into Phase 1 clinical trials. The Company intends to explore the development of its 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 the Company's Phase 1 program, in the first half of 2017 the Company expects to initiate a Phase 1/2 clinical trial with 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. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

8. Commitments and Contingencies

The Company currently has an operating lease agreement with a commitment for $16,255,927 for laboratory and office facilities through 2027.

At December 31, 2016, 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	
2017	1,299,845
2018	1,457,008
2019	1,500,718
2020	1,545,740
2021	1,592,112
Thereafter	8,860,504
	$ 16,255,927

Rent expense for the years ended December 31, 2016, 2015 and 2014 was $1,419,940, $1,385,207 and $853,504, 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 50% on the first 6% of contributions made by participants. Participant and Company contributions vest immediately. During the years ended December 31, 2016, 2015 and 2014, the Company recorded matching contribution expense of $157,244, $109,963 and $84,757, 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 for approximately 16,753 square feet of useable

10. Related Parties (continued)

laboratory and office space **.** The lease has a term of 12 years. The deferred rent balance will begin to decrease incrementally in the first quarter of 2017. 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 2016 and 2015 quarterly statements of operations.

The following table sets for the Company's unaudited condensed consolidated statements of operations for the 2016 quarters ended:

2016 Quarter Ended	December 31,	September 30,	June 30,	March 31,
Revenue	$ 97,895	$ 4,362	$ 228,445	$ —
Net loss	(27,485,039)	(30,265,327)	(30,834,454)	(27,841,449)
Basic and diluted net loss per share	$ (0.64)	$ (0.70)	$ (0.71)	$ (0.64)

The following table sets for the Company's unaudited condensed consolidated statements of operations for the 2015 quarters ended:

2015 Quarter Ended	December 31,	September 30,	June 30,	March 31,
Revenue	$ 30,659	$ —	$ 57,390	$ 3,315
Net loss	(28,834,516)	(32,160,483)	(21,511,318)	(22,286,824)
Basic and diluted net loss per share	$ (0.67)	$ (0.91)	$ (0.61)	$ (0.72)

Exhibit 10.3

Execution Version

S UPPLY A GREEMENT

This Agreement is made as of January 4, 2017 (the Effective Date) between

Siegfried Evionnaz SA

Route du Simplon 1, 36, 1902 Evionnaz, Switzerland

(Siegfried)

and

ITI Limited

Clarendon House, 2 Church Street, PO Box HM 666, Hamilton, HM CX, Bermuda

(ITI)

Recitals

A. ITI engages in the business of research, development and commercialization of pharmaceutical compounds and products;

B. Siegfried has substantial expertise in process development, scale-up and manufacturing of active pharmaceutical ingredients and drug products; and

C. ITI and Siegfried desire to enter into this Agreement to provide the terms and conditions upon which Siegfried shall manufacture Product in commercial quantities after the completion of a validation campaign.

Now, therefore, in consideration of the foregoing recitals and mutual covenants, agreements, representations, warranties and obligations expressed herein, and intending to be legally bound hereby, the Parties agree as follows:

1. Definitions

Unless elsewhere defined in this Agreement, each of the capitalized terms used in this Agreement (other than the names of the Parties and the headings of the Sections) shall have the meanings indicated below. Such meanings shall apply equally to all forms of such terms, including singular and plural forms, unless otherwise clearly indicated.

1.1 **Act** shall mean the United States Food, Drug and Cosmetic Act of 1938, including any amendments thereto and all rules and regulations promulgated thereunder.

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

1.2 **Affiliate** shall mean with respect to any Party any person or entity controlling, controlled by, or under common control with a Party at any time during the term of this Agreement. For purposes of this definition, the term **control** shall mean the power to direct or cause the direction of the management and policies of an entity, whether through the ownership of voting stock, by contract or otherwise. In the case of a corporation, the term Control shall mean the direct or indirect ownership of at least fifty per cent (50%) of the outstanding voting stock.

1.3 **Agreement** shall mean this Supply Agreement including its Annexes (and appendices, if applicable), as amended from time to time according to the terms and conditions of this Agreement.

1.4 **API** shall mean active pharmaceutical ingredient.

1.5 **Applicable Laws** means, with respect to ITI, all laws, ordinances, rules and regulations, currently in effect or enacted or promulgated, and as amended from time to time, of each jurisdiction of the Territory (in which the Product is manufactured, marketed, distributed, used or sold); and with respect to Siegfried, all laws, ordinances, rules and regulations, currently in effect or enacted or promulgated, and as amended from time to time, of the jurisdiction in which it performs the Services, and cGMP Regulations.

1.6 **Business Day** shall mean a day (not being a Saturday or Sunday) on which banks are open for business in New York, U.S.A. and Zurich, Switzerland.

1.7 **cGMP Regulations** shall mean the regulations defining and regulating current Good Manufacturing Practices (GMP) as contained from time to time in the Act and related regulations, or any successor laws or regulations governing the manufacture, handling, storage and control of the Product, including without limitations, regulations promulgated by the FDA under 21 C.F.R. §§ 210, 211, EC Directive 2003/94/EC, and the World Health Organization (WHO) “Guide to good manufacturing practice (GMP) requirements, and the International Conference on Harmonization (ICH), Guidance for Industry Q7A GMP Guidance for APIs.

1.8 **Confidential Information** shall mean any information of whatever kind, and all tangible and intangible embodiments, and oral disclosures thereof, of any kind whatsoever, which has been or will be disclosed by one Party (**Disclosing Party**) to the other Party (**Receiving Party**) in connection with this Agreement, and which is confidential or proprietary to the Disclosing Party or an Affiliate thereof, including, without limitation, for ITI, any and all information pertaining to the Product and the Specifications, and for both Parties information which relates to the business of such Party, including without limitation business plans, strategies, operations, policies, procedures, pricing, techniques, technical and scientific information, accounts, marketing plans, financial plans and status, and personnel of either Party, that is designated or marked at the time

of the disclosure as confidential or proprietary, or disclosed or made available under circumstances under which a reasonable person would understand the information to be confidential or proprietary, including without limitation which are obtained by Receiving Party through inspection or observation of Disclosing Party's, or its Affiliates', property or facilities (whether in writing, or in oral, graphic, electronic or any other form).

1.9 **Consigned Materials** shall mean the samples and materials, if any, that are to be provided to Siegfried by or on behalf of ITI for the Manufacture of the Product, as listed in ANNEX C.

1.10 **EMA** shall mean the European Medicines Agency or any successor entity.

1.11 **End Market Product** shall mean any pharmaceutical product containing the Product in the finished packed form for marketing, distribution and sale in the Territory.

1.12 **Facility** means Siegfried's manufacturing facility located at [***] or such other manufacturing facility of Siegfried or its Affiliates as agreed between the Parties.

1.13 **FDA** shall mean the United States Food and Drug Administration or any successor entity.

1.14 **Governmental Authority** shall mean any governmental authority or authorities which are responsible for approving the conduct of clinical trials, or the manufacture, marketing, use and sale of pharmaceutical products in their respective markets of the Territory, such as the FDA and the EMA.

1.15 **Hidden Defects** shall mean a failure of Product to conform to the Specifications, such failure not being discoverable upon reasonable physical inspection or standard testing upon receipt of Product.

1.16 **Improvement** shall mean any result, data, documentation, invention, know-how, improvement, modification, adaptation, enhancement or new application to or for any part of the Product or the techniques or processes involved in its manufacture, which is conceived, derived, reduced to practice, made or developed by or for Siegfried in its performance of Services under this Agreement.

1.17 **Independent Improvement** shall mean an Improvement which is independent of ITI's Confidential Information and which is not solely applicable to the Product.

1.18 **Intellectual Property Rights** shall mean all inventions, patent applications, patents, registered or unregistered design rights, copyrights, database rights, trademarks, trade names, know-how, trade secrets and other industrial or intellectual property rights of whatever kind.

1.19 **Manufacture/Manufacturing/Manufactured** shall mean all activities with respect to the manufacturing and supply of the Product, including, without limitation, the purchase and incoming inspections, storage and handling of Materials, quality control testing (including in-process, release and stability testing, when applicable), and packaging, release and delivery of Products.

1.20 **Master Batch Record** means the document approved in writing by both Parties, and as may be amended from time to time in accordance with this Agreement and the Quality Agreement, specifying or referencing the complete set of formal instructions for the Manufacture of Product, including, but not limited to material descriptions, the formula, processing procedures, and in-process testing specifications, Specifications and packaging and shipping specifications.

1.21 **Materials** shall mean Raw Materials and Consigned Materials.

1.22 **Order** shall mean a purchase order issued by ITI in accordance with this Agreement.

1.23 **Order Confirmation** shall mean a confirmation issued by Siegfried that an Order posted by ITI shall be executed.

1.24 **Party/Parties** shall mean either ITI or Siegfried, or both, as the context may require.

1.25 **Product** shall mean the API as set out in ANNEX A.

1.26 **Quality Agreement** shall mean the signed agreement between ITI and Siegfried which defines the responsibilities of each Party (Delinitation of Pharmaceutical Responsibility) with respect to the practices to be followed to ensure Product quality and compliance under cGMP Regulations, which shall be made part of this Agreement by reference (as such Quality Agreement may be amended from time to time).

1.27 **Raw Materials** shall mean all raw and other materials, excluding any Consigned Materials, which are used to Manufacture the Product in accordance with the Requirements and Specifications, as applicable.

1.28 **Regulatory Approval** means any approval or authorizations (including supplements and amendments thereof) of any Governmental Authority in each country of the Territory.

1.29 **Requirements** means compliance with Applicable Laws, cGMP Regulations, the Quality Agreement and the Master Batch Records.

1.30 **Services** means the Manufacture of Product, and all other activities to be performed by Siegfried under this Agreement.

1.31 **Specifications** shall mean the description of technical requirements the Product has to conform to, as set out in detail in ANNEX A.

1.32 **Territory** shall mean the United States of America (with its territories, possessions, and protectorates, such as the Commonwealth of Puerto Rico), Bermuda, the member states of the European Union and/or European Economic Area (EU/EEA), Switzerland, Japan and any other country, which the Parties agree in writing to add to this definition of Territory in an amendment to this Agreement.

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Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

2. Manufacture, Purchase and Supply of Products

2.1 This Agreement covers the purchase, Manufacture, and supply of commercial quantities of Product after completion of a validation campaign during the term of the Agreement as set forth in Section 10 below.

2.2 ITI shall purchase the Product from Siegfried in accordance with the purchase requirements and all other commercial terms set forth in ANNEX B.

2.3 Siegfried shall Manufacture the Product in accordance with the Requirements and solely at the Facility. Siegfried may not deviate from the Requirements without ITI's prior written consent in each instance. Siegfried shall notify ITI of any proposed changes to the Specifications and/or Master Batch Record in accordance with the Quality Agreement, and may not implement such change without ITI's prior written consent.

2.4 Promptly after the Effective Date and thereafter at least [***] prior to the start of each month, ITI shall submit to Siegfried an [***] rolling forecast covering ITI's anticipated requirements of Product during such period (each, a **Forecast**). The first twelve (12) months of each such Forecast shall be binding and [***]. ITI acknowledges that Siegfried will rely on the accuracy of ITI's Forecasts in planning its acquisitions of Raw Materials. If at any time ITI finds that a Forecast is inaccurate, ITI shall inform Siegfried without delay and submit a modified forecast for the period in question.

2.5 ITI shall make all purchases hereunder by submitting Orders to Siegfried regarding ITI's requirements of Product in accordance with Section 2.4 above. Each such Order shall be in writing and shall specify the (i) Product ordered, (ii) quantity ordered, (iii) price, (iv) delivery location(s) pursuant to ANNEX B, and (v) delivery date.

2.6 In accordance with Sections 2.3 and 2.5, ITI shall purchase [***] of the corresponding Forecast by respective Orders and Siegfried shall execute and fulfill such Orders which [***] of such Forecast. Orders [***] of the corresponding Forecast shall be discussed between the Parties, and Siegfried will use commercially reasonable efforts to fulfill such excess, but are only binding upon confirmation by Siegfried. ITI hereby accepts [***].

2.7 Within [***] from the date of the receipt of an Order from ITI, Siegfried shall confirm to ITI by way of an Order Confirmation that it will meet ITI's quantity requirements in accordance with the delivery date(s), whereupon the Order shall be confirmed, final, and binding on the Parties. Siegfried may not reject any Order that is consistent with the terms of Sections 2 and 3.

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2.8 Without limiting ITI's remedies or Siegfried's obligations hereunder, Siegfried shall promptly notify ITI in writing of any anticipated delay or of any circumstance(s) rendering it unable to Manufacture and/or supply Product in accordance with the delivery date(s) and the estimated duration of such delay/circumstance(s) and the Parties shall discuss in good faith about the steps to be taken to overcome such delay. Siegfried will keep ITI regularly informed of the progress of such Orders.

2.9 The Product shall be delivered from Siegfried to ITI according to the commercial terms and at the price as set out in ANNEX B. ITI assumes all responsibilities and liability arising out of the transport, storage, handling and use of the Product after delivery by Siegfried to ITI.

2.10 ITI acknowledges and agrees that Siegfried will Manufacture and supply the Product in volumes to fulfil all Orders specified in Section 2.5 to the extent that such volumes in any contract year do not exceed the capacity of [***] based on the validated batch size of [***]/batch.

3. Materials

3.1 Siegfried shall order sufficient quantities of all Raw Materials from its selected and qualified vendors to manufacture and supply Product in accordance with ANNEX B and this Agreement. [***], where such change is agreed by the Parties in writing.

3.2 If ITI designates certain vendors in accordance with and if set forth in the Quality Agreement, then Siegfried shall obtain respective Raw Material(s) only from such designated vendors. [***]. In no event shall Siegfried be liable or responsible for any acts or omissions of such designated vendor, including without limitation, any delayed delivery, delivery of non-conforming Raw Material or other supply failure.

3.3 ITI shall supply Consigned Materials in sufficient quantities and of good quality as necessary to enable Siegfried to perform all Services, manufacture and supply Product in accordance with the Requirements, at ITI's costs and expenses. At ITI's option, the Consigned Materials may be delivered directly from ITI's vendor to Siegfried at the vendor's or ITI's costs and expenses.

3.4 Consigned Materials shall be delivered to Siegfried by the delivery date or timeframe specified in the ANNEX B. In no event shall Siegfried be liable or responsible for any acts or omissions caused by third party or ITI activities under Section 3.2 and/or 3.4, including without limitation, any delayed delivery, delivery of non-conforming Consigned Materials or other supply failure.

3.5 Siegfried agrees that Consigned Materials shall: (i) be used solely for the purpose of Manufacture or performing other services under this Agreement; (ii) be used in compliance with all Applicable Laws; and (iii) not be transferred to any third party, except to any permitted subcontractor of Siegfried, or except as provided for under a specific Work Order.

3.6 Siegfried agrees to use all reasonable and appropriate precautions in handling and storing Consigned Materials and to inform ITI promptly in writing of any adverse effects experienced by persons handling Consigned Materials.

3.7 ITI shall retain all right, title and interest in and to all Consigned Material delivered to Siegfried and shall insure the Consigned Materials against loss and damage. Siegfried shall only be liable for any loss of or damage to Consigned Material after delivery to Siegfried if such loss or damage was caused by Siegfried's [***]. Following receipt of Consigned Materials, Siegfried shall inspect such items, in accordance with the procedures set forth in the Quality Agreement and/or the Master Batch Record, to verify their quantity and quality, and shall give ITI, as soon as reasonably possible, notice of any quantity or quality shortcoming. Any Consigned Materials not rejected by Siegfried within such time period shall be deemed accepted, unless they have Hidden Defects. In case the Consigned Materials are rejected by Siegfried, Siegfried shall follow ITI's written instructions in respect of return or disposal of defective Consigned Materials, at ITI's costs and risks. Upon delivery of any Order, Siegfried shall notify ITI of any excess Product or Consigned Materials in its possession, and unless ITI directs otherwise within [***] after receipt of such notice, Siegfried shall store all such material at its facility at an agreed rate.

3.8 Siegfried may subcontract its Manufacturing activities (including to any Affiliate) only upon ITI's prior written consent. If ITI gives its consent (in its sole reasonable discretion) Siegfried will execute a subcontractor agreement with the third party subcontractor or Affiliate that contains terms at least as protective of ITI, its rights under this Agreement, and its Intellectual Property Rights as the terms in this Agreement, including, without limitation terms that, at a minimum, provide for compliance by the subcontractor with Applicable Laws, provide for ownership and allocation of Intellectual Property Rights in accordance with Section 9, and for obligations of confidentiality of information, record-keeping, access, and rights to data that are consistent with the intent and terms of this Agreement. Siegfried shall remain liable at all times for the performance of any of its obligations hereunder that it delegates to a subcontractor, and for each such subcontractor's actions and omissions.

4. Product Inspection

4.1 Siegfried shall take reasonable precautions and institute procedures to ensure that the Manufacture of Product is and remains fully compliant with the Requirements.

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4.2 Upon receipt of the Product, ITI shall examine the Product within [***] in order to determine compliance with the Specifications. If, in ITI's opinion, the Product delivered does not comply with the Specifications, then ITI shall notify Siegfried in writing thereof. If ITI does not notify Siegfried within [***] after receipt of the Product by ITI, then the Product is deemed accepted. ITI retains the right to reject the Product for a period of [***] after delivery in case of Hidden Defects, provided that ITI notifies Siegfried in writing within [***] of discovering the Hidden Defect. Any claims by ITI regarding Product delivered shall specify in reasonable detail the nature and basis for the claim and cite Siegfried's relevant batch numbers or other information to enable specific identification of the Product involved. If ITI rejects any Product under this Section, then it may reject the entire batch from which such Product was derived. Siegfried shall promptly review any written claim made by ITI regarding the quality of the Product and promptly provide ITI with the results of such review. If such review and testing by Siegfried, using reasonable and documented methods in accordance with its standard operating procedures, confirms that the identified Product did not meet the Specifications, then the Parties shall proceed according to Section 12.1. ITI shall, at Siegfried's expense, dispose or deliver the nonconforming Product to such destination as Siegfried shall direct in writing, provided that such directions are in compliance with applicable environmental laws and regulations. ITI shall not knowingly use or dispose of any Product that does not, or shall not use or dispose of any Product of which ITI claims that it does not, conform to the Specifications without Siegfried's prior written consent. Siegfried may not make rejected Product available to any third party. ITI need not pay for any Product that it rejects until the Parties establish whether or not the rejection was proper as described in this Section 4.2 and in Section 4.3.

4.3 If Siegfried, using reasonable and documented methods in accordance with its standard operating procedures, does not agree with ITI that a delivered quantity of Product does not conform to the Specifications, the Parties shall have the batch in dispute tested and further analyzed by an independent testing laboratory selected by agreement between the Parties. The decision of the independent testing laboratory shall be deemed final as to any dispute over Product quality. Should the laboratory's testing determine that the delivered Product does not conform to the Specifications, then Siegfried shall bear all costs for the independent laboratory testing, ITI shall have the right to reject such batch, Siegfried's disposition of rejected Products shall be made in accordance with the Quality Agreement and the Parties shall proceed according to Section 12.1. However, in case of wrongful rejection of Product by ITI, then ITI shall bear the expenses of the laboratory testing and all costs incurred due to the wrongful rejection of the Product. Siegfried's disposition of rejected Products must be made in accordance with the Quality Agreement or ITI's instructions.

4.4 In the event a batch is rightfully rejected by ITI pursuant to Section 4.2 or by the independent testing laboratory pursuant to Section 4.3, upon request of ITI, Siegfried shall perform and complete an investigation with root cause analysis and corrective

actions determined to prevent further batch rejections in accordance with the Quality Agreement, which corrective actions and sharing of costs shall be agreed to in writing by the Parties. Siegfried shall perform such investigations, root cause analysis and corrective actions reasonably diligently and expeditiously.

4.5 Subject to the terms of the Quality Agreement,Siegfried shall be responsible for release testing of Product, and shall release each batch to ITI as set forth in the Master Batch Record. In connection with release of a batch of Product, Siegfried shall provide to ITI promptly in response to its request [***].

5. Audits, Notification and Recall

5.1 Siegfried shall keep and maintain true, complete and accurate records, notes, accounts, reports and other records and materials with respect to all Manufacturing activities required by cGMP Regulations (" **Records** "). Records shall be maintained in accordance with Applicable Laws and shall be kept in a secure area reasonably protected from fire, theft and destruction. Siegfried shall store all Records during the term of this Agreement and for [***] thereafter, or longer if required pursuant to the Quality Agreement or in accordance with Applicable Laws.

5.2 ITI has the right to review and inspect Records, other than financial records, during the term of this Agreement and for [***] thereafter. During the term of this Agreement, ITI may carry out compliance and cGMP Regulation audits on the site(s) of Manufacture up to [***] during the term of this Agreement, or more frequently for cause. Access shall be granted at mutually agreed dates, during normal business hours only and upon [***] prior written notice or sooner for cause. If necessary for such audits, Siegfried may grant ITI reasonable access to Siegfried's personnel relevant to Manufacture of the Product. ITI shall comply with all of Siegfried's on-site policies regarding, safety, health, data protection, confidentiality and the like which Siegfried, in its sole reasonable discretion, provides to ITI in writing. From time to time throughout each calendar year this Agreement is in place, ITI may request, as a matter of oversight and direction, to send [***] who are employees of ITI to the Facility to observe the Manufacture of Product, the conditions of which shall be discussed in good faith between the Parties, and Siegfried shall use its reasonably commercial endeavors to accomodate ITI's request. If circumstances arise that may adversely affect the quality of Product, Siegfried shall immediately notify ITI thereof in accordance with the Quality Agreement and the Parties may agree on ITI's reasonable access to relevant Siegfried areas and records.

5.3 Siegfried shall permit any Governmental Authority to inspect relevant facilities, equipment and records at their request and shall resolve any issues raised by a Governmental Authority. Siegfried shall immediately notify ITI of any inquiry, audit or inspection by any Governmental Authority if such audit or inspection relates to a

Product, and ITI shall have the right to be present at such audit or inspection [***]. Siegfried shall promptly provide to ITI all correspondence and reports that it receives from a Governmental Authority directly relating to a Product, and shall give ITI the opportunity, if reasonably possible, to comment on any responses by Siegfried.

5.4 Each Party shall notify the other in writing within [***] of receipt of a complaint related to Product, or within any other timeline set forth in the Quality Agreement. Complaints related to Manufacturing issues with respect to Product will be fully and promptly investigated by Siegfried, and an investigation report will be prepared and sent to ITI within [***] of receipt of the complaint or of the notification of such complaint by ITI, or within any other timeline set forth in the Quality Agreement. ITI, and not Siegfried, will correspond with complainants on all complaints associated with Products. Siegfried shall maintain such traceability records as are sufficient and as may be necessary to permit a recall or field correction of any Product

5.5 In the event either Party believes it may be necessary to conduct a recall or other similar action with respect to the Product (each a **Recall**), the Parties shall consult with each other as to how best to proceed. If any Government Authority issues a directive, order or written request that any Product be Recalled, or ITI determines in its reasonable discretion that any Product should be Recalled, Siegfried will cooperate with ITI with respect to such Recall as requested by ITI, and any such cooperation will be at ITI's expense except as provided below. If any Recall results from Siegfried's failure to Manufacture Products in accordance with the Requirements (unless such failure arises from defects in Consigned Materials or in Raw Materials provided by vendors designated by ITI), Siegfried shall promptly, at ITI's election and without limiting its other remedies, either: (i) refund the invoice price for such defective Product; (ii) offset the invoice price for such defective Product against other amounts due to Siegfried hereunder; or (iii) replace such Product with conforming Product without any further cost to ITI. To the extent a Recall results from negligence by Siegfried to Manufacture Product in accordance with the Requirements (unless such failure arises from defects in Consigned Materials or in Raw Materials provided by vendors designated by ITI), Siegfried shall also be responsible for the documented out-of-pocket expenses of such Recall incurred by ITI (as well as its own expenses in cooperating with ITI as required under this Agreement), as subject to Section 12.7. In all other circumstances, Recalls shall be made at ITI's cost and expense. Under no circumstances shall either Party be prohibited hereunder from taking any action that it is required to take by Applicable Law.

6. Compensation and Terms of Payment

6.1 In consideration for the Manufacture and supply of the Product under the terms of this Agreement, ITI shall pay Siegfried the prices specified in, and in accordance with the payment terms set forth in ANNEX B. ITI hereby acknowledges and agrees that after the validation campaign the Parties will either confirm or adjust (on commercially reasonable terms) the price indications set forth in ANNEX B.

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Siegfried	ITI

6.2 [***]. In case the total amount of an Order exceeds this limit, then Siegfried shall have the right to demand a reasonable prepayment on a lump-sum basis.

6.3 All pricing, payments, credits, allowances or other monetary adjustments under this Agreement shall be in Swiss Francs (CHF), unless otherwise agreed in writing. If provided for in ANNEX B, the Parties shall adjust the price (up or down) upon written agreement with regard to (i) documented Raw Material price increases, (ii) changes in relevant indices, (iii) exchange rate variations, and (iv) as otherwise set forth in ANNEX B, subject to this Section 6.

6.4 In case any undisputed invoices are not paid in accordance with such terms of payment, then ITI shall pay interest at an annual rate of [***]% on the amount of the late sum (from original due date until the late sum is paid).

6.5 ITI shall pay any and all taxes, duties, assessments and other charges and expenses imposed by any Governmental Authority in connection with delivery of the Product and the other services provided to ITI and payments made by ITI under this Agreement.

6.6 All payments made to Siegfried pursuant to this Agreement shall be (i) made by wire transfer and (ii) are non-refundable and the expiration or termination of this Agreement shall not relieve ITI of its obligation to pay any outstanding balances due.

6.7 Shortage of Supply: In the event of any shortage in the availability or supply of Raw Materials that Siegfried orders under section 3.1 of this Agreement and utilizes both in connection with the Manufacture of the Product and in connection with the production of other pharmaceutical products for third parties, Siegfried shall use commercially reasonable efforts to allocate equitably such Raw Materials among ITI and such third parties.

7. Regulatory Affairs

7.1 ITI shall be solely responsible for all regulatory filings for the Product and End Market Product. All information, documents and updates with regard to the Manufacture of Product which are in the possession of Siegfried and required by any Governmental Authority shall, as reasonably requested by ITI in connection with such submissions and filings, be provided by Siegfried, at ITI's cost, to ITI or to the Governmental Authority, if requested by ITI.

7.2 Siegfried shall further provide ITI, at ITI's requests, costs and expenses, with reasonable assistance in preparing or reviewing regulatory submissions or formulating responses to

any questions and/or inquiries (i.e., deficiency letters) with respect to the above submissions. Without limiting the foregoing, Siegfried shall provide to ITI directly all information as ITI may reasonably require for purposes of applying for and maintaining Regulatory Approval, and Siegfried hereby allows ITI to provide such information to a Governmental Authority as necessary to support any application for authorization to conduct clinical trials or Regulatory Approval of a Product or in response to the requests or requirements of such Governmental Authority, provided however that ITI shall take appropriate steps to limit the disclosure of Siegfried's Confidential Information to the extent necessary to accomplish the purpose. ITI shall be responsible for preparing all submissions to Governmental Authorities with respect to the Product. Siegfried will assist ITI with all regulatory matters relating to Product, at ITI's request and expense. The parties intend and commit to cooperate to allow each party to satisfy its regulatory obligations under Applicable Laws relating to performance of this Agreement.

7.3 ITI shall provide, and Siegfried shall review those portions of ITI's proposed regulatory submissions relating to Siegfried's Manufacturing procedures or otherwise related to Siegfried's key obligations hereunder before the submissions are filed with relevant Governmental Authorities and ITI shall consider Siegfried's comments relating to the accuracy thereto in good faith.

7.4 The Parties acknowledge that the ultimate decision of whether any End Market Product will be approved for marketing and sale rests with the Governmental Authorities of the respective market in the Territory and that Siegfried shall not be liable for the failure of the Governmental Authorities to issue such approval. Accordingly, Siegfried makes no warranties or does not in any way guarantee that the Governmental Authorities approves any regulatory filing and any or all of the End Market Products for marketing and sale in any given market in the Territory for the treatment of any or all of the indications listed in any regulatory filing.

8. Confidential Information

8.1 Each Receiving Party agrees to retain in strict confidence any Confidential Information of the Disclosing Party (or its Affiliate), whether disclosed prior to, or after the Effective Date or the date of prior agreements and not to use any such Confidential Information for any purpose except pursuant to, and in order to carry out, the terms and objectives of this Agreement, and not to disclose, divulge or otherwise communicate any such Confidential Information to any third party.

8.2 The Receiving Party may disclose Confidential Information of the Disclosing Party to the Receiving Party's (and its Affiliate's) officers, directors, employees, agents, consultants, licensees, representatives or (for Siegfried, permitted) subcontractors (each an **Entitled Person**), who, in each case, (i) need to know such information for purposes of the

implementation and performance by the Receiving Party of this Agreement, and (iii) are subject to confidentiality restrictions covering the Confidential Information that are at least as stringent at those contained in this Section 8. The Receiving Party is liable and responsible for such Entitled Persons' compliance with the terms of this Section 8.

8.3 The provisions of this Section 8 shall not apply to any Confidential Information disclosed hereunder which (a) was independently developed or known by the Receiving Party prior to its disclosure to the Receiving Party by the Disclosing Party, as evidenced by the Receiving Party's written or electronic records kept in the ordinary course of its business; or (b) was before or after the date of such disclosure in the public domain, other than through the Receiving Party's fault or breach; or (c) is lawfully disclosed to the Receiving Party by an independent, unaffiliated third party rightfully in possession of the Confidential Information and not under any confidentiality obligation towards the Disclosing Party with regard to such Confidential Information. The fact that any portion of the Confidential Information may be subject to one of the foregoing exceptions (a) through (c) shall not automatically exclude any combination of Confidential Information from protection under this Agreement unless the entirety of such Confidential Information also falls under the same exception(s). Specific information disclosed as part of the Confidential Information shall not be deemed to be in the public domain or in prior possession of the Receiving Party merely because it is included in more general information in the public domain or in the prior possession of the Receiving Party.

8.4 The Receiving Party may disclose the Disclosing Party's Confidential Information to the extent such Confidential Information is required to be disclosed by the Receiving Party to the officials of a Governmental Authority or to comply with Applicable Laws, to defend or prosecute litigation, or to comply with judicial orders or valid subpoenas, provided that the Receiving Party provides prior written notice of such intended disclosure to the Disclosing Party and takes reasonable and lawful actions to avoid and/or minimize the degree of such disclosure, and reasonably assists the Disclosing Party in its efforts (if any) to oppose such disclosure. The burden of proof of the foregoing exceptions shall lie with the Receiving Party.

8.5 Except as otherwise provided for in this Agreement, nothing herein shall be construed as giving either Party any right, title or interest in or ownership of the Confidential Information of the other Party.

8.6 The Parties acknowledge that any breach of this Section 8 will cause irreparable harm and damage for which monetary damages may be difficult to ascertain, or may not be an adequate remedy, and that the non-breaching Party shall be entitled to specific performance or injunctive relief to enforce this Section 8 or to prevent a breach of this Section 8, in addition to whatever remedies such Party may otherwise be entitled to at law or in equity.

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Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

8.7 Upon termination or expiration of this Agreement, or at any other time during the term of the Agreement upon the other Party's written request, provided that it does not prevent the Receiving Party from performing its obligations under this Agreement, each Party shall immediately deliver to the other Party (and cause any of its Entitled Persons to so deliver), at such Party's expense, all Confidential Information of the other Party in such Party's possession or control, including without limitation any and all copies, duplications, summaries and/or notes thereof or derived thereof, regardless of the format, and Siegfried shall return to ITI all remaining samples of Product, provided however, that both Parties may keep original documents, copies and samples as required by law or for archival purposes (all of which shall continue to be subject to the terms of this Section 8).

9. Intellectual Property

9.1 Subject to Section 9.5, and unless otherwise required by law or specified in writing, the results of the Manufacture performed pursuant to and during the term of this Agreement, including, but not limited to, any Intellectual Property Right(s) arising out of any Improvements (other than an Independent Improvement) shall be the property of ITI and all rights, title and interest therein shall be vested in ITI. Siegfried shall have no responsibility for prosecuting, maintaining and enforcing any patents or other Intellectual Property Rights that ITI obtains pursuant to this Agreement.

9.2 Siegfried shall assign and hereby irrevocably assigns to ITI all title and interest Siegfried and its Affiliates and its permitted subcontractors may have in any Intellectual Property Right(s) arising out of any Improvements (other than an Independent Improvement).

9.3 ITI shall have the sole right to file and seek protection for any Intellectual Property Right(s) arising out of any Improvements (other than an Independent Improvement). To the extent that ITI deems it reasonable to seek protection for, ITI shall bear the costs (including, but not limited to attorney's fees) and the responsibility associated with developing, applying for, and maintaining such protection as may be granted. In the event ITI decides to file and prosecute patent applications on any Improvement (other than an Independent Improvement), Siegfried shall provide ITI with reasonable assistance to obtain and defend such patents at ITI's costs and expenses.

9.4 During the term of this Agreement and for a period of [***] thereafter, upon request by ITI, and at ITI's expense, Siegfried shall promptly execute, acknowledge and deliver any papers reasonably deemed necessary by ITI to document, protect, or otherwise perfect such rights of ITI, including, without limitation, all documents necessary to obtain or perfect any protection of Intellectual Property Rights and/or to effect an assignment of ownership of the same to ITI, at ITI's cost and expenses.

NC	MH
Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

9.5 All rights related to any Independent Improvements shall be the sole property of Siegfried. Upon ITI's request, Siegfried shall grant and hereby grants ITI a non-exclusive, worldwide, irrevocable, royalty-free license to use Independent Improvements to the extent that, and limited to, the manufacturing, sale, commercialization or any other use of the Product is dependent upon such license.

10. Term and Termination

10.1 This Agreement shall become effective on the Effective Date and, unless earlier terminated in accordance with this Section 10, shall continue in full force and effect for five (5) years.

10.2 Either Party may terminate the Agreement immediately, [***] after becoming aware of such event, by providing written notice to the other Party upon the occurrence of any of the following events:

(a) the liquidation or dissolution of the other Party, or the commencement of insolvency procedures or any proceeding under any bankruptcy, insolvency or moratorium law, or any other law or laws for the relief of debtors which proceeding is not dismissed within ninety (90) days, or the appointment of any receiver, trustee or assignee to take possession of the properties of the other Party; or

(b) the cessation of all or substantially all of the other Party's business operations.

10.3 If a Party breaches a material term or condition of this Agreement, the non-breaching Party shall have the right to terminate this Agreement [***] prior written notice to the other Party unless any such breach is cured within [***]. Termination shall be in addition to all other rights and remedies available to the non-breaching Party at law or in equity.

10.4 Termination of this Agreement shall automatically terminate each outstanding Order unless ITI instructs Siegfried to fulfill such Order. Neither the expiration nor the termination of this Agreement shall relieve the Parties of their rights or obligations incurred prior to such expiration or termination. All provisions that, by their express or implied terms, are meant to survive termination of the Agreement, in particular all rights and obligations set forth in Sections 6 (Compensation and Terms of Payment), 8 (Confidential Information), 9 (Intellectual Property), 10.5, 12 (Liability and Indemnity), 13 (Miscellaneous) and 14 (Applicable Law and Dispute Resolution) shall continue irrespective of such termination.

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Siegfried	ITI

11. Representations and Warranties

11.1 Each Party represents and warrants to the other Party:

(i) that such Party has the legal power, authority and right to enter into this Agreement and to perform its obligations set forth herein,

(ii) It has and shall have throughout the term of the Agreement the required expertise, permits and approvals to perform its obligations under the Agreement.

(iii) that this Agreement has been duly executed and delivered by such Party and constitutes the valid and binding obligation of such Party, enforceable against such Party in accordance with its terms,

(iv) that it is not and will not become a party to any agreement, contract, arrangement or the like with any third party, which in any way limits or conflicts with its ability to fulfill any of its obligations under this Agreement,

(v) that it is not and will not be under any obligation or restriction, including, without limitation, pursuant to its charter document(s) or by-laws, which in any way limits or conflicts with its ability to fulfill any of its obligations under this Agreement, and

(vi) that such Party nor, to its knowledge, any of its employees, affiliates or agents has been (a) debarred or (b) convicted of a crime for which a person can be debarred, under Section 335(a) or 335(b) of the Act, and such Party represents that it has never been and, to its knowledge, none of its employees, affiliates, or agents has ever been (y) threatened to be debarred under the Act or (z) indicted for a crime or otherwise engaged in conduct for which a person can be debarred under the Act; such Party shall promptly notify the other Party if it receives notification of any such debarment, conviction, threat or indictment, in which case the other Party may terminate this Agreement upon notice and without liability.

11.2 Siegfried represents and warrants that:

(a) Each Product will conform in all respects to the Requirements at the time of its release.

(b) Each Product, when delivered to ITI, will not be adulterated, misbranded, or otherwise prohibited from sale within the meaning of the Act or Applicable Laws.

(c) It will procure, maintain and comply with all non-Product-specific licenses, permits, certifications and approvals required under Applicable Law for the Facility, and the portion of Facility used to Manufacture Product.

(d) It and the Facility are registered with all applicable Regulatory Authorities pursuant to and in accordance with all Applicable Laws.

Siegfried will provide ITI with prompt written notice of any facts or circumstances (whether occurring prior to or after the Effective Date) which cause any of the representations and warranties contained in this Section 11.2 not to be true, accurate, and complete in any material respect as of the Effective Date or as of any date during the term of this Agreement.

11.3 ITI warrants that (i) all quantities of Consigned Material, if any, delivered to Siegfried shall be free from defects and, if applicable, conform to the Specifications of such Consigned Material and (ii) except as set out otherwise in any particular Order, none of the processes, procedures, substances or materials, including any Consigned Material, supplied by ITI or its designee and used by Siegfried in the performance of the Services or the Manufacture of Product infringes or misappropriates or will infringe or misappropriate the Intellectual Property Rights of any third party.

ITI will provide Siegfried with prompt written notice of any facts or circumstances (whether occurring prior to or after the Effective Date) which cause any of the representations and warranties contained in this Section 11.3 not to be true, accurate, and complete in any material respect as of the Effective Date or as of any date during the term of this Agreement.

11.4 EXCEPT AS EXPRESSLY WARRANTED IN THIS AGREEMENT, SIEGFRIED AND ITI EXTEND NO OTHER WARRANTIES OR REPRESENTATIONS COVERING THE PRODUCT OR MATERIALS OR RELATING TO THIS AGREEMENT, EXPRESS OR IMPLIED, AND EACH PARTY EXPRESSLY DISCLAIMS ALL IMPLIED WARRANTIES, INCLUDING THE WARRANTY OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. EITHER PARTY'S LIABILITY UNDER THIS AGREEMENT SHALL BE STRICTLY LIMITED TO THE REMEDIES PROVIDED FOR UNDER THIS AGREEMENT.

12. Liability and Indemnity

12.1 If Siegfried is unable to meet the agreed time lines regarding the delivery of Product, or in case the Product is rightfully rejected by ITI in accordance with Sections 4.2 or 4.3 of this Agreement, Siegfried shall either (i) promptly deliver the delayed Product, or replace the rejected Product with Product that conforms with the Specifications as soon as possible, in each case at no additional cost to ITI (including reasonable costs of purchasing additional Consigned Materials, if necessary but only to the extent such costs are consistent with the costs usually borne by ITI for the supply of the Consigned Materials) or (ii) if delivery of conforming Product is not possible within reasonable additional time, refund to ITI within [***] all amounts theretofore paid by ITI to Siegfried

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Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

for such late or rejected Product. Except in the case of Siegfried's gross negligence or willful misconduct such delivery, replacement or refund shall be the only remedy available to ITI in case of late deliveries or Product not conforming to the Specifications.

12.2 Siegfried shall indemnify, defend and hold ITI, its directors, officers, employees and Affiliates, harmless against losses, damages, costs and expenses (including reasonable attorneys' fees) alleged by a third party in a claim, action, demand or proceeding brought against any of the foregoing persons or entities to the extent arising out of the breach of any of Siegfried's obligations, warranties and representations under this Agreement, except to the extent such claims, actions, demands or proceedings are caused by ITI's negligence or willful misconduct.

12.3 ITI shall indemnify, defend and hold Siegfried, its directors, officers, employees and Affiliates harmless against losses, damages, costs and expenses (including reasonable attorneys' fees) alleged by a third party in a claim, action, demand or proceeding brought against any of the foregoing persons or entities to the extent arising out of (i) the breach of any of ITI's obligations, warranties and representations under this Agreement, (ii) the death of or injury to any person or any damage to property, resulting from side effects, characteristics or defects of the Product and/or End Market Product, or (iii) the infringement of any third party's Intellectual Property Rights based upon the manufacture, use or sale of the Product; except in each case to the extent such losses are caused by Siegfried's negligence or willful misconduct.

12.4 With respect to any indemnification obligation under this Agreement, the following conditions shall be applicable:

(a) The Party seeking to be indemnified shall notify the indemnifying Party promptly in writing of any claim which may give rise to an obligation on the part of the indemnifying Party under this Section 12; provided, however, that failure to promptly notify shall not excuse the indemnifying Party from its obligations under this Section unless such failure materially prejudices its ability to defend the claim; and

(b) the indemnifying Party shall be allowed to timely take the sole control of the defense of any such action and claim, including all negotiations for the settlement, or compromise of such claim or action at its sole expense; and

(c) the Party to be indemnified shall, at the expense of the indemnifying Party, render reasonable assistance, information, co-operation and authority to permit the indemnifying Party to defend such action; and

(d) no settlement or compromise shall be binding on the indemnifying Party hereto without its prior written consent.

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The indemnified Party may participate in the defense of the claim with independent counsel at its own expense.

12.5 During the term of this Agreement, Siegfried and ITI shall each obtain and carry in full force and effect adequate commercial, general liability insurance as common in the industry, including product liability insurance. Such insurance shall be written by a reputable insurance company and shall be endorsed to include product liability coverage. A Party shall provide another Party on request with a copy of certificates of insurance evidencing the same.

12.6 NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR INCIDENTAL, INDIRECT, OR CONSEQUENTIAL DAMAGES OF THE OTHER PARTY, INCLUDING BUT NOT LIMITED TO CLAIMS BASED ON LOST PROFITS, LOSS OF TIME, LOSS OF OPPORTUNITY OR ANY OTHER ECONOMIC LOSS SUFFERED OR INCURRED AS A RESULT OF THIS AGREEMENT, WHETHER SUCH LOSS OR DAMAGE MAY BE BASED UPON PRINCIPLES OF CONTRACT, WARRANTY, NEGLIGENCE OR OTHER TORT, BREACH OF ANY STATUTORY DUTY, PRINCIPLES OF INDEMNITY OR CONTRIBUTION, OR THE FAILURE OF ANY LIMITED OR EXCLUSIVE REMEDY TO ACHIEVE ITS ESSENTIAL PURPOSE OR OTHERWISE.

12.7 [***].

12.8 SECTION 12.6 AND SECTION 12.7 SHALL NOT APPLY, FOR DAMAGES CAUSED BY A PARTY'S BREACH OF SECTION 8, DAMAGES CAUSED BY A PARTY'S WILLFUL MISCONDUCT OR GROSS NEGLIGENCE, FOR DEATH OR PERSONAL INJURY RESULTING FROM NEGLIGENCE, OR FOR FRAUD.

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Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

13. Miscellaneous

13.1 *No set-off.* Neither Party shall be entitled to set off any of its rights or obligations under this Agreement against the rights or obligations of another Party without having first obtained the prior written consent of that other Party.

13.2 *Force Majeure*. A Party shall be excused from performing its obligations under this Agreement (other than obligations of payment) to the extent that its performance is delayed or prevented by any unforeseeable cause beyond such Party's reasonable control and not due to such Party's negligence, which may include, but is not limited to, Act of God, fire, explosion, weather, disease, war, insurrection, civil strike, riots, government action power failure or energy shortages (**Force Majeure Event**). Performance shall be excused only to the extent of and during the reasonable continuance of such disability. Any deadline or time for performance specified in this Agreement that falls due during or subsequent to the occurrence of any of the disabilities referred to herein shall be automatically extended for a period of time equal to the period of such disability. The prevented Party shall immediately notify the other Party if, by reason of any Force Majeure Event affecting its performance of this Agreement. In the event that such Force Majeure Event prevents or delays a Party's performance for [***] or more, then the non-prevented Party may at any time after the expiration of such period, by written notice to the other Party, either (i) suspend this Agreement for as long as such Force Majeure Event continues to exist, or (ii) terminate this Agreement with immediate effect; in each case without liability for either Party.

13.3 *Precedence of Agreement*. Unless expressly agreed otherwise in writing, the terms outlined in this Agreement shall prevail over any terms and conditions outlined in any Order or Order Confirmation for Product and any general terms and conditions of a Party, and such terms and conditions are hereby expressly excluded. In case of discrepancies between this Agreement and an Annex hereto, the provisions of this Agreement shall prevail. In the event of a conflict between any of the provisions of this Agreement and the Quality Agreement with respect to quality-related activities, including compliance with cGMP Regulations, the provisions of the Quality Agreement shall govern. In the event of a conflict between any of the provisions of this Agreement and the Quality Agreement with respect to any commercial matters, including allocation of risk, liability and financial responsibility, the provisions of this Agreement shall govern.

13.4 *No assignment*. This Agreement is binding upon and shall inure to the benefit of the Parties hereto and their successors and permitted assigns. This Agreement and any rights or obligations hereunder may be assigned or delegated only (i) with the consent of the other Party, not to be unreasonably withheld, conditioned or delayed, or (ii) to the

successor to all or substantially all of the business of a Party (whether by merger, consolidation, asset transfer or similar transaction) to which this Agreement relates, or (iii) to an Affiliate of such Party, or (iv) by ITI to a successor to the Product. Any other assignment or delegation by either Party without the prior written consent of the other Party is void.

13.5 *No waiver*. The failure by either Party at any time to enforce any of the terms, provisions or conditions of this Agreement or to exercise any right hereunder shall not constitute or be construed to constitute a waiver of the same or affect that Party's rights thereafter to enforce or exercise the same. A waiver by a Party of any term or condition of this Agreement must be in writing to be effective.

13.6 *Independent Parties*. Nothing in this Agreement shall be deemed or construed to constitute or create between the Parties hereto a partnership, joint venture, agency, or other relationship other than as expressly set forth herein. Neither Party shall be responsible for the acts or omissions of the other Party, and neither Party shall have authority to speak for, represent or obligate the other Party in any way without prior written consent of the other Party.

13.7 *Entire Agreement*. This Agreement (together with the Quality Agreement) contains the full understanding of the Parties with respect to the subject matter hereof and supersedes all prior understandings and writings relating thereto. No alteration or modification of any of the provisions hereof shall be binding unless made in writing and signed by the Parties.

13.8 *Severability*. If any portion of this Agreement is held invalid by a court of competent jurisdiction, such portion shall be deemed to be of no force and effect and this Agreement shall be construed as if such portion had not been included herein, provided however, if the deletion of such provision materially impairs the commercial value of this Agreement to either Party, the Parties shall attempt to renegotiate such provision in good faith. The fact that any provision of this Agreement shall be prohibited or unenforceable in any jurisdiction shall not invalidate or render unenforceable such provision in any other jurisdiction. To the extent permitted by applicable law, the Parties to this Agreement waive any provision of law that renders any provision of this Agreement prohibited or unenforceable in any respect.

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Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

13.9 *Notices* . Any notice required under this Agreement shall be effective only if it is in writing and (i) delivered in person or (ii) deposited with an internationally recognized overnight courier service, or (iii) dispatched by an acknowledged e-mail (pdf), in which case such notice is to be confirmed by one of the alternate means within five (5) Business Days; in either case any notice is to be addressed to the applicable address set forth below.

if to Siegfried	**Siegfried Evionnaz SA** Route du Simplon 1, 36, 1902 Evionnaz, Switzerland Attention: [***] Email: [***].
with a copy to:	**Siegfried AG** Untere Brühlstrasse 4, 4800 Zofingen, Switzerland Legal Department Email: [***]
if to ITI:	ITI Limited Clarendon House, 2 Church Street, PO Box HM 666, Hamilton, HM CX, Bermuda Attention: Michael Halstead Email: [***]

Either Party may change its above addresses, but no such change shall have any effect until the other Party has been properly notified with written notice of the change of the address.

13.10 *Compliance with Laws.* Each Party shall comply with all Applicable Laws governing its performance of the terms of this Agreement, including, but not limited to, those relating to health, safety and the environment, fair labor practices, unlawful discrimination, debarment, anti-corruption and anti-bribery laws.

13.11 *Hardship.* If during the term of this Agreement, the performance of the Agreement should lead to unreasonable hardship for the one or the other Party, both Parties shall undertake reasonable endeavors to discuss a possible amicable resolution or possible amendment to this Agreement in light of the change in circumstances; provided, however, that neither Party shall have any obligation to amend this Agreement or to waive or modify any of its rights under this Agreement.

14. Applicable Law and Dispute Resolution

14.1 This Agreement shall be governed by New Jersey law without regard to its conflict of laws provisions, and the provisions of the UN-Convention regarding Contracts on the International Sale of Goods (Vienna Convention) are expressly excluded.

14.2 All disputes arising out of or in connection with this Agreement, including disputes on its conclusion, binding effect, amendment or termination, shall be resolved exclusively by the courts of New Jersey.

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Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

List of Annexes

Annex	Description	Content
A	Product, Specifications	Details and technical description of Product
B	Commercial terms	Sales prices and other commercial terms for Product
C	Materials	Description of Raw Materials and Consigned Materials

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Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

In Witness Whereof, the Parties have executed this Agreement as of the Effective Date.

Siegfried Evionnaz SA

/s/ T. Rouillet
T. Rouillet, Quality Director

Name / function

/s/ N. Chappot
N. Chappot, Head of Finance

Name / function

Siegfried Evionnaz SA
Route du Simplon 1, 36
CH - 1902 Evionnaz

ITI Limited

/s/ Sharon Mates

Name / function Share Mates/CEO

/s/ Michael Halstead

Name / function Michael Halstead/
General Counsel

NC
Siegfried

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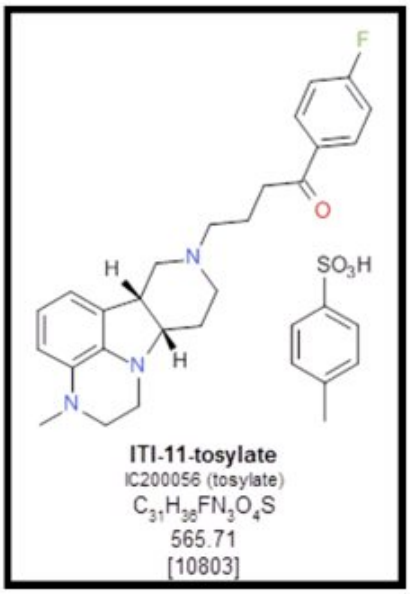
ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

ANNEX A

Product and Specification

Product: ITI-007



Specification: as set forth in the Quality Agreement

NC	MH
Siegfried	ITI

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ANNEX B

Commercial Terms

Scope:	Post-validation of ITI-007 (Siegfried Code: ITI-11 tosylate). Manufacture will be carried out in Siegfried's GMP facility in [***] based on the process as demonstrated in Siegfried's 2015 campaign.
Delivery terms:	FCA Siegfried Manufacturing facility in [***] (as per Incoterms 2010, made a part hereof by reference).
Payment:	Undisputed Invoices are payable net without discount within [***] after the receipt of invoice.
Costs:	

Post Validation Commercial Production Cost Indications

- The following price indications are provided based on the production of ITI-007 using the same yield and batch size validation assumptions as described above.
- The cost indications for milling are provided separately as these costs will have to be confirmed following the validation campaign.

Volume	Total ($/kg)	Manufacturing ($/kg)	Raws ($/kg)
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]

Milling	Total ($/kg)
[***]	[***]
[***]	[***]

NC	MH
Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Future Cost Savings Opportunities

- If the volumes grow to exceed [***] a complementary validation can be considered to increase the batch sizes, which would reduce the price and shorten the production lead-times. Two potential options include:

  1. [***].

  - [***]

  2. [***].

NC	MH
Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

ANNEX C

Materials

Raw Materials:

Raw Materials have an overall anticipated lead-time of [***].

Consigned Materials:

The key starting material [***] (Siegfried Code: [***]) will be provided by ITI free of charge and delivered at least [***] prior to the start of the respective campaign.

NC	MH
Siegfried	ITI

Portions of this Exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Exhibit 21.1

Subsidiaries

ITI, Inc., a Delaware corporation

ITI Limited, a Bermuda company

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-213495) of Intra-Cellular Therapies, Inc.,

(2) Registration Statement (Form S-8 No. 333-205070) of Intra-Cellular Therapies, Inc. pertaining to the Intra-Cellular Therapies, Inc. Amended and Restated 2013 Equity Incentive Plan,

(3) Registration Statement (Post-Effective Amendment No. 3 to Form S-1 on Form S-3 No. 333-191238) of Intra-Cellular Therapies, Inc., and

(4) Registration Statement (Form S-8 No. 333-193310) of Intra-Cellular Therapies, Inc. pertaining to the ITI, Inc. 2003 Equity Incentive Plan, as amended, and the Intra-Cellular Therapies, Inc. Amended and Restated 2013 Equity Incentive Plan;

of our reports dated March 1, 2017, with respect to the consolidated financial statements of Intra-Cellular Therapies, Inc. and the effectiveness of internal control over financial reporting of Intra-Cellular Therapies, Inc. included in this Annual Report (Form 10-K) of Intra-Cellular Therapies, Inc. for the year ended December 31, 2016.

/s/ Ernst & Young LLP

Baltimore, MD
March 1, 2017

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

I, Sharon Mates, Ph.D., certify that:

1. I have reviewed this annual report on Form 10-K of Intra-Cellular Therapies, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2017

/s/ Sharon Mates, Ph.D.

Sharon Mates, Ph.D.
Chairman, President and Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Lawrence J. Hineline, certify that:

1. I have reviewed this annual report on Form 10-K of Intra-Cellular Therapies, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2017

/s/ Lawrence J. Hineline

Lawrence J. Hineline
Vice President of Finance and Chief Financial Officer
(principal financial officer and principal accounting officer)

Exhibit 32.1

CERTIFICATIONS UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Intra-Cellular Therapies, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2016 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 1, 2017

/s/ Sharon Mates, Ph.D.

Sharon Mates, Ph.D.
Chairman, President and Chief Executive Officer
(principal executive officer)

Dated: March 1, 2017

/s/ Lawrence J. Hineline

Lawrence J. Hineline
Vice President of Finance and Chief Financial Officer
(principal financial officer and principal accounting officer)