

2013 ANNUAL REPORT

Included in the 2013 Annual Report:

Form 10-K filed with the U.S. Securities and Exchange Commission on February 28, 2014 (without exhibits)



6320 Quadrangle Drive, Suite 360 Chapel Hill, NC 27517

To the Shareholders of Cempra:

I believe Cempra is well-positioned to transition from late clinical stage to initiating commercialization activities in 2014, following a transformational and event-filled year of solid execution and advancement in 2013. Over the past year we have achieved several significant milestones and propelled our company into late-stage clinical development while strengthening our financial position.

Solithromycin is a novel, potent, and well tolerated macrolide antibiotic that has advanced to Phase 3 clinical trials: Solitaire-Oral, the first global Phase 3 study of solithromycin in community-acquired bacterial pneumonia (CABP) patients and Solitaire-IV, our global solithromycin intravenous (IV)-to-oral Phase 3 clinical trial, in patients with CABP. In addition, we further characterized solithromycin's activity and safety profiles. We presented positive results of a Phase 2 gonorrhea study, which showed 100% efficacy. We also announced promising safety data through a hepatic insufficiency study, in which solithromycin was well tolerated, and, in early 2014, a Thorough QT study, where solithromycin demonstrated no effect on the Q-T interval.

We signed an exclusive license and development agreement for solithromycin in Japan with Toyama Chemical Co., Ltd. (Fujifilm subsidiary). Cempra received an upfront payment of \$10 million, and could receive up to \$60 million in milestone payments based on the achievement of certain objectives. We were also awarded a five-year contract with the Biomedical Advanced Research and Development Authority (BARDA), valued at up to \$58 million if all options are authorized by BARDA, for the development of solithromycin for pediatric use in all dosing regimens, intravenous, capsules and pediatric suspension. This is the first novel oral suspension in development in over 20 years. BARDA funds are also directed toward studying solithromycin for the treatment of infections by bioterror threat pathogens. Finally, we completed a public offering of Cempra's common stock from which we raised approximately \$54.2 million after fees.

We also made progress with Taksta which is currently enrolling a Phase 2 trial for prosthetic joint infections (PJI), an indication that has been granted orphan drug designation by the FDA in 2013.

A Year of Significant Achievement

In 2013, we successfully advanced our solithromycin and Taksta clinical programs:

Solithromycin: We are very excited about solithromycin's broad potential. As a 4th generation macrolide, it represents significant potential for use in a number of large indications with urgent need. It has the right spectrum of activity to compete in the hospital and community setting, it is to be available in multiple dosage formulations and the safety profile to date is very promising. We are also encouraged with solithromycin's emerging potent anti-inflammatory activity, which is a property of the macrolide class, and its potential for use beyond anti-infection.

- In February 2013, the National Institute of Allergy and Infectious Diseases (NIAID) awarded a grant to Richard C. Boucher, M.D., Kenan Professor of Medicine and director of the Cystic Fibrosis and Pulmonary Research and Treatment Center at the University of North Carolina School of Medicine, to investigate the anti-inflammatory activity of solithromycin and its effect on mucin secretion in models for CF.
- In April 2013, we presented Phase 2 data at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Berlin, demonstrating solithromycin's potential to treat gonorrhea infections in all patients treated in the clinical trial.
- In May 2013, we presented data at the American Thoracic Society International Conference (ATS 2013) demonstrating the antibacterial and enhanced immunomodulatory activity of solithromycin versus levofloxacin in Cempra's prior Phase 2 clinical trial in outpatients with CABP.
- In September 2013, we announced that solithromycin demonstrated safety and tolerability in a hepatic insufficiency study of 24 patients with chronic liver disease. An important finding was that these patients did not require dose adjustments to obtain appropriate blood levels of solithromycin.
- In November 2013, we announced results of an *in vivo* preclinical study suggesting that solithromycin may provide an effective antimicrobial approach for the prevention and treatment of intrauterine infections during pregnancy. Currently, these patients have few treatment options.
- In 2013, the FDA granted solithromycin two Qualified Infectious Disease Product (QIDP) designations, one for the oral product and the second for the IV product for the indication of community-acquired bacterial pneumonia, allowing us to benefit from certain incentives for the development of new antibiotics, including priority review, and a five-year extension of new chemical entity (NCE) exclusivity. Early, in 2014 we obtained one more QIDP designation from the FDA for the oral capsule product for the treatment of gonorrhea.

Taksta: We are encouraged by the results we have seen to date from our Taksta Phase 2 study in PJI, as data are consistent with a positive effect of Taksta in this indication. Along with the very strong results from studies worldwide of fusidic acid in PJI, the active antibiotic of Taksta, the key learnings from the Phase 2 study will be applied to define the pivotal studies.

- In October 2013, the FDA granted orphan drug designation to Taksta for the treatment of PJI.
- In May 2013, the United States Patent and Trademark Office (USPTO) issued a patent with claims directed to the company's novel dosing regimen for Taksta.
- In December 2013, we provided a clinical update on the Phase 2 study in PJI.

Strong Financial Position

In 2013, we had \$4.3 million of revenue from our licensing agreement with Toyama and \$3.5 million of revenue from our work under our BARDA contract which helped to offset our expenses. We reported cash and equivalents of \$96.5 million as of December 31, 2013. The increase compared to December 31, 2012, was primarily due to proceeds from the public offering of common stock, the upfront payment from the Toyama agreement, payments for work under the BARDA contract and a \$5 million draw on a venture debt arrangement less operating expenses incurred during the year.

Looking Ahead and Moving Forward

We look forward to continuing the successful advancement of our two lead clinical-stage candidates and executing our business strategy in 2014 and beyond. We believe we are well-positioned to achieve our upcoming milestones, including the completion of SOLITAIRE-Oral Phase 3 patient enrollment in the fourth quarter of 2014 and reporting top-line data in the first quarter of 2015, as well as obtaining feedback from the FDA on the Phase 3 plan for Taksta.

On behalf of the Company and its Board of Directors, I thank our shareholders for their support as we move forward in building Cempra into a leading antibiotics company that will, hopefully, help diminish current problems with hospital acquired infections, allowing patients to switch to oral therapy and restore the quality of life to patients.

Sincerely,

Prabhavathi Fernandes, Ph.D.

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-K

	TO SECTION 13 OR 15(d) OF THE SECURIT For the fiscal year ended December 31, 2013	TIES EXCHANGE ACT OF 1934
☐ TRANSITION REPORT PURSU	ANT TO SECTION 13 OR 15(d) OF THE SEC	URITIES EXCHANGE ACT OF 1934
	For the Transition Period from to	
	Commission File Number: 001-35405	
	CEMPRA, INC.	
	(Exact name of registrant specified in its charter)	
Delaware (State or Other Jurisdiction of Incorporation or Organization)	2834 (Primary Standard Industrial Classification Code Number)	45-4440364 (I.R.S. Employer Identification No.)
	6320 Quadrangle Drive, Suite 360 Chapel Hill, NC 27517 (Address of Principal Executive Offices)	
	(919) 313-6601 (Telephone Number, Including Area Code)	
Securities	Registered Pursuant to Section 12(b) of the Exc	hange Act:
Title of Each Class	Name of	Exchange on which Registered
Common Stock, \$0.001 P	ar Value Na	sdaq Global Market
Secur	rities Registered Pursuant to Section 12(g) of the Act:	None
Indicate by check mark if the registrant is a we	ell-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 ⊠
	(1) has filed all reports required to be filed by Section 13 uch shorter period that the registrant was required to file No □	
	has submitted electronically and posted on its corporate of Rule 405 of Regulation S-T during the preceding 12 m in files). Yes ⊠ No □	
	uent filers pursuant to Item 405 of Regulation S-K is not itive proxy or information statements incorporated by respective proxy.	
	is a large accelerated filer, an accelerated filer, or a small d "smaller reporting company" in Rule 12b-2 of the Excl	
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 Exch	ange Act). Yes □ No ⊠
aggregate market value was computed by refer 2013. For purposes of making this calculation	k held by non-affiliates of the registrant, as of June 28, 20 rence to the closing price of the common stock as reported only, the registrant has defined affiliates as including only of the registrant as of June 28, 2013.	d on the Nasdaq Global Market on June 28,
As of February 20, 2014 there were 33,19	2,972 shares of the registrant's common stock, \$0.0	001 par value, outstanding.
DC	OCUMENTS INCORPORATED BY REFEREN	CE
	Proxy Statement for its 2014 Annual Meeting of Stockhol	

CEMPRA, INC.

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This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements are subject to risks and uncertainties, including those set forth under "Item 1A. Risk Factors" and "Cautionary Statement" included in "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this report, that could cause actual results to differ materially from historical results or anticipated results.

PART I

Item 1. Business

Summary

We are a clinical-stage pharmaceutical company focused on developing differentiated antibiotics for the acute care and community settings to meet critical medical needs in the treatment of bacterial infectious diseases, particularly respiratory tract infections and chronic staphylococcal infections. Our goal is to develop antibiotics with broad therapeutic potential and the right spectrum of activity to target pathogenic bacteria in adults and children. Broad therapeutic potential means addressing several disease indications. The right spectrum of activity means that, in addition to having activity against bacteria that have become resistant to many currently available antibiotics, the drug does not cause collateral damage to important bacteria such as intestinal microflora so that unintended side effects do not occur.

Our lead product, solithromycin (CEM-101), is in Phase 3 clinical trials. We are developing solithromycin in oral capsules, intravenous, or IV, and suspension formulations, initially for the treatment of community acquired bacterial pneumonia, or CABP, one of the most serious infections of the respiratory tract. Solithromycin is a potent new fourth generation macrolide and the first fluoroketolide in clinical development. As a macrolide, solithromycin has broad use potential against many types of infections and in many patient populations, including pediatrics and pregnancy. Solithromycin's potency comes from its unique chemical structure, which provides greater ability to fight resistant bacteria. Increasingly, resistance is a major threat to the efficacy of currently available antibiotics. Solithromycin has excellent organ and tissue distribution and intracellular activity, which allows it to reach bacteria at body sites that other antibiotics may not. Solithromycin is active against many key CABP pathogens as well as against pneumococcal strains resistant to other macrolides. Our prior pre-clinical and clinical studies have demonstrated the efficacy and safety of solithromycin. This record makes solithromycin a possible treatment for all age groups, including pediatrics. Finally, solithromycin offers flexibility of dosing, whether IV or oral, which we believe will be attractive to both physicians and patients.

We are conducting two Phase 3 trials which we believe will support our planned new drug application, or NDA, for solithromycin to treat CABP: one trial with oral solithromycin, which we initiated in December 2012, and another with IV solithromycin progressing to oral solithromycin that we began in December 2013. This development program was structured through the draft guidance published by and dialogue with the U.S. Food and Drug Administration, or FDA. We also have received feedback from several European Union, or EU, member countries regarding our plan to submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, within a short period of time after our planned filing of the NDA for solithromycin with the FDA.

We also are pursuing the development of solithromycin as a treatment for pediatric populations suffering from CABP and other respiratory infections as well as other infections. There is an urgent need for a new antibiotic for use in pediatric infections. The Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human Services, or BARDA, is funding the development of oral, IV and suspension formulations of solithromycin for pediatric use in bacterial pneumonia. Solithromycin is the first new antibiotic being developed as a suspension for all pediatric age groups in over 20 years.

In addition to CABP, we are pursuing a second indication, uncomplicated bacterial urethritis, primarily *Neisseeria gonorrheae* and *Chlamydia trachomatis*, for which there is an urgent public health need. In this indication, our Phase 2 study demonstrated that solithromycin was highly effective in treating uncomplicated gonorrhea, with successful treatment of all 43 evaluable patients.

BARDA also is funding studies to test the efficacy of solithromycin in treating bioterror pathogens such as tularemia and anthrax. These tests are being conducted in non-human primates, based on which we expect to conduct pilot studies in 2014.

We have global rights (other than the Association of South East Asian Nations, or ASEAN, countries, which are Brunei Darussalam, Cambodia, Indonesia, Laos, Malaysia, Myanmar (Burma), the Philippines, Singapore, Thailand and Vietnam) to solithromycin. We have licensed solithromycin to Toyama Chemical Co., Ltd., or Toyama, for development and commercialization in Japan while retaining the rights to the rest of the world. Toyama has initiated Phase 1 studies in healthy Japanese volunteers. After these studies are completed, Toyama plans to conduct Phase 2 studies in other respiratory tract infections. Toyama and we are sharing the results of our respective development activities.

The FDA has designated each of oral and intravenous solithromycin as a Qualified Infectious Disease Product, or QIDP, for the indication of CABP, and also has designated the oral form as a QIDP for the treatment of uncomplicated gonococcal infections. The QIDP designation is expected to enable us to benefit from certain incentives for the development of new antibiotics, including priority review, and a five-year extension of new chemical entity, or NCE, exclusivity.

Our second product is Taksta, an antibiotic known as fusidic acid, that has been used for decades outside the U.S., including western Europe, but which has never been approved in the U.S. We are developing Taksta exclusively in the U.S. as a long term oral treatment of prosthetic joint infections, or PJI, caused by staphylococci, including *S. aureus* and methicillin-resistant *Staphylococcus aureus*, or MRSA. Currently, there is no oral, chronic antibiotic for treating these infections. We hope to develop Taksta as an oral treatment with the same efficacy of currently available IV drugs but with the safety and convenience of oral administration. Taksta successfully completed a Phase 2 clinical trial in patients with acute bacterial skin and skin structure infections, or ABSSSI, which is frequently caused by MRSA, demonstrating a tolerability profile and comparable efficacy to linezolid (sold under the brand name Zyvox®), the only oral antibiotic currently approved for the treatment of MRSA approved by the FDA. Having shown that Taksta is well tolerated and is active against current strains of MRSA in the U.S., in December 2012, we initiated a Phase 2 trial with Taksta for the treatment of primarily stapylococcal infections of infected prosthetic joint infections, hip and knee joints. Currently, there are 14 active sites in the U.S. and additional sites are expected. We designed a Phase 2 study with a clear end point comparing vancomycin, which is the standard of care, with oral fusidic acid and rifampin. There is no FDA guidance on the design of PJI trials and also no FDA-approved antibiotic for this indication. Although the Phase 2 trial continues to enroll, we believe we have met our primary objectives of a Phase 2 trial, namely safety and efficacy, to determine the study design and dose of our planned Phase 3 trial.

In October 2013, the FDA granted orphan drug designation for fusidic acid for the treatment of PJI, which confers regulatory and economic benefits in the development process. In December 2013, PJI was classified as a very rare disease by the National Institutes of Health, or NIH. With these designations in hand, we have submitted a proposal for a Phase 3 trial for Tasksta as a treatment for PJI, which could lead to an NDA. If we receive concurrence from the FDA on the planned Phase 3 trial, we plan to stop the Phase 2 trial and roll into the Phase 3 trial.

Overview of Solithromycin (CEM-101)

Solithromycin is a potent new fourth generation macrolide, the first fluoroketolide, that we are developing in oral capsule, IV and suspension formulations (for pediatric use) for the treatment of respiratory tract infections, including CABP, which is one of the most common serious infectious diseases of the respiratory tract and the primary cause of death from an infection, and bacterial urethritis, including gonorrhea, the second most common reportable infectious disease in the world. Solithromycin is differentiated from other antibiotics because of its broad therapeutic potential and the right spectrum of activity to target pathogenic bacteria. Broad therapeutic potential means a drug that can be used in the treatment of several disease indications, such as bacterial pneumonia, chronic obstructive pulmonary disease, or COPD, cystic fibrosis, other respiratory tract infections, infections in children, infections caused by bacterial urethritis, *Helicobacter* gastritis, eye infections, infections in pregnancy, and others. Targeting the bacteria responsible for CABP and other respiratory infections without causing major effects on the intestinal microflora is a benefit of the macrolide class and solithromycin.

Macrolides, as a class, have been used broadly for treating respiratory and other infections in adults and children because of their excellent safety and efficacy profile. However, resistance to the older macrolides, like azithromycin (Zithromax, Z-Pak) is increasingly common, as high as 44% in the U.S. and 95% in some parts of Asia. A new macrolide which is active against resistant strains, while maintaining the safety of older macrolides, is needed. Solithromycin has the potency and spectrum to characterize it as a fourth generation macrolide. Solithromycin owes its potency to its unique chemical structure that binds to bacterial ribosomes in three sites while earlier generation macrolides bind in only one or two sites on the ribosome. Therefore, bacteria must mutate at three sites on the ribosome to become resistant to solithromycin. To date, we have seen no resistance to solithromycin in our clinical trials, and resistance was rare in our pre-clinical studies. Macrolide use for serious infections has generally been replaced by fluoroquinolones, despite this class having a less desirable safety and tolerability profile than macrolides. The current oral standard of care for CABP is levofloxacin or moxifloxacin, which are fluoroquinolones. As with respiratory tract pathogens, gonorrhea, has become resistant to macrolides, including azithromycin, a widely used macrolide, and other classes of oral antibiotics. Solithromycin can be used in monotherapy to treat CABP and also gonorrhea, chlamydia and mycoplasma infections. We believe solithromycin, with its unique chemical structure, retains and improves on the beneficial features of macrolides and can overcome the shortcomings of existing therapies.

We are conducting two pivotal Phase 3 trials for solithromycin to treat CABP. The first is a Phase 3 trial for oral solithromycin, which was designed based on FDA guidance documents and comments from the FDA, which we initiated in December 2012. We also began in December 2013 a second Phase 3 trial to treat CABP with IV solithromycin progressing to oral solithromycin. We believe that these two Phase 3 trials will be sufficient to support our planned NDA for solithromycin to treat CABP. These trials are randomized, double-blinded studies being conducted using a respiratory fluoroquinolone, moxifloxacin (Avelox), for which we will have to show non-inferiority for efficacy and acceptable safety and tolerability. Moxifloxacin was selected as the comparator because

it is administered at the same dose, 400 mg once a day worldwide, while levofloxacin, the respiratory fluoroquinolone used in our Phase 2 trial, is used at 750 mg in the U.S. and 500 mg in the rest of the world. Being a global study, the same dose was required to be used in our Phase 3 trials. Non-inferiority for efficacy means solithromycin will have to prove it is statistically as effective as a comparator drug within a pre-defined margin.

CABP is the number one cause of death from an infection and the sixth most common cause of death from all causes in the U.S. and a leading cause of death worldwide. There are 5 to10 million CABP cases annually, with 1.1 million patients hospitalized per year. Mortality rates are higher in hospitalized CABP patients. Most cases occur in adults 65 years and older, which is a growing population in the U.S. Pneumococcal infections cause more deaths per year in U.S. than breast or prostate cancer. In addition, respiratory disease incidence is increasing because of the growing numbers of COPD and asthma patients. CABP infection in pediatrics is quite common. The rate ranges from 74–92 (≤2yrs) and 33–52 (3–6 yrs) per 1,000 children. Early appropriate therapy is critical to positive outcomes and the treatment is empiric because, in clinical practice, a definitive microbial diagnosis of CABP is not feasible, which leads to empiric therapy to provide broad spectrum coverage to treat the pathogen. Multiple pathogens can be involved, including Grampositive, Gram-negative and atypical bacteria. Although pneumococcus is the most frequent cause of CABP, because of the multiple pathogens that could cause the disease, broad spectrum antibiotics and multiple antibiotics are used to treat CABP. For this reason, the American Thoracic Society, or ATS, and the Infectious Diseases Society of America, or IDSA, recommend treating CABP with broad spectrum coverage consisting of intravenous cephalosporin (e.g., ceftriaxone) and hospitalization. Often, azithromycin is added to treat *Legionella* and *Mycoplasma*, an atypical bacteria, however, pneumococcci are frequently resistant to azithromycin. The second choice is to use fluoroquinolones that are available in oral and IV formulations, such as levofloxacin or moxifloxacin. While these products are available in IV and oral form and have broad spectrum activity, they are not in favor for treating CABP because:

- treatment failures occur because of resistant strain selection;
- their broad spectrum kills intestinal microflora which is associated with C.difficile colitis;
- adverse effects such as, tendonitis, Achilles tendon rupture, hepatotoxicity and peripheral neuritis; and
- fluoroquinolones are not approved for use in pediatrics.

Solithromycin's spectrum of activity includes all of the pathogens involved in CABP and has demonstrated potent activity in vitro in animal models of infection and in our Phase 2 trial using solithromycin to treat CABP in monotherapy. Solithromycin can be used intravenously or orally and patients starting on IV therapy can be changed to oral therapy, which could lead to early discharge from the hospital.

The FDA has designated each of oral and intravenous solithromycin as a QIDP for the indication of CABP. The QIDP designation is expected to enable us to benefit from certain incentives for the development of new antibiotics, including priority review, and a five-year extension of NCE exclusivity.

We also are studying solithromycin for the treatment of bacterial urethritis, including uncomplicated gonorrhea. The current standard of treatment for gonorrhea is a single intramuscular injection of ceftriaxone. Until recently, cefixime (Suprax) had been recommended for oral treatment of patients as well as for treatment of their potentially infected partners. However, as of August 2012, the Centers for Disease Control, or CDC, no longer recommends cefixime for the treatment of gonorrhea, which leaves no oral treatment option. In our Phase 2 open-label study completed in 2013 in patients with suspected gonococcal infection, microbiological eradication of gonococci was achieved in 100% of all evaluable patients at all body sites. In addition to detecting the gonococcus, we also diagnosed *Chlamydia trachomatis* and *Mycoplasma genitalium*, which are atypical bacteria that can cause sterility in young girls as well as other ill effects. In most cases when diagnosed, solithromycin was effective against these pathogens also. Current treatment of bacterial urethritis includes two drugs: ceftriaxone administered intramuscularly and oral azithromycin, which is added to treat co-infections with chlamydia. Azithromycin at the 1000 mg dose that is recommended is not well tolerated. The FDA has asked that both gonococcus and chlamydia be monitored in our planned Phase 3 study and has indicated that a single Phase 3 trial in bacterial urethritis could be sufficient for approval.

In May 2013, we entered into a license agreement with Toyama whereby we licensed to Toyama the exclusive right, with the right to sublicense, to make, use and sell any product in Japan that incorporates solithromycin as its sole active pharmaceutical ingredient, or API, for human therapeutic uses, other than for ophthalmic indications or any condition, disease or affliction of the ophthalmic tissues. Toyama also has a nonexclusive license in Japan and certain other countries, with the right to sublicense, to manufacture or have manufactured API for solithromycin for use in manufacturing such products, subject to limitations and obligations of the concurrently executed supply agreement. Toyama has granted us certain rights to intellectual property generated by Toyama under the license agreement with respect to solithromycin or licensed products for use with such products outside Japan or with other solithromycin-based products inside or outside Japan. Toyama is conducting Phase 1 studies in healthy Japanese volunteers and, after completion, plans to conduct Phase 2 studies in other respiratory tract infections. Toyama and we are sharing the results of our respective development activities.

In May 2013 we entered into an agreement with BARDA for the evaluation and development of solithromycin for the treatment of bacterial infections in pediatric populations and infections caused by bioterror threat pathogens, specifically anthrax and tularemia. BARDA is funding the development of solithromycin suspension formulation for pediatric use in CABP. This is the first new antibiotic being developed as a suspension for pediatric use in over 20 years. The pediatric study plan, or PSP, was submitted and accepted by the FDA and a pediatric investigation plan, or PIP has been submitted to the EMA. There is an urgent need for a new oral and intravenous antibiotic for use in pediatric infections. Together with Toyama, we have completed pilot suspension formulation and taste masking work and we have begun taste testing in the U.S. and plan to move into manufacturing for use in Phase 1 studies. We also have initiated a Phase 1 study in adolescent children in the U.S., using the oral capsule formulation. Once the suspension formulation is available, younger children can be enrolled in a Phase 1b study. The IV formulation is also planned to be tested in these Phase 1 trials.

BARDA also is funding studies in non-human primates to test the efficacy of solithromycin in treating bioterror pathogens such as tularemia and anthrax. We expect to conduct pilot studies in 2014.

Infections in pregnancy are difficult to treat because of the nature of the infecting pathogens, such as Group B beta hemolytic streptococci and *Ureaplasma*. These infections can cause sepsis and also preterm birth. All pregnant women are screened for *Group B* beta hemolytic streptococci infections and can be treated with penicillin successfully. However, in penicillin-allergic patients there is no viable option today because of resistance. In patients infected with ureaplasma, penicillin is not effective and azithromycin has been the drug of choice. Recently resistance to azithromycin has increased and there is no optimal treatment option for these infections. In addition drugs that penetrate the amniotic fluid and placenta, in sufficient levels are important to fight infection and azithromycin has low penetration, which inhibits its efficacy in treating the infection. Consequently, there is a need for a safe and effective antibiotic that can be administered maternally but reach effective concentrations in fetal blood so that the infection at these sites can be effectively treated. Solithromycin has demonstrated in vitro activity against Group B beta hemolytic streptococci as well as ureaplasma. In November 2013, we reported that solithromycin may provide an effective antimicrobial approach for the prevention and treatment of intrauterine infections during pregnancy, including ureaplasma and Group B hemolytic streptococcus. A study in which the IV formulation of solithromycin was administered in pregnant sheep, which is a validated model for human pregnancy, resulted in effective concentrations of solithromycin in fetal plasma and amniotic fluid. According to the CDC, preterm births account for 75% of perinatal mortality. Bacterial infection of amniotic cavity is associated with preterm birth, or PTB. It is estimated that infection may be implicated in as many as 40% of PTB cases. In a 2007 study, bacterial vaginosis was shown to approximately double the risk of PTB and miscarriages were six times more likely. Pregnant women could be an additional patient population for solithromycin. BARDA is funding a segment 3 toxicology study which, if successful, could allow solithromycin to be tested in pregnancy.

Our prior Phase 1 and Phase 2 clinical trials and pre-clinical studies to date have shown that solithromycin has the following attributes:

- favorable safety and tolerability profile;
- comparable efficacy to levofloxacin, the standard of care in the U.S., with a lower incidence of treatment emergent adverse events than levofloxacin;
- potent activity against a broad range of bacteria with excellent tissue distribution and intracellular activity;
- lower incidence of resistance development;
- potential for IV, oral and suspension formulations that may allow it to be used in broad patient populations and settings;
- potential for special populations, including pediatric and pregnant patients;
- anti-inflammatory qualities to help patients feel better sooner during treatment; and
- chemical stability at room temperature.

Overview of Taksta

Taksta is a therapy that we are developing in the U.S. for the oral chronic, or long term, treatment, of prosthetic joint infections, which are frequently caused by staphylococci, including *S. aureus*, MRSA, coagulase negative staphylococci and other Gram-positive bacteria. MRSA is a qualified infectious disease pathogen. Taksta is a novel and proprietary dosing regimen of fusidic acid, which is an approved antibiotic that has been sold by Leo Laboratories, Ltd. primarily for staphylococcal infections, including skin, soft tissue and bone infections, for several decades in Europe and other countries outside the U.S. and has a long-established safety and efficacy profile. Fusidic acid, however, has never been approved for use in the U.S. We believe Taksta has the potential to be used in hospital and community settings on both a short-term and chronic basis. Since prosthetic joint infection is primarily treated with a combination of IV and oral drugs, we believe that Taksta would enable out-patient treatment of many patients who would otherwise require hospitalization and/or intravenous therapy, which we also believe would provide pharmacoeconomic advantages, be well received by

doctors and be more convenient for patients. In May 2013, we were issued a patent for our proprietary dosing regimen which has been shown with pharmacodynamics experiments to limit resistance development. In addition, in the Phase 2 study for ABSSSI, Taksta was well tolerated and no resistant strains were isolated. Further, fusidic acid is eligible for market exclusivity under the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act. In October 2013, the FDA designated Taksta as an orphan drug for the treatment of prosthetic joint infections, which will provide seven years of market exclusivity if Taksta is approved by the FDA for such treatment. In addition, orphan drug designation gives us an opportunity to develop an NDA study design acceptable to the FDA for a planned NDA. We have designed what we believe is an innovative Phase 3 trial that may be a path toward an NDA. We plan to submit the proposed Phase 3 trial protocol to the FDA in early 2014 and discuss our strategy with the FDA in the first half of 2014 in a Type C meeting.

As an orphan drug, we would also be eligible for a tax credit for 50% of the clinical cost for the continued development of Taksta and a possible waiver of PDUFA fees for an NDA. Taksta would also be eligible for an additional five years of exclusivity based upon the Generating Incentives for Antibiotics Now, or GAIN Act, since MRSA is listed in the law as a qualified infectious disease pathogen. Therefore, Taksta could qualify for as much as 12 years of statutory exclusivity in total. Taksta also could receive an additional six months exclusivity if approved for pediatric indications. In addition, our patent on our loading dose regimen for Taksta provides patent protection tom 2029.

According to a survey of physicians conducted by Decision Resources, MRSA is the most important pathogen of concern in patients with osteomyelitis and prosthetic joint infection. Bone infections often begin with skin infections where bacteria enter the bloodstream through breaks in the skin or mucous membrane that occur as a result of a wound or due to a surgical, medical or dental procedure.

In 2010, we successfully completed a Phase 2 clinical trial with Taksta in ABSSSI patients. In this trial, the Taksta loading dose regimen demonstrated efficacy, safety and tolerability that was comparable to linezolid, the only FDA-approved oral treatment for MRSA. Like ABSSSI, prosthetic joint infections are often caused by *S. aureus*, including MRSA. In December 2012, we initiated a Phase 2 trial of Taksta for treatment of primarily stapylococcal infections of infected prosthetic joint infections, hip and knee joints.. Currently, there are 14 sites in the U.S. and additional sites are expected. Despite the lack of FDA guidance for clinical trial design for treating PJI we designed a Phase 2 trial with a clear end point that compares vancomycin, which is the standard of care, with oral fusidic acid and rifampin. Although the Phase 2 trial continues to enroll, we believe we have met our primary objectives of the Phase 2 trial, namely safety and efficacy, to determine the study design and dose of our planned Phase 3 trial.

In October 2013, the FDA granted orphan drug designation for fusidic acid for the treatment of PJI. In December 2013, PJI was classified as a very rare disease by the NIH. With these designations in hand, we have submitted a proposal for a Phase 3 trial for Taksta as a treatment for PJI, which could lead to an NDA. If we receive concurrence from the FDA on the planned Phase 3 trial, we plan to stop the Phase 2 Trial and roll into the Phase 3 trial. We also are developing Taksta exclusively for the U.S. market.

Our prior clinical trials and pre-clinical studies, as well as historical data from outside the U.S., have shown that Taksta has the following attributes:

- established safety profile;
- comparable efficacy to linezolid, the only FDA-approved oral treatment for MRSA;
- ability to be used orally and for long term, chronic use as a treatment for all types of *S. aureus*, including MRSA;
- lower frequency of resistance development due to our loading dose regimen; and
- potential to be used in patient populations not well served by current treatments.

The Limitations Associated with Antibiotics

The widespread use of antibiotics has led to development of resistant strains of bacteria, which limits the effectiveness of existing drugs. This led the World Health Organization to state in 2010 that antibiotic resistance is one of the three greatest threats to human health. The CDC estimates that more than 70% of U.S. hospital infections are resistant to at least one of the antibiotics most commonly used to treat them. The CDC also estimates that each year more than 2,000,000 people are sickened with antibiotic-resistant infections, with at least 23,000 dying as a result. Antibiotic-resistant infections also increase the costs to the U.S. healthcare system.

Antibiotic resistance is primarily caused by genetic mutations in bacteria selected by exposure to antibiotics where the drug does not kill all of the bacteria. In addition to mutated bacteria being resistant to the drug used for treatment, many bacterial strains can also be cross-resistant, meaning that the use of a particular treatment to address one kind of bacteria can result in resistance to other kinds of bacteria as well as to other antibiotics. As a result, the effectiveness of many antibiotics has declined, limiting physicians' options to

treat serious infections and creating a global health issue. For example, it is estimated that in the U.S. approximately 44% of pneumococci, the primary pathogen involved in respiratory tract infections, are resistant to azithromycin and other macrolides commonly used to treat them. In addition, no new antibiotic has been developed for pediatric use in 20 years and this population also is showing growing resistance to currently available antibiotics. Resistance also is growing to antibiotics currently used to treat infections in pregnant women. Antibiotic resistance has a significant impact on mortality and morbidity and contributes heavily to health care system costs worldwide.

In addition to resistance issues, current antibiotic therapies also have other limitations, including serious side effects. These side effects may include: severe allergic reaction, decreased blood pressure, nausea and vomiting, suppression of platelets, pain and inflammation at the site of injection, muscle, renal and oto toxicities, optic and peripheral neuropathies and headaches. Some of these side effects may be significant enough to require that therapy be discontinued or not used. As a result, some treatments require clinicians to closely monitor patients' blood levels and other parameters, increasing the expense and inconvenience of treatment.

Further, many of the existing antibiotics used to treat serious infections are difficult or inconvenient to administer. Many drugs are given twice daily for seven to 14 days or more and patients can be hospitalized for much or all of this period or require in-home IV therapy. While IV treatment can deliver the drug more rapidly and in a larger dose than is possible orally, once a patient is stabilized, a switch to oral treatment allows for more convenient and cost-effective out-patient treatment. We believe that there is a need for new antibiotics that have improved potency and pharmacokinetics, effectiveness against resistant bacterial strains, improved side effect profiles and more flexible administration formulations.

Recognizing the seriousness of growing antibiotic resistance, in July 2012, Congress passed the GAIN Act to provide economic incentives to promote the development of antibiotics designed to treat specific qualified infections disease pathogens identified by the FDA. Among the pathogens that the FDA has identified as qualified infectious disease pathogens are MRSA, vancomycin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*. The incentives will be granted for an antibiotic that is designated by the FDA as a qualified infectious disease product or QIDP. QIDP designation provides certain incentives for the development of new antibiotics, including priority review, and a five year extension of new chemical entity exclusivity. Pursuant to the GAIN Act, in 2013, the FDA designated each of the oral and IV formulations of solithromycin as a QIDP for the indication of CABP, which was designated a qualified infectious disease pathogen by the FDA in 2013. In 2014, the FDA designated oral solithromycin as a QIDP for the treatment of uncomplicated gonococcal infections, which were designated as a qualified infectious disease pathogen by the FDA in 2014.

Solithromycin

Overview

We are developing solithromycin, a fourth generation macrolide and the first fluoroketolide, to treat multiple infectious diseases in multiple patient populations. We are initially developing solithromycin for respiratory tract infections, including CABP and also for treating chronic staphylococcal infections, including bacterial urethritis. Traditionally, macrolides have been among the most commonly prescribed drug for respiratory tract infections because of their combination of spectrum of activity, safety for use in adult and pediatric patients, tissue distribution and activity against intracellular pathogens, pharmacokinetics allowing use in oral and IV formulations, and anti-inflammatory properties. However, the effectiveness of macrolides for treating serious respiratory tract infections such as CABP has declined due to resistance issues related to earlier generations of macrolides. We believe our clinical and pre-clinical results suggest that solithromycin retains and improves on the benefits of, and overcomes the shortcomings of, earlier generation macrolides.

We also believe that solithromycin can be used as a monotherapy to treat CABP, due to its potency and planned availability in IV and oral formulations.

Solithromycin Market Opportunity

We are developing solithromycin in both oral (including a suspension formulation) and IV formulations initially as a treatment for CABP, which is a respiratory tract bacterial infection acquired outside of a hospital setting. Respiratory tract infections can range from severe diseases such as pneumonia (CABP), to similar infections of the respiratory tract such as pharyngitis (which is usually referred to as strep throat), bronchitis, chronic sinusitis and middle ear infections (which are especially common in children). CABP is one of the most common serious infectious diseases of the respiratory tract and is the most frequent cause of death due to bacterial infections. There are 1.6 million fatal cases of pneumococcal disease annually worldwide which is more than the deaths caused annually by breast or prostate cancer. There are approximately five to six million cases of CABP in the U.S. every year, approximately one million of which require hospitalization. Typical bacteria that cause CABP include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis* and *Staphylococcus aureus*. These four bacteria account for approximately 85% of CABP cases. Other organisms, called atypical bacteria, may be involved in CABP and include *Legionella pneumophila*, *S. aureus*, *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae*.

Many respiratory tract infections, including CABP, involve multiple bacteria. The routine diagnostic tests available to a physician can only identify a pathogen in 10% to 25% of cases and that diagnosis can take several days. Since infections can be serious and potentially life threatening, physicians cannot delay treatment while waiting for the results of these diagnostic tests to identify the pathogens involved in the disease. As a result, physicians seek to begin treatment with the antibiotic or combination of antibiotics that has the broadest activity against the bacteria thought to be causing the infection.

CABP and other respiratory tract infections can be treated with numerous classes of antibiotics, including macrolides, tetracyclines, fluoroquinolones, penicillins and cephalosporins. Each class has a different mechanism of action and resulting spectrum of activity. Each class, however, whether used alone or in combination, has limitations that can impede the treatment of CABP infections. Historically, macrolides have been among the most commonly prescribed drug for respiratory tract infections because of their broad spectrum of activity and relative safety. Azithromycin, a second generation macrolide which is sold as Zithromax and Z-PAK and as a generic, is the most widely prescribed macrolide with total U.S. prescriptions of 52 million in 2010, according to IMS Health, and sales of \$1.1 billion, according to Medical Marketing & Media.

In recent years, the effectiveness of earlier generation macrolides, including azithromycin, to treat serious infections such as CABP has declined due to resistance issues. The most recently approved macrolide, telithromycin (Ketek), has seen limited use because of serious side effects. For these reasons, fluoroquinolones, such as levofloxacin, now are commonly used for serious CABP infections. Although levofloxacin is efficacious, it has serious side effects including *C. difficile* enterocolitis, tendonitis, hepatotoxicity and central nervous system effects. Beta-lactams, such as cephalosporins, which are commonly used in CABP, also have limitations, including limited coverage against several important bacteria such as *Legionella* and *Mycoplasma*. In addition, the newer cephalosporins can only be administered intravenously, which is a disadvantage if the patient does not need to be hospitalized or needs to move to oral therapy to enable treatment on an out-patient basis. The American Thoracic Society, or ATS, and the Infectious Diseases Society of America, or IDSA, recommend a macrolide together with a beta-lactam (such as a cephalosporin) to treat CABP; the macrolide is added to cover atypical bacteria. Alternatively, ATS and IDSA recommend physicians treat CABP with fluoroquinolones. The recommended combination of a macrolide with a beta-lactam has been shown to enhance survival; when a macrolide is not used, an increase in mortality has been shown.

We believe that the initial market acceptance of Ketek, which, according to IMS Health, in 2005, its first full year after FDA approval, generated 3.4 million prescriptions and \$193 million in sales in the U.S., demonstrates the potential for a new macrolide therapy. However, soon after its U.S. approval in 2004, Ketek was found to cause reversible visual disturbances, loss of consciousness, exacerbate myasthenia gravis (a neurological disorder characterized by improper muscle regulation) and cause liver toxicity resulting in liver failure. Ketek was withdrawn in 2007 for use in all infections other than CABP, and as a result, the large market predicted for Ketek has not developed. While Ketek is a macrolide, solithromycin has a different chemical structure from Ketek, and therefore we believe is not likely to have the safety issues associated with Ketek. Our research, which was published in a peer-reviewed article in *Antimicrobial Agents and Chemotherapy*, suggests that pyridine, a chemical component of Ketek, is the agent that causes liver toxicity and other problems associated with Ketek. Solithromycin and older generation macrolides, including azithromycin and clarithromycin, do not have a pyridine component and have not been observed to cause the serious side effects associated with Ketek. We believe that solithromycin has the potential to be more successful than older macrolides because of the activity against resistant pathogens and potency if the Phase 3 trials confirm the efficacy and safety profile demonstrated in our previous trials.

As a result of the limitations of current therapies for CABP, we believe there is an opportunity to introduce the fourth generation macrolide that is more potent and effective against bacteria that are resistant to older generations of macrolides, while retaining the traditional safety and anti-inflammatory properties that macrolides are known to exhibit. To date, our Phase 1 and Phase 2 clinical trials have demonstrated that solithromycin is potent and effective against resistant bacteria and is well tolerated, with no serious adverse events. We also believe that developing IV and oral formulations will provide flexibility to physicians to treat patients according to the severity of their disease and transition some patients from IV to oral, enabling them to leave the hospital sooner. If approved by the FDA, solithromycin would be the first macrolide approved with both IV and oral capsule and suspension formulations since azithromycin was approved more than 20 years ago.

Further, we believe that the designation by the FDA of solithromycin as a QIDP for the treatment of CABP provides us with advantages in its development, namely priority review, and a five year extension of new chemical entity (NCE) exclusivity.

In addition to CABP, there is a large public health need for a new and effective oral treatment for treating bacterial urethritis. Resistance has emerged to cefixime, which is the only remaining oral therapy for gonococci infections, such as bacterial urethritis. Our Phase 2 trial conducted in 2013 demonstrated that solithromycin is active against most bacterial pathogens known to be involved in bacterial urethritis including gonococci, chlamydia and mycoplasma. The CDC has identified N. gonorrhea as one of the three pathogens that pose an immediate public health threat that require urgent and aggressive action. In addition, the CDC and key opinion leaders have expressed the need for an oral antibiotic as a replacement for cefixime because of resistance development. The development of solithromycin for bacterial urethritis would present an additional market opportunity for solithromycin and all of the

patient data gathered in any trials would also contribute to the safety data base for CABP development. The FDA has indicated to us that a single Phase 3 trial for solithromycin in bacterial urethritis could be sufficient for approval. In 2014, the FDA designated solithromycin as a QIDP for the treatment of uncomplicated gonococcal infections, which would provide us with the same development advantages discussed above for solithromycin as a treatment for CABP.

We also believe that solithromycin, because of its safety and tolerability as a macrolide, as well as its excellent tissue distribution and intracellular activity, may be effective in the treatment of infections in special populations, including pediatric and pregnant patients.

Key Attributes of Solithromycin

We believe the following key attributes of solithromycin will make it a safe and effective treatment for CABP and bacterial urethritis/gonorrhea as well as other infectious diseases and in many patient populations, including pediatrics and pregnancy.

Solithromycin has demonstrated a favorable safety and tolerability profile. Solithromycin has been tested in over 500 subjects in our Phase 1 and 2 clinical trials and has been shown to be safe and well tolerated to date. There were no clinically significant laboratory abnormalities in the Phase 1 trials. In the Phase 2 trial, there were fewer adverse events compared to levofloxacin, none of which required the patient to prematurely discontinue treatment with solithromycin, and no serious adverse events determined by the investigator to be related to solithromycin. Patients in our single and multi-dose Phase 1 IV trial showed no clinically significant liver enzyme changes associated with solithromycin at the selected therapeutic doses, indicating no liver toxicity. Additionally, in this study solithromycin did not produce dose-limiting nausea or vomiting, or effect the heart, which are common side effects of other macrolides. Safety and tolerability also were demonstrated in our Phase 2 trial for bacterial urethritis as well as in our study in patients with mild to severe chronic liver disease. We believe that solithromycin's safety and tolerability profile will allow it to be used in many patient populations, including pediatrics and pregnancy.

Solithromycin has demonstrated comparable efficacy to the current standard of care for CABP. In our Phase 2 trial in 132 CABP patients comparing the oral formulation of solithromycin to levofloxacin, solithromycin successfully demonstrated efficacy comparable to levofloxacin. In addition, solithromycin was highly effective in our Phase 2 trial of bacterial urethritis.

Solithromycin is potent against a broad range of bacteria and has excellent tissue distribution and intracellular activity. In preclinical studies, solithromycin was shown to be generally eight to 16 times more potent against respiratory tract bacteria *in vitro* than azithromycin as well as retains activity against azithromycin resistant strains. These pre-clinical studies also showed that solithromycin is potent against many bacteria that are resistant to levofloxacin and other fluoroquinolones. In addition to respiratory tract infections, solithromycin is active against bacteria causing other types of infections such as urethritis, malaria, and tuberculosis. Solithromycin has demonstrated activity against bacterial strains that are not susceptible to older generations of macrolides. In preclinical studies, solithromycin has demonstrated a longer post-antibiotic effect, meaning that after exposure to solithromycin, bacteria take longer to regrow than after exposure to other macrolides, supporting the potential for once-daily dosing. Solithromycin has also demonstrated excellent organ and tissue distribution and intracellular activity, addressing not only bacteria located in the blood but also in organs and cells in which they multiply. Bacteria therefore cannot escape from the action of the drug. As a result of its potency, spectrum of activity and pharmacokinetic and pharmacodynamic properties, we believe that solithromycin could eventually be used as a monotherapy for the treatment of CABP.

Solithromycin has a greater ability to fight resistant bacteria and to overcome resistance development due to its chemical structure. Solithromycin has a unique structure that binds to bacterial ribosomes in three sites while earlier generation macrolides have only one or two binding sites. Therefore, bacteria must mutate at three sites on the ribosome to become resistant to solithromycin. To date, we have seen no resistance to solithromycin in our clinical trials, and resistance was rare in our pre-clinical studies.

Solithromycin has the potential for IV, oral and suspension formulations. We are developing oral (including suspension) and IV formulations to allow patients with severe CABP to be treated in both hospital and out-patient settings. Providing both the IV and oral formulations will enable IV-to-oral step-down therapy. We believe this would be more convenient and cost-effective for patients and provide pharmacoeconomic advantages to health care systems. The suspension formulation would be used to treat bacterial infections in the pediatric population as well as elderly patients who may be unable to swallow a capsule.

Solithromycin has improved anti-inflammatory qualities. In CABP and other bacterial infections, the body's immune response to the bacteria results in inflammation and tissue damage, which worsens symptoms. In addition to their antibacterial effects, macrolides also have anti-inflammatory properties which help patients feel better earlier. Our pre-clinical data suggest that solithromycin could have significantly greater anti-inflammatory properties than azithromycin and clarithromycin, which are used to treat patients with cystic fibrosis, or CF, and COPD, primarily for their anti-inflammatory properties.

Clinical Data

Phase 2 Oral CABP Trial. We successfully completed a Phase 2 trial of the oral formulation of solithromycin in the third quarter of 2011. The trial was a randomized, double-blinded, multi-center study to evaluate the efficacy and safety of oral solithromycin compared to oral levofloxacin in 132 patients with CABP. Levofloxacin, which is a respiratory fluoroquinolone, is the current standard of care and widely prescribed for the treatment of CABP. Patients were randomized to receive solithromycin or levofloxacin for five days. Solithromycin patients received once-daily dosing of 800 mg on Day 1 and 400 mg on Days 2 through 5. Patients randomized to levofloxacin treatment received the standard dosing regimen of 750 mg per day for five days. The trial compared clinical success rates and safety and tolerability parameters for solithromycin and levofloxacin. The primary outcome measure was continued improvement or complete resolution of baseline signs and symptoms in the intent to treat, or ITT, and the clinically evaluable, or CE, populations at the Test of Cure, or TOC, visit, which was completed five to 10 days after the last dose of the drug.

Outcomes were assessed for several populations within the study. The ITT population consisted of all randomized patients, among whom 85.6% were in the CE group. To be clinically evaluable, key inclusion and exclusion criteria had to be validated, confounding antibiotics for other infections could not have been administered, and key visits and assessments had to have been performed. Patients for whom a microbial pathogen, or the bacteria responsible for the pneumonia, had been identified comprised the microbial-ITT, or mITT, population. Those mITT patients who were also in the CE study group constituted the microbial-evaluable or ME group. Since pneumonia can also be caused by viruses which antibiotics cannot treat, the FDA has placed emphasis on proof of clinical success in the mITT and ME groups.

Solithromycin demonstrated comparable efficacy to levofloxacin. The clinical response rate in the ITT population was 84.6% for solithromycin and 86.6% for levofloxacin. Similarly, clinical response rates for solithromycin and levofloxacin in the mITT and ME populations were well balanced (77.8% vs. 71.4% and 80.0% vs. 76.9%, respectively). The clinical response rates at TOC for the ITT, CE, mITT and ME populations are presented in Table 1.

Table 1. Solithromycin Oral Phase 2 Results: Clinical Response at Test of Cure (Days 5 to 10 after Last Dose).

<u>Population</u>	Clinical Response	Solithromycin 800/400 mg once daily No. of patients (%)	Levofloxacin 750 mg once daily No. of patients (%)
ITT	Number of patients	65	67
	Success	55 (84.6)	58 (86.6)
	95% Confidence Interval	(73.5-92.4)	(76.0-93.7)
	Failure(1)	10 (15.4)	9 (13.4)
	Failure	9 (13.8)	7 (10.4)
	Indeterminate	1 (1.5)	2 (3.0)
CE	Number of patients	55	58
	Success	46 (83.6)	54 (93.1)
	95% Confidence Interval	(71.2-92.2)	(83.3-98.1)
	Failure	9 (16.4)	4 (6.9)
mITT	Number of patients	18	14
	Success	14 (77.8)	10 (71.4)
	95% Confidence Interval	(52.4-93.6)	(41.9-91.6)
	Failure(1)	4 (22.2)	4 (28.6)
	Failure	3 (16.7)	4 (28.6)
	Indeterminate	1 (5.6)	0(0.0)
ME	Number of patients	15	13
	Success	12 (80.0)	10 (76.9)
	95% Confidence Interval	(51.9-95.7)	(46.2-95.0)
	Failure	3 (20.0)	3 (23.1)

⁽¹⁾ Includes clinical response of failure and indeterminate.

In the CE population, the numerical success rate was higher in the levofloxacin arm (93.1%), with broadly overlapping confidence intervals. This in large part is due to exclusion of a larger number of failure patients from the levofloxacin arm and exclusion of treatment successes from the solithromycin arm on the basis of pre-established study criteria including validation of key inclusion and exclusion criteria and the completion of key visits and assessments.

Under the proposed FDA guidance for the conduct of CABP clinical trials, drug developers will be required to assess early responses to therapy as a primary endpoint. Therefore, we assessed markers of clinical success at the Day 3 visit. A clinical response was achieved if a patient was clinically stable and had experienced an improvement in severity without worsening in any of these signs or symptoms. The early clinical response rate in the ITT population was 72.3% for solithromycin patients, and 71.6% for levofloxacin patients.

Safety was an important focus of this Phase 2 trial. In the trial, patients receiving levofloxacin reported more adverse events and severe adverse events than solithromycin patients. There were 19 patients (29.7%) in the solithromycin group with treatment emergent adverse events, or TEAE, compared with 31 patients (45.6%) in the levofloxacin group. There were no patients in the solithromycin group that discontinued the study due to a TEAE as compared to six patients (8.8%) in the levofloxacin group. The overall incidence of TEAE was greater in the levofloxacin arm, at all degrees of severity. Notably, gastrointestinal disorders, including abdominal discomfort, nausea, and vomiting, all occurred with greater frequency among levofloxacin recipients. The results are summarized in Table 2 below.

Table 2. Solithromycin Oral Phase 2 Results: Treatment-emergent Adverse Events with 2% Incidence in Any Treatment Group.

	Solithromycin 800/400 mg once daily (No. of patients, n=64)			Levofloxacin 50 mg once daily . of patients, n=68	once daily	
By System/Organ	Mild n (%)	Moderate n (%)	Severe n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Subjects with at least one TEAE	10 (15.6)	6 (9.4)	3 (4.7)	14 (20.6)	11 (16.2)	6 (8.8)
Gastrointestinal Disorders	5 (7.8)	4 (6.3)	0(0.0)	11 (16.2)	5 (7.4)	0(0.0)
Musculoskeletal and Connective Tissue Disorders	2 (3.1)	3 (4.7)	0(0.0)	2 (2.9)	1 (1.5)	0(0.0)
Nervous System Disorders	3 (4.7)	2 (3.1)	1 (1.6)	5 (7.4)	2 (2.9)	1 (1.5)

In addition to TEAEs, the trial also recorded serious adverse events, which are adverse events of particular severity that, among other defining criteria, might result in hospitalization or threaten overall health or survival. There were nine patients who experienced one or more serious adverse events during the study, two solithromycin recipients and seven levofloxacin recipients. The study site trial investigator determined that both of the serious adverse events reported in solithromycin recipients were unrelated to solithromycin, while one of the seven reported in levofloxacin recipients was unrelated to levofloxacin.

Patients treated with solithromycin had no drug-related clinically significant liver toxicities and reported no visual adverse events. Severe liver toxicities and visual disturbances led the FDA to require the drug label for Ketek to include a strengthened warning section regarding specific drug-related adverse events and contributed to Ketek being withdrawn for the treatment of all infections other than CABP.

Phase 1 IV Trial. The objective of our Phase 1 IV trial for solithromycin was to demonstrate safety and tolerability as well as to select the therapeutic dose after IV administration for our planned second Phase 3, IV to oral trial. We tested escalating IV doses of 25 mg, 50 mg, 100 mg, 200 mg, 400 mg, 800 mg and 1000 mg administered as single doses or 200, 400, 600 and 800 mg doses administered once daily for seven days. Patients were randomized into solithromycin and placebo arms. In the trial, the most common adverse events, or AEs, were general disorders and administration site conditions related to infusion discomfort or pain. Our Phase 1 trial also tested infusion solutions designed to minimize injection site pain. No AEs were reported in any of the studies that resulted from clinically significant changes in physical examinations, vital signs, or ECG data. In healthy subjects who received repeat-dose IV solithromycin (200, 400, or 800 mg QD for up to seven days) in the Phase 1 study 20% had asymptomatic and reversible ALT elevations. One subject, who received three daily doses of 800 mg, had a reversible and asymptomatic Grade 4 ALT elevation without bilirubin elevation. These ALT elevations were reversible and not associated with symptoms, bilirubin elevation or cholestasis. No loss-of-consciousness, myasthenia exacerbations, or visual disturbances were observed. Among patients receiving repeated doses of 400 mg daily for up to seven days, no clinically significant systemic adverse events were observed, except injection site pain in some subjects. In addition, the desired PK profile was achieved, with clinically relevant mean peak solithromycin concentrations of 4 micrograms/mL. Modeling of the PK data suggest that initial intravenous dosing with 400 mg once-daily, with a switch to oral administration when clinically appropriate to the same dose as in the oral program, i.e. 800 mg loading dose and 400 mg maintenance dose, will achieve concentrations of the drug that warrant its evaluation in the treatment of moderate to severe community acquired bacterial pneumonia caused by pathogens including azithromycin-resistant pneumococcus, Legionella, Mycoplasma, Moraxella, Hemophilus influenzae, and Staphylococcus aureus, including methicillin susceptible and community-acquired methicillin-resistant Staphylococcus aureus, all of which are infections that could require elevated concentrations of antibiotics. Based on this study, we selected a therapeutic dose of 400 mg administered once daily for up to seven days for our Phase 3 IV-to-oral trial with the option of stepping down to oral treatment of solithromycin when appropriate as decided by the physician based on decreased symptoms.

Phase 1 Oral Trials. In earlier Phase 1 oral trials beginning in 2008 and continuing into 2011, 159 subjects were exposed to solithromycin. The Phase 1 trials were designed to examine the safety of solithromycin and the properties of the drug when absorbed into the bloodstream. There were no clinically relevant changes in patient laboratory values, including liver enzymes. There were very limited gastrointestinal adverse events and no dose-limiting nausea or vomiting, a common side effect of macrolides. Absorption of solithromycin into the bloodstream after oral administration was not affected by food, meaning solithromycin may be taken with or without food.

The results from our first Phase 1 dose escalation study demonstrated that doses of solithromycin from 200 mg to 600 mg had a favorable safety profile and were well tolerated in healthy subjects and that the compound's pharmacokinetic profile was supportive of once-daily dosing. In this study, solithromycin was administered orally once-daily for seven days at 200 mg, 400 mg and 600 mg. The bioavailability of solithromycin was calculated to be 67% whereas azithromycin's bioavailability is 38% as reported in its package insert. The concentration of solithromycin was measured in the plasma on Day 1 and Day 7. The compound showed moderate accumulation over the seven days of dosing, indicating that a loading dose regimen followed by a maintenance dose would be suitable, as has been noted with macrolides like azithromycin in the past. These blood levels were subjected to a sophisticated computer model based on efficacy studies in mouse models, which led to identifying a loading dose of 800 mg with a maintenance dose of 400 mg as the therapeutic dose. At these doses solithromycin is expected to be clinically effective against 99.99% of pneumococci with a minimum inhibitory concentration, or MIC, of 2 μ g/ml or less, while no pneumococcal strains with an MIC of >1 mcg/ml have been identified in any of the surveillance programs. Mild, clinically insignificant gastrointestinal side effects were the most common adverse events observed in each dose group. Importantly, there were no clinically significant adverse events.

In CABP, the lung is the target organ where pathogens replicate. Therefore, in the first quarter of 2010, we conducted a Phase 1 pharmacokinetic study of solithromycin in 31 healthy human volunteers to measure the concentration of solithromycin in the epithelial lining fluid, or ELF, and in alveolar macrophages, or AM, compared to the concentration in plasma. After five days of dosing (400 mg per day, without loading), we performed bronchoalveolar lavage (BAL), a medical procedure to collect fluid and cells in the lung. BAL analysis was performed in groups of six at 3, 6, 9, 12 or 24 hours following the last solithromycin dose on Day 5, and solithromycin concentrations were measured in each of the ELF, AM, and plasma. The concentration of solithromycin in ELF was 10 times that of plasma and in AM it was 100 times that of plasma. As shown in Table 3, solithromycin's drug levels are higher than those achieved by azithromycin and solithromycin reaches the site of infection at concentration levels several fold in excess of the levels necessary to kill the relevant bacteria according to our pre-clinical studies. Higher drug levels also inhibit bacterial regrowth and resistance development during intervals between dosages.

Table 3: Solithromycin Oral Phase 1 Results: Pulmonary Levels of Solithromycin and Azithromycin at Time of BAL.

Antibiotic	Dose	Plasma Cmax (μg/mL)	ELF Cmax (µg/mL)	AM Cmax (μg/mL)
Solithromycin	400 mg qd/5 d	0.7	7.6	102
Azithromycin ⁽¹⁾	500 mg qd/1 d; 250 mg qd/4 d	0.1	2.2	57

⁽¹⁾ Zithromax Prescribing Information with loading dose of 500 mg on Day 1 followed by 250 mg daily for four days, Foulds, et.al., 1990.

We also conducted three drug-drug interaction studies in 2010 and 2011 in which solithromycin was co-administered with rifampin, midazolam or ketoconazole to test its effects on these drugs. These studies have been successfully concluded and the data confirm that solithromycin's interactions with CYP3A4, an enzyme in the liver that metabolizes a number of drugs, are consistent with older macrolides' interactions with CYP3A4.

Thorough QT (TQT) Study. Macrolides are known to cause QT prolongation that may be associated with risk of arrhythmia. In 2013, the U.S. drug label for azithromycin, the most commonly prescribed macrolide antibiotic in the U.S., was updated to include a warning of possible QTc prolongation and the risk for sudden death. This label change followed publication of a study that suggested a higher risk of cardiovascular death in persons treated with a 5-day course of azithromycin compared to persons treated with amoxicillin, ciprofloxacin, or no drug. We conducted a TQT study of solithromycin, the top line results of which demonstrated no QT effects at single intravenous (IV) doses of 800 mg. In ouor solithromycin TQT study, 48 subjects were enrolled in a three-way randomized dosing sequence cross-over design to receive 800 mg of IV solithromycin infused over 40 minutes to obtain maximal cardiac exposure (Cmax), 400 mg of oral moxifloxacin, which was used as the positive control along with IV physiologic saline to maintain study blinding, or IV physiologic saline as the negative control. There was a seven-day washout period between dosing intervals. Data were collected continuously for 25 hours, starting one hour before dosing, using 12-lead ECG Holter monitors. Electrocardiograms were analyzed by a core laboratory. No significant QT effects were seen with solithromycin. The study's assay sensitivity was confirmed by the observation of QTc prolongation following dosing with moxifloxacin. The study thereby constitutes a solidly negative TQT study as defined by the ICH E14 guidance. Solithromycin at the supratherapeutic exposures achieved in this study had no significant effect on the OT interval.

Hepatic Insufficiency Phase 1 Study. In 2013, we conducted a safety and pharmacokinetic study of oral solithromycin in patients with chronic liver disease. The study demonstrated that no dosage adjustment is needed when administering solithromycin to patients with mild, moderate, or severe hepatic impairment. Solithromycin was well tolerated in this patient population and no significant differences in safety, compared to healthy controls, were noted. The most commonly reported adverse effects were mild diarrhea and mild headache.

Phase 2 Trial in Gonorrhea. Emerging resistance to available therapies, including oral and intramuscular cephalosporins and azithromycin, has resulted in an urgent medical need for new therapies for gonorrhea. Solithromycin, a new fourth generation macrolide with three ribosomal binding sites, has greater in vitro potency against gonococci than azithromycin and is active against most azithromycin- and cephalosporin-resistant strains. In our Phase 2 trial in patients with suspected gonococcal infection, microbiological eradication of gonococci was achieved in 100% of all evaluable patients. In addition to detecting the gonococcus, we also diagnosed Chlamydia trachomatis and Mycoplasma genitalium, an atypical bacteria that can sterility in young girls as well as other ill effects. In most cases when diagnosed, solithromycin was effective against these pathogens also. Current treatment of bacterial urethritis includes two drugs: ceftriaxone administered intramuscularly and oral azithromycin. Azithromycin at 1000 mg dose that is recommended is not well tolerated. Solithromycin was generally well-tolerated, with mild gastrointestinal AEs, the most common of which was mild diarrhea followed by mild nausea. Solithromycin could be used as a monotherapy that would cover gonorrhea and chlamydia, rather than the current treatment with two drugs, replacing the need for intramuscular injection of ceftriaxone.

Pre-Clinical Data

Our pre-clinical studies support four of the key attributes of solithromycin: potency against a broad range of bacteria, potential to have a low incidence of resistance, intracellular activity and anti-inflammatory qualities associated with macrolides.

Potency. We have extensively studied solithromycin's *in vitro* activity and potency against a variety of respiratory and non-respiratory bacteria. solithromycin was tested against clinical isolates including pneumococci, *Hemophilus*, *Legionella*, *Moraxella*, *Chlamydia*, *Neisseria*, beta-hemolytic streptococci, *Mycoplasma*, *S. aureus* (including MRSA), coagulase negative staphylococci, enterococci and many other bacteria. These studies found that solithromycin exhibited two to four times greater potency compared to Ketek, and superior potency compared to other macrolides against most bacteria causing CABP. In another study, solithromycin demonstrated superior activity against several serotypes of *Legionella pneumophila* compared to other macrolides, particularly erythromycin and azithromycin, which are commonly used to treat Legionellosis. *Legionella* are atypical bacteria and are not susceptible to penicillins and cephalosporins commonly used to treat CABP, but are susceptible to fluoroquinolones such as levofloxacin. The results of these studies are presented in Table 4 below. Potency against a panel of bacterial strains is measured by MIC₉₀, which refers to the concentration needed to inhibit the growth of 90% of a panel of bacterial strains isolated from patients. A lower MIC₉₀ indicates greater potency against a particular bacterium.

Table 4. Solithromycin Pre-Clinical Data: Solithromycin in vitro Activity Against CABP Bacteria.

Organism (# strains tested)	Solithromycin MIC ₉₀ (µg/ml)	Azithromycin MIC ₉₀ (μg/ml)	Levofloxacin MIC ₉₀ (μg/ml)	Amox/Clav MIC ₉₀ (μg/ml)
Streptococcus pneumoniae (150)	0.25	>16	1.0	>8
Streptococcus pyogenes (100)	0.03	>16	1.0	0.25
Hemophilus influenzae (100)	2	2	0.12	2.0
Legionella pneumophila (30)	0.015	2	0.5	NE
Mycoplasma pneumoniae (36)	0.000125	0.0005	0.5	NE
Chlamydophila pneumoniae (10)	0.25	0.125	NT	NE

NE = Not effective, as the target of these antibiotics do not exist in these pathogens.

NT = Not tested.

Resistance. Solithromycin was tested against pneumococcal strains that have become resistant to older macrolides as a result of mutations called erm(B), mef(A), a combination of erm(B) with mef(A), and L4 mutations. As shown by the *in vitro* potency data in Table 5 below, solithromycin was active against all tested pneumococcal strains that are resistant to older macrolides.

Table 5. Solithromycin Pre-Clinical Data: MIC_{50} and MIC_{90} Values ($\mu g/ml$) of Pneumococci with Defined Macrolide-Resistant Mechanism.

		n(B) 54)	mef(A	A) (51)	erm(mef(A			itations 27)
<u>Drug</u>	MIC ₅₀	MIC ₉₀						
Solithromycin	0.03	0.5	0.03	0.125	0.125	0.25	0.06	0.125
azithromycin	>64	>64	4	8	>64	>64	>64	>64
telithromycin	0.06	1	0.125	0.25	0.5	1	0.125	0.25
clindamycin	>64	>64	0.06	0.06	0.06	>64	0.06	0.125
amox/clav	0.5	8	0.125	2	2	8	4	8
levofloxacin	1	2	1	2	1	16	1	2
penicillin G	1	4	0.125	4	2	4	4	16

The ability to become resistant to solithromycin was analyzed by exposing eight pneumococcal bacterial strains from the above study to solithromycin. Only one strain which was already resistant to the older macrolides and were *erm* and *mef* strains developed a high-level resistance to solithromycin and only after 18 passes. This suggests that selection of resistant strains would be infrequent and additional mutations are necessary for resistance to develop to solithromycin.

We also tested a number of Group A beta-hemolytic streptococci that have become resistant to older macrolides. The data indicate that solithromycin is active against these organisms, which have different mechanisms of resistance, including erm(B), mef(A) and erm(A). The frequency of resistance was low at $<10^{-10}$, but importantly there was no cross-resistance with these organisms once they had become resistant to older macrolides. Solithromycin is active against all these resistant strains. While the strains are resistant to older generations of macrolides, no strains resistant to solithromycin could be isolated after 50 transfers in a growth medium containing solithromycin.

We have continued to study global susceptibility and resistance patterns against relevant pathogens in CABP and tested solithromycin against pathogens collected in 2011 from respiratory tract infections. Solithromycin displayed coverage against 100.0% of *S. pneumoniae* strains (2,418 strains collected from the U.S. and Europe) at $\leq 1~\mu g/mL$ (a level which is achievable in the plasma and tissues). The MIC₉₀ against *S. pneumoniae* was 0.12 $\mu g/mL$ in these studies. Resistance rates in the U.S. to macrolides have been noted to increase from previous results to 44% in 2012. The activity of solithromycin against other respiratory tract associated pathogens, such as *H. influenzae* and *M. catarrhalis*, was stable during four consecutive surveillance years (2008-2011). We believe this confirms that solithromycin could be a promising antibiotic for treatment of bacterial pathogens causing respiratory tract and other infections.

Intracellular Activity. Bacteria that cause infections can be inside cells or in tissue. During treatment if the antibiotic does not penetrate into tissues and cells, the bacteria can escape the effect of the antibiotic. Consequently, it is important that antibiotics be distributed from the blood to the tissues and intracellularly. Macrolides have been known to be effective against intracellular bacteria, which is one of their advantages. Solithromycin accumulates to concentrations that are several times higher than azithromycin, as shown below in Figure 1a, and the intracellular drug is potent against intracellular bacteria and is more active than azithromycin in killing intracellular pathogens such as Legionella pneumophila as shown in Figure 1b.

Figure 1a: Concentration after Exposure of Macrophages to Azithromycin and Solithromycin in Macrophages

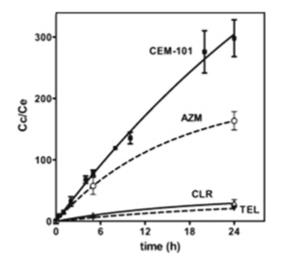
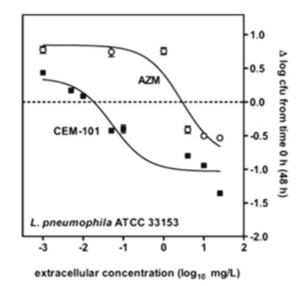


Figure 1b: Killing of Legionella Located Intracellularly by Azithromycin and Solithromycin



Anti-Inflammatory Properties. We conducted studies comparing solithromycin's anti-inflammatory properties to older macrolides. Solithromycin was more effective than the older macrolides in decreasing the production of cytokines, which are cell-signaling molecules involved in the process of inflammation. Reduction of cytokine activity would be expected to reduce inflammation and resulting tissue damage. Thus, solithromycin is expected to be effective in eradicating the infecting bacteria and reducing the inflammation resulting from the infection, which should result in a faster recovery. Older generation macrolides have also been used in the treatment of diseases like late-stage COPD and CF because of their anti-inflammatory properties. Our pre-clinical data suggest solithromycin could also be used in the treatment of these diseases.

In addition, investigators at the University of North Carolina, Chapel Hill, through funding from the National Institute of Allergy and Infectious Diseases, or NIAID are for studying solithromycin's mucin inhibitory properties and ability to restore lung physiology in cystic fibrosis model systems.

Ongoing and Planned Clinical Trials

Solithromycin as a Treatment for CABP. We have initiated our pivotal clinical trial program, which consists of two Phase 3 trials, including one trial with oral solithromycin and one trial with IV solithromycin progressing to oral solithromycin, for the approval of both IV and oral products under separate NDAs. The FDA's Anti-Infective Drugs Advisory Committee (AIDAC) convened in November 2011 to review anticipated changes in guidance to the industry for conducting clinical trials for CABP. The proposed guidance follows several FDA advisory meetings as well as recommendations of an independent advisory body called the FNIH that involved industry and academic infectious disease physicians. According to the proposed guidelines, the primary endpoint for Phase 3 CABP trials will be clinical success at an early timepoint (Day 3-5 post study drug initiation). Clinical success is defined as improvement in at least two of the following symptoms: cough, shortness of breath, chest pain, and sputum production, without worsening in any other symptom. The proposed guidelines also clarify the patient population required for these trials by specifying the percent of patients to be enrolled based on the severity of their disease. We designed our Phase 3 trials in accordance with these guidelines and met with the FDA to finalize the design. Subsequently, in January 2014, the FDA issued new draft guidelines which may decrease the number of PORT II patients as well as the overall margin which would allow a smaller study size and data base. However, we are continuing our Phase 3 trials as previously agreed upon with the FDA. The EMA has not changed its guidelines. The Phase 3 trial for oral solithromycin was initiated in the fourth quarter of 2012 and the Phase 3 trial for IV-to-oral solithromycin was begun in December 2013. The Phase 3 trials are randomized, double-blinded studies conducted against a comparator drug agreed upon with the FDA, for which we will have to show non-inferiority from an efficacy perspective and acceptable safety and tolerability. We expect to complete enrollment of the Phase 3 oral trial in the fourth quarter of 2014 and to report top line data for the Phase 3 oral trial in the first quarter of 2015.

In October 2012, we reported results from our Phase 1 trial for the IV formulation of solithromycin in which we demonstrated that IV solithromycin was well tolerated, showed a favorable pharmacokinetic (PK) profile and achieved relevant plasma concentrations. Based on this study, we selected a therapeutic dose of 400 mg administered once daily for up to seven days for the Phase 3 IV-to-oral trial.

We are working on pediatric studies for solithromycin in a range of indications for CABP through our agreement with BARDA. BARDA is funding the development of solithromycin in oral, IV and suspension formulations for pediatric use in CABP. This is the first antibiotic being developed as a suspension for all pediatric age groups in over 20 years. The pediatric plan was submitted and accepted by the FDA and a similar plan has been submitted to the EMA. There is an urgent need for a new antibiotic for use in pediatric infections. Together with Toyama, we have completed pilot suspension formulation and taste masking work and we have begun taste testing in the U.S. and plan to move into manufacturing for use in Phase 1 studies. We also have initiated a Phase 1 study in adolescent children in the U.S. Once the suspension formulation is available, younger children can be enrolled in a Phase 1b study.

Solithromycin as a Treatment for Bacterial Urethritis. We have demonstrated that solithromycin has in vitro activity against a broad spectrum of pathogens that cause bacterial urethritis, including N. gonorrhoeae, Chlamydia trachomatis, Mycoplasma genitalium, Ureaplasma urealyticum etc. In our Phase 2 trial, we demonstrated that solithromycin is effective in treating gonococcal urethritis/cervicitis, and pharyngeal and rectal gonococcal infections. In 2013, the CDC identified N. gonorrhoeae as an urgent public health threat that requires urgent and aggressive action. The CDC no longer recommends oral cefixime to be used in the treatment of gonorrohea and the recommended treatment is intramuscular injection of ceftriaxone, plus either azithromycin or doxycycline. Resistance to ceftriaxone has been reported. There is no oral antibiotic currently recommended for treating gonorrhea as well as for treatment of sexual partners of infected patients. This need has become a public health crisis and the WHO and U.S. government are looking for alternative treatments. We are discussing possible grant funding opportunities with the NIAID to pursue solithromycin in a pivotal Phase 3 trial for the treatment of bacterial urethritis, primarily gonnorhea. The FDA has asked that both gonococcus and chlamydia be monitored in our planned Phase 3 study and has indicated that a single Phase 3 trial in bacterial urethritis could be sufficient for approval.

Potential Biodefense Application for Solithromycin. Solithromycin is active against bioterror threat pathogens such as *B. anthracis, Yersinia pestis* and *Francisella tularensis*. BARDA is funding studies to test the efficacy of solithromycin in treating bioterror pathogens such as tularemia and anthrax. These tests are being conducted in non-human primates and we expect to conduct pilot studies in 2014.

Taksta (Fusidic Acid)

Overview

Taksta, our fusidic acid product candidate, is an antibiotic that we are developing in the U.S. for the oral chronic treatment of prosthetic joint infections, which are frequently caused by staphylococci, including coagulase-negative and coagulase-positive staphlycocci and MRSA. Fusidic acid is the only member of a unique class of antibiotics, called fusidanes, and has a mechanism of action that differs from any other antibiotic. Fusidic acid has been approved and sold for several decades in Europe and other countries outside the U.S. and has a long-established safety and efficacy profile, but has never been approved in the U.S. We have conducted *in vitro* tests of Taksta's activity against thousands of strains of *S. aureus* found in the U.S. and our data show that virtually all of those strains tested (99.6%) are susceptible to Taksta. In addition, we believe Taksta has the potential to be used in hospital and community settings on both a short-term and chronic basis. Our completed Phase 2 clinical study has shown Taksta to be comparably effective to linezolid, a treatment for the common skin infection *S. aureus* and the only oral antibiotic approved by the FDA to treat MRSA.

Taksta Market Opportunity

According to the IDSA, MRSA infections account for approximately 60% of skin infections seen in U.S. emergency rooms. The most common treatments for prosthetic joint infection with MRSA currently are vancomycin (available as a generic) and sometimes daptomycin (sold under the brand name Cubicin®), both of which are available only as IV formulations for systemic infections. Linezolid, which is also prescribed for prosthetic joint infections, is available in both IV and oral formulations and is the only oral antibiotic approved by the FDA for MRSA. Linezolid, however, has significant side effects, which include irreversible peripheral neuritis, or the inflammation of nerves and thrombocytopenia, or a relative decrease of platelets in blood. It is recommended that linezolid not be taken for more than 14 days without additional monitoring because of the increased possibility of these side effects. In addition, on July 26, 2011, the FDA published a drug safety communication letter regarding the use of linezolid in patients on serotonergic drugs such as SSRIs (including Prozac, Paxil and Zoloft), which are taken for depression, bipolar disease, schizophrenia and other psychiatric disorders. Given the widespread use of SSRIs and some of the other side effects associated with linezolid, we do not believe that linezolid is an option for many patients. We believe there is an opportunity to develop an oral drug that is effective against MRSA and has a safety profile that supports out-patient use, use for chronic indications and use in children.

In 2006, nearly 800,000 total knee or hip arthroplasty procedures were performed in the U.S., with an overall infection rate of approximately 1.0%. It has been predicted that the demand for knee revision surgery will double by 2015, and increase by 673% by the year 2030 as the population ages. With steadily increasing numbers of patients in the U.S. undergoing prosthetic joint surgery, we expect there will be a corresponding increase in the overall incidence of prosthetic joint infections. Prosthetic joint infections usually occur when bacteria enter the area of the prosthesis during implantation. However, they may also occur through other surgical, medical or dental procedures or by accident when the skin or mucous membrane is broken, enabling surface-level bacteria to travel to

the prosthesis. S. aureus species, including MRSA, are the most commonly identified bacterial pathogens involved in prosthetic joint infections.

The methods for the treatment for PJI are variable depending on the severity of the infection and the patient's condition. The infected prosthesis could be saved or could be replaced. The antibiotics used to treat these infections depend on the pathogens involved. Staphylococci are the most frequently identified pathogen in PJI. IDSA has recently issued guidelines for the treatment of PJI (Osmon, et al., 2013). In almost all cases intravenous vancomycin is administered for two to eight weeks, in combination with oral antibiotics such as rifampin, ciprofloxacin, levofloxacin, cefazolin, clindamycin or trimethoprim/sufamethoxazole (Bactrim). The choice of the oral antibiotic is dependent on whether the staphylococcus is MRSA. Rifampin is commonly used with other antibiotics, such as intravenous vancomycin, as its use has been noted to have better outcome. Two-stage revision replacement of an infected prosthesis is most commonly practiced in the U.S. It has been noted that greater than 85% success could be achieved by two-stage revision versus 45% success rate if the prosthesis is retained. These results are in the U.S. where fusidic acid is not available for use. In the two-stage method of treatment, the infected prosthesis is removed, an antibiotic impregnated spacer is installed and the patient is then treated with IV vancomycin for four to six weeks. After that time, the antibiotic is stopped and after six weeks, the joint is cultured to determine if the infection is cleared and a new prosthesis is introduced. Thus, in the U.S., patients undergo at least two surgeries, several weeks of intravenous therapy, as well as oral antibiotics. In Europe and Australia, two-stage revision is less common and the strategy is to debride and treat with intravenous vancomycin and oral rifampin for one to four weeks followed by oral rifampin plus fusidic acid for three months to one to two years. Other oral antibiotics have been used with less success. In the U.S., the debride and retention method is less often used in PJI patients, but when used in these patients, chronic suppression is used for years with a combination of intravenous and oral antibiotics and the treatment is often a failure. According to Data Monitor, physicians indicate that safety is a significant factor for them in choosing antibiotic therapy for osteomyelitis and prosthetic joint infections because the population of patients receiving prosthetic joints tends to be older and the treatment duration is longer. As a result, we believe there is a significant opportunity for a treatment for prosthetic joint infection that is effective against staphylococci, including MRSA, and can be used safely on a long-term basis. Outside of the U.S., fusidic acid has been used successfully in combination with rifampin to achieve high cure rates in selected patients with prosthetic joint infections, without requiring replacement of the prosthesis. In a recent review of clinical experience at an Australian teaching hospital, as well as in the Swiss teaching hospital, treatment of staphylococcal prosthetic joint infection with debridement, prosthesis retention, and oral fusidic acid and rifampin therapy achieved an approximately 88% treatment success rate at one year.

Key Attributes of Taksta

We believe Taksta can be an effective treatment for prosthetic joint infections because of the following key attributes.

Taksta has an established safety profile outside the U.S. Fusidic acid has been approved and used in certain countries in Europe and in Australia for many years, in some countries as many as 40 years, both for short-term use in complicated skin infections as well as for long-term use in other types of infections requiring long-term therapy, including osteomyelitis and prosthetic joint infections. Further, fusidic acid has been used in pediatric populations outside the U.S. and has been safe and well tolerated. As fusidic acid has been in clinical use outside the U.S. for several decades, a substantial body of safety data is in the public domain. Safety data from over 100 published clinical study results involving the oral administration of fusidic acid to over an aggregate of 4,000 patients demonstrated a safety profile consistent with non-U.S. approved product labeling. These data indicate significant worldwide use of fusidic acid, capture clinical experience in the public domain and characterize the safety profile of fusidic acid. The safety data from our Phase 1 and Phase 2 clinical trials are consistent with available historical data and establish that Taksta has a favorable safety and tolerability profile.

Taksta has demonstrated comparable efficacy to the only FDA-approved oral treatment for MRSA. In a Phase 2 trial in 155 ABSSSI patients comparing Taksta to linezolid, Taksta successfully demonstrated efficacy comparable to linezolid and confirmed its effectiveness against *S. aureus* and MRSA. Furthermore, *in vitro* data have demonstrated that Taksta has potent activity against more than 7,300 strains of *S. aureus*, including MRSA strains that are community-acquired MRSA, or CA-MRSA, hospital-acquired MRSA, or HA-MRSA, and other known types of MRSA. We have also conducted tests of Taksta's activity against strains of *S. aureus* that are found in the U.S. and our data show that virtually all of those strains (99.6%) are susceptible to Taksta. As a result of Taksta's broad range of activity against *S. aureus*, physicians could use Taksta to treat a patient with an infected wound or cellulitis without identifying the particular type of *S. aureus* causing the infection. Since fusidic acid has a unique structure and target, there is no known cross-resistance with other antibiotics.

Taksta is an oral therapy for all types of S. aureus, including MRSA. The leading treatments for prosthetic joint infections and ABSSSI caused by MRSA are available only in IV formulations. Linezolid is the only drug currently approved for use against MRSA with an oral formulation. However, its use is associated with serious side effects and cannot be used in certain patient populations without additional monitoring. We believe our ongoing Phase 2 trial and other clinical studies and historical data on fusidic acid demonstrate that Taksta has the potential to be a safe and effective oral treatment for prosthetic joint infections and ABSSSI caused by

MRSA. We believe Taksta would enable physicians to treat patients not otherwise needing hospitalization on an outpatient basis, thereby reducing hospitalization costs and avoiding the unnecessary introduction of resistant bacteria into the hospital setting.

Taksta has a lower incidence of resistance due to our proprietary loading dose regimen. Our in vitro studies have shown that the reason for resistance to fusidic acid that was reported to occur during oral treatment outside the U.S. is that it was not dosed optimally. In addition, published studies of resistance during oral treatment with fusidic acid outside the U.S. conclude that the frequency of resistance is related to the lack of initial potency, which has been addressed in the past by combination therapy. Our innovative loading dose regimen, for which we received a U.S. patent in May 2013, minimizes the development of resistance by increasing the amount of drug initially delivered to the bacteria.

Taksta can be used in patient populations not well served by current treatments. We believe Taksta could also be used for patients that are anemic, as well as patients on serotonergic drugs such as SSRIs who could be treated with an oral antibiotic, but for whom linezolid may not be a viable or convenient treatment option due to side effects and/or increased monitoring requirements. In addition, none of the antibiotics currently on the market can be used for prolonged periods of time to treat chronic staphylococcal infections due to safety concerns. We believe Taksta could fulfill the need for a safe, long-term oral therapy to treat chronic infections such as prosthetic joint infections and osteomyelitis. Furthermore, there are few treatment options for children infected with *S. aureus*, especially MRSA, because in children, IV antibiotics have unpredictable blood levels and are inconvenient to dose. Fusidic acid is available in an oral formulation and has been used in pediatric populations outside the U.S. We intend to develop a pediatric formulation of Taksta to address the need for a safe and effective oral treatment of staphylococci and streptococci in children.

Clinical Data

Fusidic acid has been used outside the U.S. for approximately four decades. However, fusidic acid has never been approved in the U.S. As a result, we must demonstrate that Taksta is active against current strains of staph, including MRSA, that are responsible for infections in the U.S., as well as to show that it is well tolerated at the dosing regimen that we are developing.

Phase 2 Clinical Trial. We have successfully completed a Phase 2 clinical trial in ABSSSI, comparing Taksta to linezolid, which is the only oral antibiotic approved by the FDA for treating MRSA infections. The trial demonstrated that our Taksta loading dose regimen has a favorable safety and tolerability profile with efficacy comparable to linezolid. In this study, patients were stratified by the type of infection, such as wounds and cellulitis, and, through the first 127 patients, were randomized in a 1:1:1 ratio to receive a Taksta non-loading regimen (Taksta 600 mg twice per day which is similar to the dose practically used in the E.U.), a Taksta loading dose regimen (Taksta 1500 mg twice per day on Day 1, followed by 600 mg twice per day), or linezolid (600 mg twice per day, which is the standard approved dose), each administered for 10-14 days. After interim analysis of the initial 127 patients demonstrated comparable safety and tolerability of the two Taksta regimens, the Taksta non-loading dose regimen was dropped in favor of the Taksta loading dose regimen, which was shown to have a lower resistance profile in *in vitro* models, and the remaining patients were randomized in a 1:1 ratio to receive the Taksta loading dose regimen or the linezolid regimen. A total of 155 patients received either the Taksta loading dose regimen or linezolid. The loading dose followed by maintenance dose strategy was designed to ensure a higher concentration of Taksta in the bloodstream at the beginning of the treatment period to rapidly reduce the bacterial population load in an infection, thus limiting resistance development, and to then allow a reduced dose to maintain steady state levels of Taksta in the bloodstream, which increases tolerability.

The results from the Phase 2 trial demonstrated a clinical cure rate comparable to linezolid as described in Table 6 below. The clinical success rates for the Taksta loading dose regimen were comparable to those for the linezolid regimen in the ITT, mITT, CE and ME populations. Respective clinical success rates at the TOC in Taksta loading dose and linezolid treatment groups in the ITT population were 85.9% and 94.8%; in the mITT population, they were 88.1%, and 93.1%; in the CE population, they were 92.3% and 98.5%; and in the ME population, they were 96.0% and 98.0%. Importantly, in patients with documented *S. aureus* infection at baseline, clinical success rates were 95.8% and 97.9%, and with MRSA 96.8% and 100.0%, in the ME population in the Taksta loading dose and linezolid groups, respectively.

Table 6. Taksta Phase 2 Results: Clinical Response at the TOC.

	Treatment Group				
	Ta	ksta	Linezolid		
Population	No. of patients	Success rate, % (95% CI)	No. of patients	Success rate, % (95% CI)	
Intent-to-treat (ITT)		85.9		94.8	
, , ,	67/78	(76.2-92.7)	73/77	(87.2-98.6)	
Microbiological intent-to-treat (mITT)		88.1		93.1	
	52/59	(79.9-95.1)	54/58	(83.3-98.1)	
Clinically evaluable (CE)		92.3		98.5	
	60/65	(83.0-97.5)	67/68	(92.1-100)	
Microbiologically evaluable (ME)		96.0		98.0	
	48/50	(86.3-99.5)	48/49	(89.2-100)	
S. aureus (ME)		95.8		97.9	
	46/48	(85.8-99.5)	47/48	(88.9-100)	
MRSA (ME)		96.8		100.0	
	30/31	(83.3-99.9)	37/37	(90.5-100)	
S. pyogenes (ME)*	1/1	100.0	2/2	100.0	
Streptococcus agalactaie (ME)*	1/2	50.0	0	N/A	
Beta-hemolytic streptococcus, other (ME)*	1/1	100.0	0	N/A	

^(*) Types of beta-hemolytic streptococci.

In August 2010, the FDA published new guidance regarding assessment of outcomes for ABSSSI clinical trials, with an emphasis on assessment of the early response to therapy in the ITT population. Following this guidance, 87.2% of study subjects randomized to the Taksta loading dose arm achieved an early response (defined as both cessation of spread of lesion and absence of fever on treatment Day 3, in patients not otherwise considered a treatment failure) compared to 90.9% of the linezolid subjects, as shown in Table 7 below.

Table 7. Taksta Phase 2 Results: Early Clinical Response (Day 3 Visit) in the ITT Population.

	Taksta Loading Dose (No. of patients, N=78) n (%)	Linezolid (No. of patients, N=77) n (%)
Success	68 (87.2)	70 (90.9)
95% Confidence Interval	77.7-93.7	82.2-96.3
Failure	10 (12.8)	7 (9.1)
Reason for Failure		
Increase in lesion length or width only	6 (7.7)	7 (9.1)
Febrile only	0 (0.0)	0(0.0)
Both increase in lesion length or width and febrile	0 (0.0)	0 (0.0)
Missing lesion data only	0 (0.0)	0(0.0)
Missing temperature data only	0 (0.0)	0(0.0)
Missing both lesion size and		
temperature data	2 (2.6)	0(0.0)
Clinical failure on or prior to Day 3 Visit	2 (2.6)	0 (0.0)

The results of the trial demonstrated Taksta has a favorable safety and tolerability profile with data comparable to linezolid as shown in Table 8 below. Since the study was blinded, we were required to exclude any patient taking SSRIs, who would have required additional monitoring if administered linezolid. Adverse events were reported in 61.5% of patients in the Taksta loading dose group and in 63.6% of patients in the linezolid group. There were no clinically relevant differences between treatment groups in the types or frequency of adverse events, including gastrointestinal events. Notably, the frequency and intensity of nausea and/or vomiting were similar in the Taksta loading dose and the linezolid treatment groups. There were more nervous system adverse events reported for linezolid (16.9% vs. 10.3%) than for Taksta, the majority of which were headaches.

Table 8. Taksta Phase 2 Results: Adverse Events.

Event	Taksta Loading Dose (No. of patients, N=78) n (%)	Linezolid (No. of patients, N=77) n (%)
Any adverse event	48 (61.5)	49 (63.6)
Serious adverse event	3 (3.8)	0 (0.0)
Discontinued treatment due to adverse event	3 (3.8)	0 (0.0)
Adverse event		
Gastrointestinal disorders	31 (39.7)	32 (41.6)
General disorders and administration site condition	5 (6.4)	4 (5.2)
Infections and infestations	8 (10.3)	10 (13.0)
Injury, poisonings, and procedural complications	5 (6.4)	0 (0.0)
Metabolism and nutrition disorders	5 (6.4)	5 (6.5)
Nervous system disorders	8 (10.3)	13 (16.9)
Respiratory, thoracic, and mediastinal disorders	5 (6.4)	2 (2.6)
Skin and subcutaneous tissue disorders	7 (9.0)	13 (16.9)

Three patients in the Taksta loading dose group had at least one serious adverse event (*Herpes simplex*, a serious kidney infection, and head injury and back pain) none of which were considered by the investigator to be related to the study medication. Three patients in the Taksta group discontinued the study medication due to adverse events (nausea and chills; blister and maculopapular rash; and nausea, vomiting and anorexia).

Phase 1 Results. We previously completed Phase 1 single dose, multi-dose and loading dose trials with Taksta between 2007 and 2009. These trials were randomized, double-blinded, placebo-controlled, dose-escalation studies to determine the pharmacokinetics and tolerability of single and multiple doses of Taksta. The effect of food on oral bioavailability was measured and food did not have a significant effect on the oral bioavailability, meaning Taksta can be taken with or without food. There were few adverse events and all were mild in severity. No serious adverse events were seen at the 1650 mg dose. Based on these data, loading dose regimens followed by maintenance dose regimens were considered safe and well tolerated up to a combination of 1650 mg/825 mg of Taksta.

The pharmacokinetics, or PK, of Taksta were investigated in three Phase 1 trials. The first trial of 28 subjects evaluated the relative bioavailability of Taksta 250 mg tablets compared to Fucidin® tablets, the marketed product in Europe, which contains the same API as Taksta but is a different sized tablet, manufactured with different components and dosed differently. This trial also compared the PK of a single oral dose of Taksta 500 mg in the fed versus fasted states. The second trial assessed the PK of multiple oral doses of Taksta 500 mg (2 × 250 mg) administered three times a day for 4.5 consecutive days in 24 healthy subjects. The third trial evaluated the PK of single, multiple, and loading dose regimens of Taksta administered to healthy subjects.

In each trial, Taksta was shown to be generally safe and well tolerated. These trials showed that Taksta had a long plasma half-life and therefore the drug accumulates in the blood over time when administered at the same high dose daily, as evidenced by Taksta showing higher PK after the dose in the second and subsequent periods as compared to the first period. The results of the trial led to the design of the loading dose which would provide high drug levels on Day 1 followed by a steady concentration of Taksta of approximately 80 mcg/ml, which is well over 10 times the MIC_{90} , or the concentration level needed to inhibit 90% of staphylococci and streptococci, the two organisms most frequently found in skin infections.

Pre-Clinical Data

We evaluated the *in vitro* activity of Taksta against prevalent community-acquired, hospital-acquired, and epidemic clones including strains non-susceptible to anti-MRSA agents. We have conducted tests of Taksta's activity against strains of *S. aureus* that are found in the U.S. and our data show that virtually all of those strains (99.6%) are susceptible to Taksta. A collection of 56 MRSA strains from the Network on Antimicrobial Resistance in *Staphylococcus aureus*, or NARSA, and Eurofins Medinet repositories were tested for susceptibility to Taksta and comparators by broth microdilution, a method of testing susceptibility using a semi-solid or liquid growth medium to conduct dilutions in small volumes, in accordance with current Clinical and Laboratory Standards Institute, or CLSI, guidelines. Isolates included those with rare resistance phenotypes, linezolid and daptomycin non-susceptible isolates and isolates from prevalent community, hospital, and epidemic clones. Against the selected resistant MRSA, Taksta had an MIC range of 0.06-8 μ g/mL with an MIC₅₀ and MIC₅₀ of 0.12 μ g/mL. With the exception of one vancomycin intermediate *Staphylococcus aureus*, or VISA, isolate (with an MIC of 1 μ g/mL), two daptomycin non-susceptible isolates (with MICs of 4 μ g/mL), and one linezolid non-susceptible isolate (with an MIC of 8 μ g/mL), Taksta's MICs were 0.06-0.12 μ g/mL against MRSA with rare but emerging resistance phenotypes. Against a subset of 10 community, 10 hospital, and five epidemic clones, Taksta's MICs were 0.06-0.12 μ g/mL. Taksta had potent *in vitro* activity against MRSA non-susceptible to currently approved antibiotics vancomycin, linezolid, and daptomycin. Taksta was also active against USA100 and USA300 MRSA clones of MRSA most likely to be encountered clinically in the U.S. today. Based on its potency and activity, these results highlight the potential of Taksta for the treatment of MRSA in the U.S.

We have continued to determine in vitro activity of Taksta against recent strains S. aureus including MRSA collected in the U.S. The activity of Taksta against *S. aureus* was stable over the four surveyed years (2008-2011). Taksta showed excellent activity against *S. aureus* 3,539 strains collected in the U.S. in 2011, including MRSA strains, with 100% of MRSA from the U.S. susceptible to Taksta. Only eight (0.2%) *S. aureus* strains displaying elevated Taksta MIC values (>1 µg/mL) were detected in the U.S., which likely carried acquired genes *fusB* and *fusC* that confer low level resistance (MIC, 2-8 µg/mL). These genes are usually part of plasmids that can be co-selected by other antimicrobial agents due to the presence of additional resistance genes. These results continue to demonstrate that Taksta could be a valuable alternative for the treatment of staphylococcal infections in the U.S. since the population has not been previously exposed to fusidic acid and resistance is rarely observed among endemic *S. aureus*. Furthermore, low *S. aureus* resistance rates of fusidic acid in Europe are encouraging and suggest that after many years of clinical use, fusidic acid is still a reliable option for the treatment of serious staphylococcal infections.

As required by FDA regulations, we conducted pre-clinical animal studies of Taksta to determine its absorption. The studies indicated that Taksta was not very well absorbed and has a short half-life in animals, resulting in minimum exposure levels which limited the ability to test Taksta in animal models. All pre-clinical tests were benign and indicated no safety or tolerability issues. However, because fusidic acid has been used for several decades in humans outside the U.S. and there is sufficient human clinical trial data for Taksta, we believe that this animal absorption data will not adversely impact our development efforts for Taksta at the FDA.

Compassionate Use Data. We have treated one patient with severe chronic osteomyelitis under our FDA-approved compassionate use program with Taksta. This patient had been treated unsuccessfully with many known antibiotics over a period of two years and was scheduled for a leg amputation. After being treated with Taksta, the patient recovered and the large leg lesion healed; the patient was treated with Taksta for approximately two years. In Canada, where fusidic acid tablets are available, a single patient with S. aureus infected prosthetic joints in both elbows following severe rheumatoid arthritis had failed on all possible oral medications and was scheduled for amputation of one arm. After treatment with higher doses than recommended in Canada and similar to our loading dose regimen, the arm was saved from amputation and the patient has continued on fusidic acid therapy for over four years to date. These results, while encouraging, are preliminary, from a small number of patients and of limited value because they were not obtained in a controlled clinical trial. Furthermore, these results may not be predictive of our future trial results, including the result of our ongoing Phase 2 trial regarding prosthetic joint infections.

Published Ex-U.S. studies of Sodium Fusidate in the Treatment of Bone and Joint Infections. Fusidic acid has been used for more than three decades for treatment of bone and joint infections in Europe and Australia. Atkins and Gottlieb [Atkins 1999] reviewed published experience with fusidic acid in the treatment of bone and joint infections, citing its utility in the treatment of acute and chronic osteomyelitis, vertebral infection, septic arthritis, and prosthetic and other device related infections. The authors considered achievement of effective bone and joint fusidic acid concentrations a key factor in its historical efficacy in the treatment of these conditions.

We used several European and Australian studies as the basis for our ongoing Phase 2 study design for Taksta for the treatment of prosthetic joint infections. The study was published in 2007 by the European Society of Clinical Microbiology and Infectious Diseases. Between 1998 and 2003, 20 patients in St. Vincent's Hospital, a teaching hospital in Melbourne, Australia, were treated for staphylococcal prosthetic joint infection with debridement, prosthesis retention, and IV antibiotic followed by oral fusidic acid and rifampin. Of the patients, 13 had hip joint replacements and seven had knee joint replacements. The median duration of IV treatment was 12 days, the median duration of hospitalization was 20 days and the median duration of oral treatment was 12 months. Two patients reported nausea that was severe enough to require a change of treatment. Two patients reported transient nausea, but continued treatment. No hepatotoxicity was reported. There was no evidence of treatment failure for 18 patients and 16 patients retained their original prosthesis without any evidence of infection after 26 months of follow-up. The cumulative success of treatment after one year was approximately 88%. In a retrospective study of patients with MRSA orthopedic device-related infection in Geneva University Hospitals between 2000-2008, of 41 patients with a median follow up of 391 days, 18 patients experienced treatment failure, involving MRSA persistence or recurrence (Ferry et al., 2010) while none of the 12 patients who received a rifampin-fusidic acid combination therapy followed by intravenous vancomycin and oral rifampin therapy experienced treatment failure.

Lautenbach et al. [1975] measured serum and bone fusidic acid concentrations (by agar plate diffusion methods using a susceptible bacterial strain) in 36 patients with chronic osteomyelitis during the course of therapy; bone concentrations of active drug ranged from 1 to 15 μ g/g, measured at approximately nine hours after last oral dose (in most cases, 20 to 40 mg/kg/day, divided TID). Hierholzer et al. [1966, 1974] measured bone and soft tissue concentrations at three to six hours after last oral dose (500 mg TID dosing for at least five days) in a series of patients with osteomyelitis and found fusidic acid concentrations of 2 to 15 μ g/g in bone and 4 to 17 μ g/g in soft tissue. A second group of patients studied by the same group were administered fusidic acid (500 mg TID, orally) for five to thirteen days prior to surgery for non-infected bone disease; concentrations of fusidic acid in bone were on average up to two times higher than those observed in patients with osteomyelitis, and mean concentrations ranged from 46% to 94% of those observed in serum. Chater, et al. [1972] reported fusidic acid concentrations in bone and serum from seven adult patients treated with 500 mg TID oral fusidic acid for osteomyelitis; concentrations of fusidic acid in bone were similar to those described above, and ranged from 4% to 72% of serum concentrations, with consistently higher soft tissue concentrations (ranging from 20% to >100% of serum concentrations). In summary, oral fusidic acid dosing was found to achieve drug concentrations at the infected bone and joint site that were associated with effective treatment of osteomyelitis across a number of studies.

Rifampin has emerged as a critical antibiotic in the treatment of prosthetic joint infection, attributed to its unique ability to penetrate and disperse biofilms. In a landmark study, Zimmerli and colleagues [Zimmerli 1998] demonstrated the important role of rifampin in the effective treatment of prosthetic joint infection when used in combination with initial IV therapy (vancomycin or flucloxacillin) and follow-on oral antibiotic therapy (ciprofloxacin). In that trial, patients with stable implants and a short duration of infection were effectively treated with the debride and retain strategy, with success in 100% of evaluable patients who received a three to six month course of ciprofloxacin/rifampin therapy. There were no MRSA infections in the study population. Drancourt et al. [1997] demonstrated equivalent efficacy of oral fusidic acid/rifampin to oral ofloxacin/rifampin in a randomized trial of therapy in prosthetic joint infection cases treated with the debride and retain strategy. In a third report of clinical experience with fusidic acid plus rifampin for orthopedic device related infection (comprised principally of joint prostheses and internal fixation devices), Ferry et al. [2010] reported clinical success in 12 of 12 patients. In our ongoing Phase 2 trial for treatment of prosthetic joint infection, Taksta will be co-administered with rifampin, which is believe to further decrease resistance development.

Ongoing and Planned Clinical Trials

We are testing Taksta in two-stage revision treatment of PJI, as this is the standard of care in the U.S. In our ongoing Phase 2 trial, the infected joint will be removed, cultured, a spacer inserted and the patients will then be randomized to either intravenous vancomycin only for three to four days, followed by oral rifampin and Taksta for six weeks in the study arm or an intravenous standard of care for six weeks in the comparator arm. The primary end-point is bacteriologic cure at 12 weeks, at the time the second prosthesis is introduced. The secondary end points are retention of the joint for three to six months and safety. Long-term monitoring for infection relapse or recurrence will continue for the subsequent two years. This study is expected to be conducted in 50 patients with hip or knee PJIs, and the intent is to show non-inferiority to the standard of care for efficacy and to show that two oral drugs can replace an intravenous drug for four to six weeks of treatment. Success in this study could demonstrate a pharmacoeconomic advantage to patients, payers and hospitals, while improving the quality of life. We also have a compassionate use program for those PJI patients where two-stage revision is not possible or necessary. Such a study would replicate the use of fusidic acid overseas and could provide even greater pharmacoeconomic advantages.

We began the open-label Phase 2 trial of Taksta in patients with prosthetic joint infections in December 2012. Based on discussions with the FDA, we revised the protocol to clarify interpretation of end points and expedite trial enrollment. There is no FDA guidance for developing antibiotics for treating PJI, and we designed a Phase 2 trial with a clear endpoint that compares vancomycin, which is the standard of care, to oral fusidic acid and rifampin. Currently, there are 14 sites in the U.S. and additional sites are expected. Although the Phase 2 trial continues to enroll, we believe we have met our primary objectives of the Phase 2 trial, namely safety and efficacy, to determine the study design and dose of our planned Phase 3 trial. We plan to submit the proposed Phase 3 trial protocol to the FDA in early 2014 and discuss our strategy with the FDA in the first half of 2014 in a Type C meeting.

While we previously completed a successful end of Phase 2 meeting with the FDA for Taksta in ABSSSI, at this time, we do not intend to pursue Taksta as a treatment for ABSSI.

Earlier Stage Pipeline Programs

Our earlier stage programs include developing other uses for solithromycin and Taksta, as well as the development of newly discovered compounds as antibiotics and for the treatment of other diseases.

Solithromycin. In the future we may pursue secondary indications for solithromycin to treat other respiratory tract infections such as pharyngitis, sinusitis and chronic bronchitis, as well as other infectious diseases such as infections in CF patients, otitis media (middle ear infection), *Helicobacter* gastritis, malaria, tuberculosis, eye infections and COPD. Of these additional indications, we are currently most interested in COPD and CF infections. In COPD, older macroldies are used, because of their anti-inflammatory properties, to lower the dose of steroids. Solithrormycin has demonstrated anti-inflammatory properties and we plan to test it in a small group of COPD patients.

In CF, the second most common bacteria that infects the lung is *S. aureus*, against which solithromycin has demonstrated activity. In addition, our pre-clinical work suggests that solithromycin is likely to have greater anti-inflammatory properties than azithromycin, which is commonly used in CF patients for its anti-inflammatory properties. Solithromycin has also been demonstrated to have in vitro activity against enterocci, including vancomycin resistant enterocci (VRE).

Taksta. Given the historical use of fusidic acid and its safety profile, we believe Taksta can also address osteomyelitis and infections related to CF, all of which tend to require long-term or chronic treatment, as well as ABSSSI that generally requires seven to 14 days of treatment. Fusidic acid is used in certain countries in Europe to treat *S. aureus* infections in CF patients and is active against 40 *S. aureus* strains isolated from CF clinics in the U.S. All *S. aureus* strains were susceptible to fusidic acid. A CF patient has been treated under our compassionate use program for approximately eight months with some demonstrated symptomatic relief.

Other Research Programs. Shortly after our inception, we entered into a collaborative research and development and license agreement with Optimer Pharmaceuticals, Inc., or Optimer, which was acquired by Cubist Pharmaceuticals, Inc. in October 2013. The license agreement gives us exclusive access to a library of over 500 macrolide compounds, which we have further expanded through our own discovery efforts. Macrolides are complex structures which can be chemically modified to eliminate their antibacterial activities. We intend to use our proprietory macrolide technology platform to develop drugs with no antibiotic effect and replace offlabel use of older macrolides in inflammatory conditions and other indications such as diabetic gastroparesis. Several compounds have been identified through our screening programs that could potentially address therapeutic needs in the areas of inflammation, diabetic gastroparesis and cancer.

We are conducting pre-clinical studies for the use of macrolides in treating diabetic gastroparesis, which is related to a lack of neural response in the gastrointestinal tract of diabetic patients, and gastroesophageal reflux disease, or GERD, both likely to be helped by addressing motilin function. Motilin is a naturally occurring peptide that causes the stomach to contract to initiate the migratory motor complex that empties the stomach. Erythromycin and related antibiotics have known activity as motilin agonists. Through our discovery program, we have selected a lead candidate that is active in the motilin receptor binding assay, functional assays using cloned human motilin receptor in mammalian cells, as well as in rabbit duodenal strip contraction assays. These compounds have been optimized for pharmacokinetic properties and oral bioavailability and are in pre-clinical development.

Our Commercialization Strategy

We will pursue commercialization strategies intended to maximize the value of each product. We plan to develop our product candidates through late-stage clinical studies and, upon approval, either sell our products directly through our own hospital-based sales force, which we would need to assemble, or through partnerships, which we would need to negotiate with larger pharmaceutical companies.

Solithromycin. We expect to be actively engaged in the commercialization process during 2014. This will include commercial assessments and forecasts of key markets, product uptake and penetration studies, pricing and reimbursement research and sales force sizing scenarios. We intend the solithromycin opportunity to be maximized by having a hospital-based sales force, a specialty sales force and a primary care sales force. We believe we could build a sales force to sell directly to the hospital market or in select specialty care markets. A large pharmaceutical company with an established commercial organization may be better positioned to maximize solithromycin sales in the primary care market. There may be an opportunity to partner with a large pharmaceutical company in a manner that enables us to retain either promotion or co-promotion rights in certain markets, such as the hospital market.

We believe solithromycin represents an attractive commercialization opportunity outside the U.S. and we plan to seek commercial partners in selected regions as appropriate. To that end, in May 2013, we entered into a license agreement with Toyama whereby we licensed to Toyama the exclusive right to make, use and sell any product in Japan that incorporates solithromycin as its sole API for human therapeutic uses, other than for ophthalmic indications or any condition, disease or affliction of the ophthalmic tissues. Toyama also has a nonexclusive license in Japan and certain other countries to manufacture or have manufactured API for solithromycin for use in manufacturing such products, subject to limitations and obligations of the concurrently executed supply agreement discussed below. In addition, Toyama has granted us certain rights to intellectual property generated by Toyama under the license agreement with respect to solithromycin or licensed products for use with such products outside Japan or with other solithromycin-based products inside or outside Japan.

The Toyama license is part of our global development program. We will receive all data and information developed by Toyama in all clinical trials and other studies required in Japan. This will add to our data base, and we expect be beneficial as we seek approval for solithromycin in markets outs die of the U.S. and Japan. While we licensed the rights to solithroymcin in Japan to Toyama, we retain the rights to develop it elsewhere in the world.

We also plan to conduct the necessary trials to establish the utility of solithromycin for the treatment of a broader variety of respiratory and other infections including sinusitis, bronchitis and other forms of pneumonia, and plan to align our commercial strategy with the product life cycle plan accordingly.

Taksta. The initial market for Taksta will be in the treatment of prosthetic joint infections. Patients with prosthetic joint infections are generally admitted to the hospital to begin antibiotic treatment and determine whether a debridement procedure that retains the prosthetic joint will be performed or whether the prosthetic joint will be removed. Following whatever procedure is necessary, patients are discharged and treated on an outpatient basis. Subject to finding a collaborative partner, the next market for Taksta would be in the U.S. in the hospital emergency department for treatment of ABSSSI infections. Both markets could also be addressed by the same hospital-based sales force we may build to sell solithromycin.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. Many of our potential competitors have substantially greater financial, technical and human resources than we do and significantly more experience in the discovery, development and regulatory approvals of products, and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render solithromycin, Taksta or any other product candidates that we become obsolete or non-competitive before we can recover the expenses of developing and commercializing any product candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market, as advanced technologies become available and as generic forms of currently branded drugs become available. Finally, the development of new treatment methods for the diseases we are targeting could render our drugs non-competitive or obsolete.

In many cases, however, we believe that competition often will be determined by antibiotic class and any limitations of that antibiotic class in general, and the antibiotic in particular, in treating a particular disease or population. We believe that the key competitive factors that will affect the development and commercial success of solithromycin, Taksta and any other product candidates that we develop are efficacy, safety and tolerability profile, convenience in dosing, price and reimbursement.

We anticipate that, if approved, solithromycin will compete with other antibiotics that demonstrate CABP activity. These include well established, widely prescribed drugs, including generic versions, such as azithromycin, clarithromycin, moxifloxacin, levofloxacin, linezolid and ceftriaxone. Among macrolides, azithromycin (Zithromax, Z-Pak) is the class leader, and a generic drug. Azithromycin is available as oral tablets, lyophilized vials for intravenous and a powder for suspension, which has allowed dosing of all age groups and has been used broadly including for simple respiratory tract infections and in combination with ceftriaxone to treat CABP. Azithromycin and other macrolides are used broadly in COPD for their anti-inflammatory properties to lower the dose of steroids, in bacterial urethritis to treat gonorrhea and Chlamydia infections, and many other infections. Azithromycin is among the most widely used antibiotics. Ceftaroline was approved in CABP, but only the intravenous formulation is available; no oral or powder for suspension for pediatric use is available. For intravenous use in CABP, ceftaroline must be co-administered with azithromycin or another macrolide because it does not provide adequate coverage for atypical bacteria, such as Legionella or Mycoplasma. Patients can stay in the hospital for IV therapy or be discharged on a different, lower potency second generation cephalosporin. Ceftobiprole has failed to get approval in the U.S. and is being evaluated in Europe for CABP. However, it is very similar to ceftaroline in being available for intravenous use. Novaxel's pleuromutilin analog was licensed to Forest Laboratories and returned to them recently. This product could potentially be developed in CABP, but could be cross resistant with the oxazolidinones and chloramphenicol, binding to the same cfr site on the bacterial ribosome, thus potentially having limited ability to fight resistance. We are not aware of any other drugs in development for CABP currently; to our knowledge, the majority in development are being developed for ABSSI and for hospital acquired pneumonia, or HAP. Fluoroquinolones, such as levofloxacin and moxifloxacin, could be used in CABP and are available in oral and IV formulations. They are not approved for pediatric use because of safety. Levofloxacin is now generic and because of its lower potency, its use in CABP has been taken over by the branded moxifloxacin (Avelox). Fluoroquinolones are known for several undesirable effects such as tendonitis, achilles tendon rupture, C. difficile colitis, and hepatotoxicity and central nervous system side effects. These adverse events limit the use of these drugs in CABP. In the area of bacterial urethritis, gonococcus has become resistant to older macrolides and other drugs and only intramuscular ceftriaxone is currently available for treating these patients. A fluoroquinolone is under development for gonorrhea by Melinta Therapeutics, Inc. but has not been tested in a Phase 2 trial yet. Gonorrhea also has shown resistance to fluoroquinolones.

We anticipate that, if approved, Taksta will compete with other antibiotics that demonstrate MRSA activity. These include well established, widely prescribed drugs, including generic versions, such as vancomycin, linezolid, daptomycin, tigecycline and ceftaroline. Among these, intravenous vancomycin is the standard of care. There is no approved oral or intravenous antibiotic for use in PJI. Daptomycin, which is also available for intravenous use only, was tested in PJI and not shown to have an advantage over vancomycin. It is not approved for this indication, but is used in some patients who do not tolerate vancomycin IV. Linezolid is useful for short term oral use but is not approved for PJI and is not approved for chronic oral use. Tedizolid and other oral antibiotics in development are not being tested for chronic use.

Intellectual Property

Due to the length of time and expense associated with bringing new products to market, biopharmaceutical companies have traditionally placed considerable importance on obtaining and maintaining patent protection for significant new technologies, products and processes. solithromycin is a new chemical entity developed from the macrolide library of compounds licensed from Optimer (now owned by Cubist) and is covered by a series of patents and patent applications, which claim, among other things, the composition of matter of solithromycin. The original patents covering the composition of matter for fusidic acid have expired. Our proprietary position for Taksta has two bases. For prosthetic joint infections, if Taksta is the first fusidic acid product approved by the FDA, it would be a new chemical entity, or NCE, and would receive five years of data exclusivity under the Hatch-Waxman Act,

which would be increased to 10 years under the GAIN Act. Taksta was awarded orphan drug status for prosthetic joint infections, which, it approved by the FDA would extend the first exclusivity period to seven years which, together with the five years granted under the GAIN Act, would provide 12 years statutory exclusivity. In addition, we expect that Taksta would also be eligible for pediatric exclusivity. Our loading dose regimen, which received a U.S. patent in May 2013, provides patent protection to 2029.

Our success will depend in part on our ability to protect the proprietary nature of solithromycin, Taksta and our other product candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions, and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation, and in-licensing opportunities to develop and maintain our proprietary position.

We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our technology.

Most of our portfolio consists of intellectual property that we own ourselves or that we exclusively license from Optimer (now owned by Cubist). The intellectual property licensed from Optimer primarily relates to solithromycin and related compounds, and to other macrolide and ketolide compounds. Internally, we typically develop those compounds further and refine them to determine commercial applicability.

We have applied, and are applying, for patents directed to our three main areas of focus: (1) macrolide and ketolide antibiotics, (2) fusidic acid antibiotics, and (3) macrolides and ketolides for non-antibiotic uses, both in the U.S. and, when appropriate, in other countries. As of December 31, 2013, our owned and in-licensed patent portfolio consisted of two issued patents in the U.S., and approximately 40 other patent applications pending worldwide.

With respect to solithromycin and a broad group of macrolide antibiotics, our U.S. patent portfolio consists of two issued U.S. patents, U.S. Patent Nos. 7,601,695 and 8,012,943, each entitled "Novel Antibacterial Agents," which we exclusively license from Optimer. U.S. Patent No. 7,601,695 (US '695) issued on October 13, 2009 and is scheduled to expire in 2025, including a Patent Term Adjustment of 330 days under 35 U.S.C. § 154(b). U.S. Patent No. 8,012,943 (US '943) issued on September 6, 2011, is scheduled to expire in 2024, and does not include a Patent Term Adjustment under 35 U.S.C. § 154(b). The exclusively in-licensed portfolio also includes a continuing patent application of US '695 and US '943 pending in the U.S., corresponding patent applications pending in Canada and Europe (European Patent Convention), and a patent registration that has been initiated in Hong Kong. Prosecution is ongoing in each of those patent applications. Each of the foregoing patents and applications ultimately arise from a PCT international application filed on March 5, 2004, which claims a priority benefit to U.S. provisional applications filed on March 10, 2003, and May 6, 2003.

We have also filed additional patent applications pending in the U.S., Australia, Canada, China, Europe, Israel, India, and Japan that claim related chemical compounds, morphological forms, pharmaceutical compositions, pharmaceutical formulations, methods for treating particular infections and other diseases, and/or manufacturing processes. We are seeking to develop a strategy to increase the breadth of solithromycin coverage, particularly in the U.S., Europe, and Asia, and prosecution is ongoing in each case. We have filed patent applications eligible for worldwide coverage claiming two new crystalline forms of solithromycin. In addition, we have filed patent applications eligible for worldwide coverage claiming processes for manufacturing solithromycin and related compounds from either clarithromycin or erythromycin. Those same patent applications also claim the composition of matter of various intermediates used in those processes, solithromycin and related compounds have also been described by us in U.S. and international patent applications claiming their use in (a) treating bacterial infections arising from one or more resistant bacterial strains, including bacterial strains resistant to other macrolides or ketolides, (b) biowarfare and biodefense applications, (c) treating Mycobacterium infections, including tuberculosis and Mycobacterium avium infections, (d) treating bacterial gastrointestinal diseases, and (e) treating eye infections. We have also filed U.S. and international patent applications claiming pharmaceutical compositions and pharmaceutical formulations of solithromycin and related compounds, including lyophilized forms of solithromycin, parenteral formulations of solithromycin for IV and intramuscular delivery, and topical formulations of solithromycin for ocular delivery. We have filed, or are preparing for filing, U.S. and international patent applications covering solithromycin and other macrolides and ketolides for treating diseases other than infection, including inflammatory diseases, cystic fibrosis, motilin receptor-mediated diseases and malaria to increase the breadth of coverage of other macrolides and ketolides in the U.S., Europe, and Asia.

We have engaged, and continue to engage, in research efforts to exploit the potential of the in-licensed Optimer inventions, including solithromycin and related compounds, in new therapy areas, and to discover new forms and formulations of solithromycin and related compounds. Our research efforts have indicated that solithromycin may also be useful in treating particular bacterial infections that may be considered to be generally untreatable with macrolide antibiotics, including bacterial infections arising from one or more resistant strains. In addition, alternative physical forms and alternative formulations of solithromycin and related

compounds are being developed. If we are able to obtain issued patents for those forms and formulations, and the treatment methods, then we will have several years of additional coverage above and beyond the expiration of the patents covering the chemical composition of solithromycin.

With respect to fusidic acid, we are developing a strategy to increase the breadth of our fusidic acid coverage in the U.S., Europe, and Asia. We have filed patent applications covering fusidic acid in the U.S. and as Patent Cooperation Treaty, or PCT, international patent applications. The fusidate sodium chemical entity itself is a compound which is no longer subject to composition of matter patents in the U.S. Therefore, our pending patent applications claim new dosing protocols and uses of fusidic acid, and new formulations and packaging. In May 2013, we received a U.S. patent, and have filed a related patent application under the Patent Cooperation Treaty on the novel loading dose regimen that has been developed to overcome pre-existing limitations on a broader, more effective use of fusidic acid in the treatment of bacterial infections, including infections not previously considered to be susceptible to fusidic acid, like urethritis, and for new formulations of fusidic acid for direct bronchial and pulmonary delivery. We have also filed patent applications in the U.S. covering new formulations and packaging of fusidic acid dosage units to overcome the storage limitations of fusidic acid. Each of these applications is also eligible for international patent protection.

Our U.S. patent portfolio for Taksta consists of the loading dose regimen, U.S. Patent No. 8,450,300 entitles "Fusidic Acid Dosing Regimens for Treatment of Bacterial Infections."

In addition to filed patent applications claiming new dosing protocols and formulations of fusidic acid for treating infections, we plan to obtain regulatory exclusivity for the first use of fusidic acid through approval with the FDA. We are not aware of any competing applications before the FDA seeking approval for fusidic acid. Therefore, we believe that, if the FDA approves an NDA of ours for Taksta before the FDA approves an NDA or other application for fusidic acid use filed by any competitor, pursuant to amendments to Section 505 of the Food, Drug and Cosmetic Act enacted in 2008, we will have at least five years of regulatory exclusivity in the U.S. for the first approved indication for fusidic acid. We believe that the 2008 amendments will also provide us with three years of exclusivity for any additional uses.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the U.S., a patent's term may be lengthened by Patent Term Adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent. For a more comprehensive discussion of patent term and extensions thereto, please see "Business—Government Regulation and Product Approval."

While we pursue patent protection and enforcement of solithromycin, fusidic acid and our other product candidates, and aspects of our technologies when appropriate, we also rely on trade secrets, know-how and continuing technological advancement to develop and maintain our competitive position. To protect this competitive position, we regularly enter into confidentiality and proprietary information agreements with third parties, including employees, independent contractors, suppliers and collaborators. Our employment policy requires each new employee to enter into an agreement containing provisions generally prohibiting the disclosure of confidential information to anyone outside of our company and providing that any invention conceived by an employee within the scope of his or her employment duties is our exclusive property. We have a similar policy with respect to independent contractors, generally requiring independent contractors to enter into agreements containing provisions generally prohibiting the disclosure of confidential information to anyone outside of our company and providing that any invention conceived by an independent contractor within the scope of his or her services is our exclusive property with the exception of contracts with universities and colleges that may be unable to make such assignments. Furthermore, our know-how that is accessed by third parties through collaborations and research and development contracts and through our relationships with scientific consultants is generally protected through confidentiality agreements with the appropriate parties.

Further, we seek trademark protection in the U.S. and internationally where available and when appropriate. We have a registered trademark in the U.S. for the CEMPRA mark, which we use in connection with our pharmaceutical research and development services, and which we plan to use with our proposed products. We also have received Notices of Allowance from the U.S. Patent and Trademark Office for the TAKSTA, STRAFEX, and STAFREL marks. We plan to use the TAKSTA mark with our proposed sodium fusidate product. The remaining marks may be used with the sodium fusidate product or other proposed products. Because solithromycin will be used as monotherapy in our Phase 3 trials for CABP, we have selected the trial name of "Solitaire".

Collaborations and Commercial Agreements

Optimer Pharmaceuticals, Inc (now owned by Cubist Pharmaceuticals). In March 2006, we entered into a Collaborative Research and Development and License Agreement with Optimer, a biotechnology company focused on discovering, developing and commercializing innovative anti-infective products. Under this agreement, we obtained access to a library of over 500 macrolide compounds, including solithromycin. Optimer was acquired by Cubist in October 2013. Optimer granted us an exclusive license to

these compounds in all countries of the world except ASEAN countries, with the right to sublicense, under Optimer's patents and know-how related to certain macrolide and ketolide antibiotics and related proprietary technology. The exclusivity of our license is potentially subject to the U.S. government's right to obtain a non-exclusive, irrevocable, royalty-free, paid-up right to practice and have practiced certain patents worldwide. As partial consideration for granting us such license, we issued shares of our common stock to Optimer. We also have an obligation to make additional payments upon achievement of specified development, regulatory and commercialization milestones. The aggregate amount of such milestone payments we may need to pay is based in part on the number of products developed under the agreement. The aggregate amount would be \$27.5 million if four products are developed and gain FDA approval. Additional limited milestone payments would be due if we develop more than four products. In July 2010 and July 2012, we made \$0.5 million and \$1.0 million milestone payments, respectively to Optimer after our successful completion of the Phase 1 and Phase 2 trials for oral solithromycin, respectively. We are also obligated to make tiered, mid-single-digit royalty payments to Optimer based on annual net sales of licensed products outside the ASEAN countries, which royalties are subject to reduction in the event additional licenses are obtained from third parties in order to practice our rights under the agreement and/or we are required to grant a compulsory license to a third party.

The agreement also includes the grant of an exclusive license to Optimer and its affiliates, with rights of sublicense, under our patents and other intellectual property in any products covered by the agreement to permit Optimer to develop and/or commercialize such products in ASEAN countries. In consideration of such license, Optimer will pay us \$1.0 million in milestone payments for the first two products that receive regulatory approval or have a first commercial sale in any ASEAN country, as well as tiered, midsingle-digit royalty payments based on net sales of such products, which royalties are subject to reduction in the event additional licenses are obtained from third parties in order to practice Optimer's rights under the agreement and/or Optimer is required to grant a compulsory license to a third party. The agreement also included a collaborative research program, to be performed by the parties, which was completed on March 31, 2008.

The Optimer patents and know-how existing as of the effective date of the agreement and improvements thereof remain the property of Optimer. Except for such improvements, any know-how or inventions developed by Optimer pursuant to the agreement or that relate to the licensed products (except those generated by using grant monies provided by the U.S. government) vest in us subject to the license we granted to Optimer. Optimer has the responsibility to prosecute the Optimer patents relating to macrolide antibiotics. We will be responsible for prosecuting any patents controlled by us that relate to macrolide antibiotics other than the Optimer patents described above. We will have the first right to prosecute patents claiming joint inventions. We have the first right to control any proceeding involving alleged infringement of Optimer patents with respect to rights granted to us under the agreement and Optimer has such right regarding alleged infringement of our patents with respect to rights granted to Optimer under the agreement. Should we exercise our right to control any proceeding involving alleged infringement of Optimer patents, we will be responsible for the costs of these proceedings.

Subject to certain exceptions, on a country-by-country and product-by-product basis, a party's rights and obligations under the agreement continue until the later of: (i) the expiration of the last to expire patent rights of a covered product in the applicable country or (ii) ten years from the first commercial sale of a covered product in the applicable country. As a result, the final expiration date of the Optimer license is indeterminable until the last such patents issue and results of potential patent extensions are known, or each of the first commercial sales are made, as applicable. Upon expiration of the agreement with respect to a particular product and country, the licenses granted in the agreement with respect to such product and country will remain in effect and convert to a perpetual, unrestricted, fully-paid, royalty-free, worldwide license. Either party may terminate the agreement (i) in the event of a material breach by the other party, subject to prior notice and the opportunity to cure, (ii) in the event the other party fails to use diligent efforts to develop and commercialize products in its respective territory, or if the other party makes a determination not to develop and commercialize at least one product under the agreement, or (iii) in the event of the other party's bankruptcy. In the case of these terminations, the terminating party can elect that all licenses granted by the other party survive, subject to continuing royalty, payment and other obligations. Additionally, either party may terminate the agreement for any reason upon 30 days' prior written notice, in which case the non-terminating party can elect that all licenses granted by the other party survive, subject to continuing royalty, payment, and other obligations.

The Scripps Research Institute. Effective June 12, 2012, we entered into a license agreement with The Scripps Research Institute ("TSRI"), whereby TSRI licensed to the Company rights, with rights of sublicense, to make, use, sell, and import products for human or animal therapeutic use that use or incorporate one or more macrolides as an active pharmaceutical ingredient and is covered by certain patent rights owned by TSRI claiming technology related to copper-catalysed ligation of azides and acetylenes. The rights licensed to us are exclusive as to the People's Republic of China (excluding Hong Kong), South Korea and Australia, and are non-exclusive in all other countries worldwide, except the member-nations of the Association of Southeast Asian Nations, which are not included in the territory of the license. Under the terms of the agreement with TSRI, we paid a one-time only, non-refundable license issue fee in the amount of \$350,000 which was charged to research and development expense in the second quarter of 2012. Our rights under the agreement are subject to certain customary rights of the U.S. government that arise or result from TSRI's receipt of research support from the U.S. government.

We are also obligated to pay annual maintenance fees to TSRI in the amount of (i) \$50,000 each year for the first three years (beginning on the first anniversary of the agreement), and (ii) \$85,000 each year thereafter (beginning on the fourth anniversary of the agreement). Each calendar year's annual maintenance fees will be credited against sales royalties due under the agreement for such calendar year. Under the terms of the agreement, we must pay TSRI low single-digit percentage royalties on the net sales of the products covered by the TSRI patents for the life of the TSRI patents, a low single-digit percentage of non-royalty sublicensing revenue received with respect to countries in the nonexclusive territory and a mid-single-digit percentage of sublicensing revenue received with respect to countries in the exclusive territory, with the sublicensing revenue royalty in the exclusive territory and the sales royalties subject to certain reductions under certain circumstances. TSRI is eligible to receive milestone payments of up to \$1.1 million with respect to regulatory approval in the exclusive territory and first commercial sale, in each of the exclusive territory and nonexclusive territory, of the first licensed product to achieve those milestones that is based upon each macrolide covered by the licensed patents. Each milestone is payable once per each macrolide. Each milestone payment made to TSRI with respect to a particular milestone will be creditable against any payment due to TSRI with respect to any sublicense revenues received in connection with the achievement of such milestone. Pursuant to the terms of the Optimer Agreement, any payments made to TSRI under this license for territories subject to the Optimer Agreement can be deducted from any sales-based royalty payments due under the Optimer Agreement up to a certain percentage reduction of the royalties due to Optimer.

Under the terms of the agreement, we are also required to pay additional fees on royalties, sublicensing and milestone payments if we, an affiliate with TSRI, or a sublicensee challenges the validity or enforceability of any of the patents licensed under the agreement. Such increased payments would be required until all patent claims subject to challenge are invalidated in the particular country where such challenge was mounted.

The term of the license agreement (and the period during which we must pay royalties to TSRI in a particular country for a particular product) will end, on a country-by-country and product-by-product basis, at such time as no patent rights licensed from TSRI cover a particular product in the particular country.

Toyama Chemical Co., Ltd. On May 8, 2013, we entered into a license agreement with Toyama whereby we licensed to Toyama the exclusive right, with the right to sublicense, to make, use and sell any product in Japan that incorporates solithromycin as its sole API for human therapeutic uses, other than for ophthalmic indications or any condition, disease or affliction of the ophthalmic tissues. Toyama also has a nonexclusive license in Japan and certain other countries, with the right to sublicense, to manufacture or have manufactured API for solithromycin for use in manufacturing such products, subject to limitations and obligations of the concurrently executed supply agreement discussed below. Toyama has granted us certain rights to intellectual property generated by Toyama under the license agreement with respect to solithromycin or licensed products for use with such products outside Japan or with other solithromycin-based products inside or outside Japan.

As consideration for the execution of the license agreement, Toyama paid us an upfront payment of \$10.0 million. Toyama is also obligated to pay us up to an aggregate of \$60.0 million in milestone payments, depending on the achievement of various regulatory, patent, development and commercial milestones. Under the terms of the license agreement, Toyama must also pay us a royalty equal to a low-to-high first double decimal digit percentage of net sales, subject to downward adjustment in certain circumstances.

The term of the license agreement (and the period during which Toyama must pay royalties under the license agreement) will end, on a product-by-product basis, at the later of: (i) such time as no patent rights under the agreement cover a particular licensed product in Japan; (ii) 15 years after such product is first launched in Japan, or (iii) the first commercial sale in Japan by a third party of a generic equivalent of such licensed product.

Toyama may terminate the license agreement (i) at any time, with or without cause, upon advance notice to us, (ii) upon the occurrence of any serious adverse effect in any human clinical trial of any licensed product that would significantly impact the long term commercial viability of a licensed product in Japan, or (iii) upon our failure to obtain the issuance of certain patents or file for U.S. regulatory approvals by certain dates, or to continue certain key clinical trials. We may terminate the license agreement if Toyama or any of its sublicensees is convicted of a felony relating to the development, manufacture, use, marketing, distribution or sale of a licensed product, or upon Toyama's failure to (i) initiate certain clinical trials in Japan by certain dates, (ii) obtain regulatory approval in Japan within a certain period of completing certain clinical trials in Japan, (iii) launch and commercialize approved licensed products in Japan within a certain period of approval, (iv) use commercially reasonable efforts to market and sell licensed products, or (v) achieve expected benchmarks for net sales of licensed products. Either party may terminate the license agreement due to the other party's insolvency or for uncured material breach.

As part of the license agreement, Toyama and we also entered into a supply agreement, whereby we will be the exclusive supplier (with certain limitations) to Toyama and its sublicensees of API for solithromycin for use in licensed products in Japan, as well as the exclusive supplier to Toyama and its sublicensees of finished forms of solithromycin to be used in Phase 1 and Phase 2 clinical trials in Japan. Pursuant to the supply agreement, Toyama will pay us for such clinical supply of finished product and all

supplies of API for solithromycin for any purpose, other than the manufacture of products for commercial sale in Japan, at prices equal to our costs. All API for solithromycin supplied by us to Toyama for use in the manufacture of finished product for commercial sale in Japan will be ordered from us at prices determined by our manufacturing costs, and which may, depending on such costs, equal, exceed, or be less than such costs. The supply agreement will continue until the expiration or termination of the license agreement. Either party may terminate the supply agreement for an uncured material breach or in the event of insolvency of the other party, with Toyama's right to terminate for our breach subject to certain further conditions in the case of our failure to supply API for solithromycin or clinical supply.

Biomedical Advanced Research and Development Authority. On May 24, 2013 we entered into an agreement with the Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human Services, or BARDA, for the evaluation and development of solithromycin for the treatment of bacterial infections in pediatric populations and infections caused by bioterror threat pathogens, specifically anthrax and tularemia.

The agreement is a cost plus fixed fee development contract, with a base performance segment valued at approximately \$17.7 million, and four option work segments that BARDA may request in its sole discretion. If all four option segments are requested, the cumulative value of the agreement would be approximately \$58 million. Three of the options are cost plus fixed fee arrangements, while the second to last option is a cost sharing arrangement for which we would be responsible for a designated portion of the costs associated with that work segment. The estimated period of performance for the base performance segment is May 24, 2013 through May 23, 2015. If all option segments are requested, this estimated period of performance would be extended until approximately May 23, 2018.

Activities to be conducted for the base performance include, among other things, toxicology studies, pharmacokinetics and pharmacodynamics studies, safety studies, animal model efficacy studies, activities to develop a powder for suspension formulation, and select chemical synthesis activities. In the event that BARDA requests one or more of the option work segments, optional activities to be conducted would include, among other things, additional efficacy studies, Phase 1 and Phase 2/3 clinical studies, dose determination studies and filing of new drug applications. BARDA may terminate this agreement upon our uncurred default in our performance of the agreement or at anytime if the contracting officer determines that it is in the government's interest to terminate the agreement.

Manufacturing

We do not own or operate manufacturing facilities for the production of solithromycin, Taksta or other product candidates that we might develop, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently depend on third-party contract manufacturers for all of our required raw materials, API and finished products for our pre-clinical research and clinical trials. We employ internal resources and third-party consultants to manage our manufacturing contractors.

To date, we have ordered pre-clinical and clinical supplies for solithromycin under short-term contract orders. We employ the services of Wockhardt Limited, or Wockhardt, in Mumbai, India, to produce solithromycin API and finished oral and IV product. We do not have long-term contracts for the commercial supply of solithromycin. If solithromycin is approved for treatment of CABP by the FDA, we intend to enter into agreements with third-party contract manufacturers for the commercial production of solithromycin. We believe there are a number of qualified manufacturers who could supply clinical and commercial quantities of solithromycin.

In January 2013, we entered into a supply agreement with Wockhardt whereby we will purchase from Wockhardt at least 70% of our total annual purchases of solithromycin in any year for clinical or commercial use in humans. Pursuant to the agreement, we may develop alternative sources of solithromycin for the other 30% of our annual needs. In the event that we reasonably believe that Wockhardt will be or is unable to manufacture and/or supply us with our required amounts of solithromycin, we have the right to purchase all or any portion of our solithromycin requirements from such alternate sources. The agreement's initial term runs until December 31, 2019. After the end of the third complete calendar year (i.e. December 31, 2016), and at the end of each calendar year thereafter, the term will automatically extend for an additional year unless either party gives written notice to the other of its intent to terminate prior to the end of such calendar year, in which case the agreement will terminate at the end of the three remaining calendar years of the term.

We have a long term supply arrangement with Ercros, S.A., or Ercros, in Madrid, Spain, in which Ercros agrees to exclusively supply us with fusidic acid in the U.S., and we agree to exclusively obtain our supply of fusidic acid for commercial sale from Ercros, subject to a right to develop a second source for limited supply quantities to produce fusidic acid for Taksta. The supply agreement with Ercros will continue until at least March 2029, subject to earlier termination for our uncured material breach or our bankruptcy or insolvency. In addition, the exclusivity restrictions on Ercros are subject to termination for our failure to file with the FDA an NDA for the sale of Taksta prior to December 31, 2017. We believe Ercros is one of only two currently known manufacturers that can produce fusidic acid compliant with the purity required for human use. Fusidic acid is difficult to produce at these purity levels because of its complex fermentation process. We believe the only other manufacturer of fusidic acid with sufficient purity is Leo

Laboratories, which is using its manufacturing capacity for its own needs. We have yet to identify a viable alternate source of fusidic acid but continue to research alternatives. We intend to utilize a third-party manufacturer to produce the finished dosing formulation of Taksta.

In July 2013, we entered into a development and supply agreement with Hospira Worldwide Inc., or Hospira, whereby Hospira will assist us in the development of an IV form of solithromycin (in glass vials) and will provide our supply of that product for development purposes. If we receive regulatory approval for such form of solithromycin, we will purchase from Hospira at least 80% of our requirements of such product for commercial sale as a human pharmaceutical product in the U.S., the European Union, Canada, Norway and Switzerland (the "Territory"). We will pay one price for clinical supplies of solithromycin and another price for commercial supplies. Beginning in 2014, Hospira may increase the price of the product for commercial use once annually by the increase in Hospira's manufacture of the product or the annual increase of a specified inflation index. The per unit price of our commercial supply will decrease if we purchase specified volumes in a given year. Additionally, we will pay Hospira certain development fees, with specified amounts becoming payable at defined stages of the development of the product. Each year during which we sell the product, we are required to purchase a specified minimum percentage of our forecasted amount of product required for that year. We must supply Hospira at no cost the active pharmaceutical ingredient for the product. If Hospira fails to supply a specified percentage of product, we may purchase all or a portion of our requirements of the product from an alternative supplier until Hospira remedies the supply failure. Unless earlier terminated, the agreement will remain in effect until the end of the third year after the first commercial sale of the product in the Territory. Thereafter, the agreement will automatically renew for an indefinite period. Beginning one year after the first commercial sale of the product in the Territory, either party may terminate the agreement at will upon 24 months' notice. Prior to the completion of the development of the product or the submission of an application for regulatory approval in the Territory, either party may terminate the development project or the agreement if such party determines the development of intravenous solithromycin under the agreement is not clinically, commercially or technically feasible.

Government Regulation and Product Approval

Government authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. solithromycin, Taksta and any other antibiotic product candidate that we develop must be approved by the FDA through the NDA process before they may be legally marketed in the U.S.

U.S. Drug Development Process

In the U.S., the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- Completion of pre-clinical laboratory tests, animal studies and formulation studies according to good laboratory practices, or GLP, or other applicable regulations;
- Submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- Performance of adequate and well-controlled human clinical trials according to the FDA's current good clinical practices, or cGCP, to establish the safety and efficacy of the proposed drug for its intended use;
- Submission to the FDA of an NDA for a new drug;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's cGMPs to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the drug candidate enters the pre-clinical testing stage. Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. The sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Each new clinical protocol must be submitted to the IND for FDA review, and to an Institutional Review Board, or IRB, for approval. Protocols detail, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

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

- *Phase 1*. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2*. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- *Phase 3*. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval studies, or Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

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

U.S. Review and Approval Processes

The results of product development, pre-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, which was reauthorized under the Food and Drug Administration Amendments Act of 2007, or FDAAA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. During the drug approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the drug. If the FDA concludes REMS is needed and notifies the drug sponsor of this decision, the sponsor of the application must submit a proposed REMS; the FDA will not approve a marketing application without a REMS, if required.

In addition, under the FDAAA, all NCEs prior to approval are referred to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions, unless the Secretary of Health and Human Services provides in the action letter on the drug application a summary of the reasons why it was not referred. An advisory committee is a panel of experts who provide advice and recommendations when requested by the FDA on matters of importance that come before the agency. The FDA is not bound by the recommendation of an advisory committee but it generally follows such recommendations.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require Phase 4 testing which involves post-approval clinical trials designed to further assess a drug safety and effectiveness after NDA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Under the Orphan Drug Act, special incentives exist for companies to develop products for rare diseases or conditions, which are defined to include those diseases or conditions that affect fewer than 200,000 people in the U.S. Companies must submit their request that the FDA grant a drug orphan designation prior to submission of an NDA or biologic license application for that product. Products designated as orphan drugs are eligible for special grant funding for research and development, FDA assistance with the review of clinical trial protocols, potential tax credits for research, reduced filing fees for marketing applications, and a special seven-year period of market exclusivity after marketing approval. Orphan drug exclusivity prevents FDA approval of applications by others for the same drug and the designated orphan disease or condition. The FDA may approve a subsequent application from another entity if the FDA determines that the application is for a different drug or different use, or if the FDA determines that the subsequent product is clinically superior, or that the holder of the initial orphan drug approval cannot assure the availability of sufficient quantities of the drug to meet the public's need. A grant of an orphan designation is not a guarantee that a product will be approved. If a sponsor receives orphan drug exclusivity upon approval, there can be no assurance that the exclusivity will prevent another entity or a similar drug from receiving approval for the same or other uses.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits 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. Subject to certain limitations, 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, up to a total of five years. Only one patent applicable to an approved drug is eligible for the extension. The application for such extension must be submitted

prior to the expiration of the patent and within 60 days of the drug's approval. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications of other companies seeking to reference another company's NDA. The FDCA provides a five-year period of non-patent data exclusivity within the U.S. to the first applicant to obtain 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 to one of the patents listed with the FDA by the innovator NDA holder. 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, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example 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 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 and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of exclusivity in the U.S. Pediatric exclusivity, if granted, provides an additional six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study. The current pediatric exclusivity provision was reauthorized in September 2007 as part of the FDAAA.

We believe that both solithromycin and Taksta will benefit from the marketing incentives of the GAIN Act, enacted in 2012. This legislation rewards a Qualified Infectious Disease Product with five years of additional exclusivity (added to the five years of Hatch-Waxman exclusivity) when its NDA is approved. Pursuant to the GAIN Act, in 2013, the FDA designated each of the oral and IV formulations of solithromycin as a QIDP for the indication of CABP, which was designated a qualified infections disease pathogen by the FDA in 2013. The NDA also receives priority review, which reduces the standard 12-month review time by four months. The FDA has designated each of oral and intravenous solithromycin as a QIDP for the indication of CABP, and also has designated the oral form as a QIDP for the treatment of uncomplicated gonococcal infections.

Fusidic acid has been approved for oral use in many countries, including Western countries, outside the U.S. for more than three decades to treat ABSSSI, as well as other types of infections caused by staphylococci and β-hemolytic streptococci, but it has never been approved in the U.S. This is because of the general lack of intellectual property protection that was available for the molecule until recently. Significant patent protection expired in the 1980's, and antibiotics were not eligible for Hatch-Waxman Act data exclusivity, which affords a five-year period of data exclusivity upon approval of a new chemical entity, or NCE, in the U.S. In November 1997, the FDA Modernization Act, or FDAMA, repealed section 507 of the Federal, Food, Drug, and Cosmetic Act, or FDCA, under which marketing applications for antibiotics were previously approved. This law made antibiotics, like other drugs, eligible for Hatch-Waxman Act exclusivity. However, fusidate/fusidic acid was the subject of a marketing application received by FDA under Section 507 of the FDCA before November 21, 1997, the effective date of FDAMA. Antibiotics for which marketing applications were submitted before that date, even if the application was not approved, as was the case with fusidic acid, are known as "old" antibiotics. Old antibiotics were not eligible for the exclusivity provisions afforded by FDAMA. Consequently, although fusidic acid had never been approved in the U.S., as an old antibiotic, it was not eligible for the five-year NCE exclusivity. The passage of Public Law (PL) 110-379 on October 8, 2008, allowed old antibiotics such as fusidic acid to obtain five-year NCE exclusivity upon NDA approval, thereby making development of fusidic acid for the U.S. feasible. In response to our question based on unclear language in PL 110-379 regarding other exclusivities, we received notification from the FDA in January 2011 that old antibiotics such as fusidic acid would also be eligible for orphan and pediatric exclusivity. In October 2013, the FDA granted orphan drug designation for fusidic acid for the treatment of PJI. In December 2013, PJI was classified as a very rare disease by the National Institutes of Health, or NIH. In addition, the GAIN Act extends the NCE data exclusivity period for QIDPs such as fusidic acid from five years to 10 years. Finally, our loading dose regimen, which received a U.S. patent in May 2013, provides patent protection to 2029.

Post-Approval Requirements

Any drug product for which we receive FDA approval will be subject to continuing regulation by the FDA, including, among other things, record keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, cGMP requirements, complying with certain electronic

records and signature requirements and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Future FDA and state 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, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems (quality or safety) occur after the product reaches the market. Later discovery of previously unknown quality, safety, or other problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

In addition, from time to time, legislation is drafted, introduced and passed in the U.S. Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, in September 2007, the FDAAA was enacted giving the FDA enhanced post-market authority, including the authority to require post-market studies and clinical trials, labeling changes based on new safety information and compliance with a risk evaluation and mitigation strategy. Failure to comply with any requirements under the new law may result in significant penalties. The law also authorized significant civil money penalties for the dissemination of false or misleading direct-to-consumer advertisements and allows the FDA to require companies to submit direct-to-consumer television drug advertisements for FDA review prior to public dissemination. Additionally, the law expanded the clinical trial registry so that sponsors of all clinical trials, except for Phase 1 clinical trials, are required to submit certain clinical trial information for inclusion in the clinical trial registry data bank. In addition to this legislation, the FDA regulations and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

Other U.S. Health Care Laws and Compliance Requirements

In the U.S., our activities are subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration), other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Under the Veterans Health Care Act, or VHCA, drug companies are required to offer certain drugs at a reduced price to a number of federal agencies including U.S. Department of Veterans Affairs and U.S. Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs including Medicare and Medicaid. Recent legislative changes purport to require that discounted prices be offered for certain U.S. Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities or register their sales representatives, as well as prohibiting pharmacies and other health care entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and prohibiting certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Foreign Regulation

In addition to regulations in the U.S., we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to sell any products outside of the U.S. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

E.U. member states require both regulatory clearances by the national competent authority and a favorable ethics committee opinion prior to the commencement of a clinical trial. Under the E.U. regulatory systems, we may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, conducted by the EMA, provides for the grant of a single marketing authorization that is valid for all E.U. member states. The centralized procedure is compulsory for medicines produced by certain biotechnological processes, products with a new active substance indicated for the treatment of certain diseases such as neurodegenerative disorder or diabetes and products designated as orphan medicinal products and optional for those products which are highly innovative or for which a centralized process is in the interest of patients. The decentralized procedure of approval provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials (draft summary of product characteristics, draft labeling and package leaflet) to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

We have presented to and received feedback from several E.U. member countries regarding our plan to submit an MAA to the EMA. As part of this, we have submitted a PIP to the EMA for the suspension formulation of solithromycin to treat CABP in pediatric patients.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the U.S. and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend considerably on the availability of reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our products may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In 2003, the U.S. government enacted legislation providing a prescription drug benefit for Medicare recipients, which became effective at the beginning of 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, to obtain payments under this program, we would be required to sell products to Medicare recipients through prescription drug plans operating pursuant to this legislation. These plans will likely negotiate discounted prices for our products. In March 2010, the Patient Protection and Affordable Care Act became law, which substantially changed the way healthcare is financed by both governmental and private insurers. We anticipate that this legislation will result in additional downward pressure on coverage and the price that we receive for any approved product. Federal, state and local governments in the U.S. continue to consider legislation to limit the growth of health care costs, including the cost of prescription drugs. Future legislation could limit payments for pharmaceuticals such as the drug candidates that we are developing.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of our particular drug products to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control

company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the U.S. has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Corporate History and Information

We were formed as Cempra Holdings, LLC, a limited liability company under the laws of the State of Delaware, on May 16, 2008. Cempra Holdings, LLC was formed in connection with a reorganization whereby the stockholders of Cempra Pharmaceuticals, Inc., a corporation formed under the laws of the State of Delaware on November 18, 2005, exchanged their shares of Cempra Pharmaceuticals, Inc. stock for shares of Cempra Holdings, LLC, pursuant to a merger of a subsidiary of Cempra Holdings, LLC with and into Cempra Pharmaceuticals, Inc., as a result of which Cempra Pharmaceuticals, Inc. became a wholly owned subsidiary of Cempra Holdings, LLC. On January 29, 2012, we effected a 1-for-9.5 reverse stock split of all of our common and preferred shares. The ratio for the reverse stock split was determined by our Board of Directors. The reverse stock split was approved by the holders of our pre-conversion common and preferred shares. All share and per share amounts referred to in this report have been adjusted to reflect the effect of the 1-for-9.5 reverse stock split.

On February 2, 2012, Cempra Holdings, LLC converted from a Delaware limited liability company to a Delaware corporation and was renamed Cempra, Inc. As a result of the corporate conversion, the holders of common shares of Cempra Holdings, LLC became holders of shares of common stock of Cempra, Inc. and the holders of preferred shares of Cempra Holdings, LLC became holders of shares of common stock of Cempra, Inc. Holders of options to purchase common shares of Cempra Holdings, LLC became holders of options to purchase shares of common stock of Cempra, Inc. Holders of notes convertible into preferred shares of Cempra Holdings, LLC and associated warrants exercisable for preferred shares of Cempra Holdings, LLC became holders of shares of common stock and warrants to purchase shares of common stock of Cempra, Inc.

We effected the reverse stock split and the corporate conversion in conjunction with our initial public offering, or IPO, which closed on February 8, 2012.

We have two subsidiaries, Cempra Pharmaceuticals, Inc. and CEM-102 Pharmaceuticals, Inc. Our primary executive offices are located at 6320 Quadrangle Drive, Suite 360, Chapel Hill, NC 27517-8149, and our telephone number is (919) 313-6601. Our website address is http://www.cempra.com. The information contained in, or that can be accessed through, our website is not part of this report.

Employees

As of February 20, 2014, we had 38 employees, 15 of whom hold Ph.D. or M.D. degrees. Twenty eight of our employees were engaged in research and development activities and ten were engaged in support administration, including business development and finance. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

Item 1A. Risk Factors

This report contains forward-looking statements that involve risks and uncertainties. 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 below and elsewhere in this report and in any documents incorporated in this report by reference.

If any of the following risks, 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 are heavily dependent on the success of solithromycin and Taksta, which are still under clinical development. The FDA and foreign regulatory approval process is lengthy, time consuming and inherently unpredictable and if we are ultimately unable to obtain regulatory approval for solithromycin or Taksta our business will be substantially harmed.

We have no products that have been approved for sale. Our near-term prospects are substantially dependent on our ability to develop and commercialize solithromycin and Taksta. We cannot commercialize, market or sell either product in the U.S. without FDA approval. FDA approval, if received, is several years away at least. To commercialize solithromycin outside of the U.S., we would need applicable foreign regulatory approval. The clinical development of solithromycin and Taksta is susceptible to the risk of failure inherent in any stage of drug development, including failure to achieve efficacy across a broad population of patients, the occurrence of severe adverse events and the FDA or any applicable foreign regulatory authority determining that a drug product is not approvable.

The process required to obtain approval for commercialization from the FDA and similar foreign authorities is unpredictable, and typically takes many years following the commencement of clinical trials depending on numerous factors. In addition, approval policies, regulations, or the type and amount of clinical data necessary to obtain regulatory approval may change during the course of a product's clinical development. We may fail to obtain regulatory approval for solithromycin, Taksta or any other product candidates for many reasons, including the following:

- we may not be able to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for any indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval, and/or the FDA may require additional, expensive trials;
- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may not be able to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- we may not be able to demonstrate that a product candidate is non-inferior or superior to the current standard of care, future competitive therapies in development, or over placebo in any indications for which the FDA requires a placebocontrolled trial;
- the data collected from clinical trials of any product candidates that we develop may not be sufficient to support the submission of a new drug application, or NDA, or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- while we have a pathway based on an end of Phase 2 meeting, there can be no assurance that the FDA will not change its position and require additional trials based on results;
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- the FDA or comparable foreign regulatory authorities may not accept data generated at our clinical trial sites;
- the FDA or comparable foreign regulatory authorities may fail to approve the clinical practices of the third party clinical research organizations, or CROs, we use for clinical trials; and
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators enter into agreements for clinical and commercial supplies.

This lengthy approval process as well as the unpredictability of future clinical trial results may prevent us from obtaining regulatory approval to market solithromycin, Taksta or any future product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive, can take many years to complete and its outcome is highly uncertain. Failure can occur at any time during the clinical trial process due to inadequate performance of a drug or inadequate adherence by patients or investigators to clinical trial protocols. Pursuant to FDA guidelines, new drugs must show non-inferiority or superiority to existing approved treatments. We have conducted our solithromycin for CABP clinical trials pursuant to proposed guidelines published by the FDA for drugs being developed for the treatment of CABP. To date, those clinical trials demonstrate solithromycin are comparable to current standard of care. However, because the number of patients in our Phase 2 trial for the oral formulation of solithromycin was small, our results were not powered to show, and did not show, statistical non-inferiority. If in our ongoing and any later clinical trials solithromycin fails to demonstrate safety and/or superiority or non-inferiority according to FDA guidelines, the FDA will not approve that product candidate and we would not be able to commercialize it, which will have a material adverse effect on our business, financial condition, results of operations and prospects.

Our ongoing and planned Phase 3 trials for solithromycin may be more expensive and time consuming than we currently expect. FDA regulations require two Phase 3 trials for any drug for which an NDA is submitted. Based on FDA guidance, we believe that we will only need to conduct one Phase 3 trial for oral solithromycin and one Phase 3 IV-to-oral trial because we believe we will have developed the necessary data to support our planned NDA and satisfy the FDA requirement. However, the FDA may disagree with our assessment and may require additional clinical data to support approval. Any expanded or additional trials, for whatever reason, would add to the time and cost of solithromycin's development.

In addition, the results of pre-clinical studies and early clinical trials of product candidates may not be predictive of the results of later-stage clinical trials. A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than us, have suffered significant setbacks in Phase 2 and Phase 3 clinical trials despite achieving successful results in earlier stage trials. The failure to obtain positive results in any of our Phase 2 or Phase 3 clinical trials could seriously impair the development prospects, and even prevent regulatory approval, of solithromycin or Taksta or any candidate in our existing proprietary macrolide library.

We have no experience as a company in bringing a drug to regulatory approval.

As a company, we have never obtained regulatory approval for, or commercialized, a drug. It is possible that the FDA may refuse to accept any or all of our planned NDAs for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval of solithromycin, Taksta or any future product candidates. If the FDA does not accept or approve any or all of our planned NDAs, it may require that we conduct additional clinical, pre-clinical or manufacturing validation studies, which may be costly, and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA required studies, approval of any NDA or application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. Any delay in obtaining, or an inability to obtain, regulatory approvals would prevent us from commercializing solithromycin or Taksta, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any NDA we submit. If any of these outcomes occur, we may be forced to abandon our planned NDAs for either solithromycin or Taksta or both, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for any approval in a foreign jurisdiction.

Future legislation, and/or regulations and policies adopted by the FDA or other regulatory health authorities may increase the time and cost required for us to conduct and complete clinical trials for solithromycin, Taksta or other product candidates that we develop.

The FDA has established regulations, guidelines and policies to govern the drug development and approval process, as have foreign regulatory authorities. Any change in regulatory requirements due to the adoption by the FDA and/or foreign regulatory authorities of new legislation, regulations, or policies may require us to amend existing clinical trial protocols or add new clinical trials to comply with these changes. Such amendments to existing protocols and/or clinical trial applications or the need for new ones, may significantly impact the cost, timing and completion of the clinical trials.

In particular, drugs being tested and/or developed for the treatment of CABP, including solithromycin, are subject to proposed guidelines published by the FDA in March 2009 (with new guidelines proposed in November 2011). We have conducted our clinical trials to date according to the standards established by these proposed guidelines, but we expect the FDA will revise the proposed guidelines for CABP before we submit our NDA for solithromycin. Any new proposed guidelines may require us to conduct

additional clinical trials, re-run previously completed trials to gather data at different endpoints or according to different protocols, or otherwise materially alter our planned clinical development of solithromycin. Any such regulatory change may materially increase our costs, delay the completion of our clinical trials, and otherwise impact our ability to obtain regulatory approval for our product candidate. Furthermore, the FDA's guidance documents are not binding on the FDA. As a result, the FDA may not accept the results of clinical trials we conduct even though they follow the FDA's most recent guidance.

In addition, increased scrutiny by the U.S. Congress of the FDA's approval process, particularly in our areas of focus, may significantly delay or prevent regulatory approval, as well as impose more stringent product labeling and post-marketing testing and other requirements.

We might not successfully differentiate solithromycin from telithromycin (Ketek®), a macrolide found to cause severe side effects.

Ketek is a macrolide antibiotic that the FDA approved in 2004 for the treatment of multi-drug resistant pneumococci and other CABP bacteria. Soon after release, however, Ketek was found to cause reversible visual disturbances, exacerbate myasthenia gravis (a neurological disorder characterized by improper muscle regulation) and cause liver failure. These effects led the FDA to require the drug label for Ketek to include a strengthened warning section regarding specific drug-related adverse events and contributed to Ketek being withdrawn in 2007 for the treatment of all infections other than CABP. Our research suggests these side effects are likely caused by pyridine, which is a component of Ketek. Solithromycin and older generation macrolides, including azithromycin and clarithromycin, do not have a pyridine component, which we have demonstrated inhibits the action of nicotinic acid acetylcholine receptors that could result in the side effects caused by Ketek. If our research is proven to be incorrect or if solithromycin demonstrates similar side effects, the FDA might not approve solithromycin, or, if already approved, might withdraw approval, require us to conduct additional clinical trials or require warnings on product labeling, which would significantly harm our ability to generate revenues from solithromycin. Even if the FDA approves solithromycin, physicians may not be convinced that solithromycin is a safe and effective treatment for CABP and other infections. If physicians believe solithromycin demonstrates characteristics similar to Ketek, they might not prescribe solithromycin, which would negatively affect our revenues.

Bacteria might develop resistance to solithromycin or Taksta, which would decrease the efficacy and commercial viability of that product.

Drug resistance is primarily caused by the genetic mutation of bacteria resulting from sub-optimal exposure to antibiotics where the drug does not kill all of the bacteria. While antibiotics have been developed to treat many of the most common infections, the extent and duration of their use worldwide has resulted in new mutated strains of bacteria resistant to current treatments. We are developing solithromycin and Taksta to treat patients infected with drug-resistant bacteria. With respect to solithromycin, which is a next generation macrolide, resistance issues associated with earlier generations of macrolides have led to a decrease in their use for treating serious respiratory tract infections such as CABP. If physicians, rightly or wrongly, associate the resistance issues of earlier generation macrolides with solithromycin, physicians might not prescribe solithromycin for treating a broad range of infections. Similarly, resistance to fusidic acid has developed outside the U.S. Our *in vitro* studies have shown that the reason for resistance to the oral formulation is that it was not dosed optimally. We believe that overuse of topical formulations of fusidic acid also contributed to development of resistance outside the U.S. If Taksta is improperly dosed, or if our studies incorrectly attributed an increase in resistance to inappropriate dosing, bacteria might develop resistance to Taksta in the U.S. If these bacteria develop resistance to solithromycin or Taksta, the efficacy of these products would decline, which would negatively affect our potential to generate revenues from these products.

Delays in clinical trials are common and have many causes, and any such delays could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales as currently contemplated.

We may experience delays in clinical trials of our product candidates. Our planned clinical trials might not begin on time, may be interrupted or delayed once commenced, might need to be redesigned, might not enroll a sufficient number of patients or might not be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including the following:

- delays in obtaining regulatory approval to commence a trial;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in obtaining required institutional review board, or IRB, approval at each site;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in recruiting suitable patients to participate in a trial;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;

- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new sites;
- delays in obtaining sufficient supplies of clinical trial materials, including suitable active pharmaceutical ingredient, or API: or
- delays resulting from negative or equivocal findings of the data safety monitoring board, or DSMB, for a trial.

We were subject to such a delay in 2008 when the FDA placed a partial clinical hold on our Phase 2 clinical trial for oral solithromycin over concern about possible toxicity related to solithromycin. The FDA converted the partial clinical hold into a full clinical hold in April 2010. At the time, the FDA had concerns that solithromycin, as a fluoroketolide, may have similar toxicity issues as Ketek. While we addressed the FDA's concerns and were allowed to proceed with the trial, which we successfully completed, the trial was delayed by approximately 12 months. While the FDA reviewed our overall development plan for solithromycin, either the oral or IV-to-oral Phase 3 clinical trial could be delayed for the reasons noted above.

In addition, we are evaluating alternative IV solutions of solithromycin to develop the optimal solution and may experience delays in the commencement of our planned Phase 3 IV-to-oral trial if we cannot develop the solution in a timely or cost-effective manner.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. In addition, the timing of our clinical trials for solithromycin is dependent on the onset, degree and timing of the CABP season, which tends to occur in the winter months in each hemisphere. We could encounter delays in our clinical trials of solithromycin or Taksta if participating physician investigators encounter unresolved ethical issues associated with enrolling patients in clinical trials of solithromycin or Taksta in lieu of prescribing approved antibiotics that have established safety and efficacy profiles. Any of these delays in completing our clinical trials could increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenues.

We may be required to suspend or discontinue clinical trials due to adverse side effects or other safety risks that could preclude approval of solithromycin or Taksta or any of our future product candidates.

Our clinical trials may be suspended or terminated at any time for a number of reasons. A clinical trial may be suspended or terminated by us, our collaborators, the FDA or other regulatory authorities due to a failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, presentation of unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using the investigational drug, changes in governmental regulations or administrative actions, lack of adequate funding to continue the clinical trial, or negative or equivocal findings of the DSMB or the IRB for a clinical trial. An IRB may also suspend or terminate our clinical trials for failure to protect patient safety or patient rights. We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants. In addition, regulatory agencies may order the temporary or permanent discontinuation of our clinical trials at any time if they believe the clinical trials are not being conducted in accordance with applicable regulatory requirements or present an unacceptable safety risk to participants. If we elect or are forced to suspend or terminate any clinical trial of any product candidates that we are developing, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues, if at all, from any of these product candidates will be delayed or eliminated. Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly.

We have not completed a clinical trial of Taksta for the treatment of prosthetic joint infections and there is no guarantee that the results of our ongoing Phase 2 trial or any other trial we conduct will be consistent with the results of any trials conducted to date or will demonstrate safety and efficacy to the satisfaction of the FDA.

We initiated, in December 2012, our Phase 2 clinical trial of Taksta for the treatment of prosthetic joint infections. While we have successfully completed a Phase 2 clinical trial comparing Taksta to linezolid for the treatment of ABSSSI the results of our completed Phase 2 trial for the treatment of ABSSSI were not powered to show, and did not show, statistical non-inferiority. Comparisons to results from other reported clinical trials, including our completed Phase 2 clinical trial for the treatment of ABSSSI, can assist in evaluating the potential efficacy of Taksta for the treatment of prosthetic joint infections; however, there are many factors that affect the outcome for patients in clinical trials, some of which are not apparent in published reports, and results from different trials often cannot be reliably compared. Therefore, there is no assurance that the results of any other trials we conduct for Taksta in the treatment of prosthetic joint infections will demonstrate safety and efficacy comparable to the results of trials conducted to date or will be sufficient to attain FDA approval.

We previously completed our end of Phase 2 meeting with the FDA for Taksta with respect to the treatment of ABSSSI. In October 2013, the FDA granted orphan drug designation to Taksta for the treatment of PJI. There is no published FDA guidance for clinical trials for PJI. Further, we need to determine the impact of the orphan drug designation on our clinical development plan and the planned clinical trial to support an NDA. Although the Phase 2 trial continues to enroll, we believe we have met our primary objectives of the Phase 2 trial, namely safety and efficacy, to determine the study design and dose of our planned Phase 3 trial. We intend to submit our planned clinical trial protocol to support an NDA submission for Taksta as a treatment for prosthetic joint infections with the FDA in early 2014 and plan to discuss the protocol with the FDA in the first half of 2014. If the Phase 2 trial data results are inadequate or the FDA believes that the plan is inadequate, it could delay or prevent our ability to receive regulatory approval or commercialize Taksta for the treatment of prosthetic joint infections.

Taksta is not well absorbed in animals, which could impair our ability to obtain FDA approval.

As required by FDA regulations, we conducted pre-clinical studies of Taksta to determine its level of absorption in animals. The studies indicated that Taksta is not very well absorbed and has a short half-life in animals, resulting in minimum exposure levels which limited the ability to test Taksta in animal models. Fusidic acid, the API in Taksta, has been used for several decades in humans outside the U.S. and we believe there is sufficient human clinical trial data for Taksta to overcome the lack of absorption in animal studies. Despite this human data, and while all of our pre-clinical tests were benign and indicated no safety or tolerability issues, our limited ability to test Taksta in animal models may adversely affect our ability to obtain FDA approval.

Even if the FDA approves solithromycin for the treatment of CABP and Taksta for the treatment of prosthetic joint infections, adverse effects discovered after approval could adversely affect the market for those products.

If we obtain regulatory approval for solithromycin, Taksta or any other product candidate that we develop, and we or others later discover that our products cause adverse effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered, conduct additional clinical studies, implement a risk evaluation and mitigation strategy, or REMS, or restrict the distribution of the product;
- we could be sued and held liable for harm caused to patients and our liability insurance may not adequately cover those claims; and
- our reputation may suffer.

Any of these events could prevent us from maintaining market acceptance of the affected product candidate and could substantially increase the costs of, or prevent altogether, the commercialization of our product candidates.

We continue to have negative cash flows from operations since inception and might not be able to generate sufficient cash to service our existing indebtedness to Hercules Technology Growth Capital, Inc., the level of which indebtedness could have a material adverse effect on our business, financial condition, results of operations and prospects.

On December 20, 2011, we entered into a loan and security agreement with Hercules Technology Growth Capital, Inc., or Hercules, pursuant to which we borrowed \$10.0 million. We must repay the indebtedness on or before December 1, 2015. In addition, at the time that the loan is either due or prepaid, we must pay Hercules a fee of \$400,000. On May 31, 2013, we entered into an Amendment No. 2 to Loan and Security Agreement with Hercules, pursuant to which Hercules agreed to provide us with additional credit of approximately \$5.2 million, which amount we borrowed at closing. We paid Hercules a facility charge of \$250,000 at closing. We also received an extension through September 30, 2013 for borrowing the remaining \$10.0 million available under the loan and security agreement dated December 20, 2011; we elected not to request any additional borrowing and let the option expire on September 30, 2013. In addition, at the earlier of the time the loan is prepaid, the time it is accelerated or June 1, 2017, we must pay Hercules a fee of \$495,245. Our ability to make payments on this indebtedness depends on our ability to generate cash in the future. We expect to experience negative cash flow for the foreseeable future as we fund our operations and capital expenditures. There can be no assurance that we will be in a position to repay this indebtedness when due or obtain extensions of the maturity date. We anticipate that we will need to secure additional funding in order for us to be able to satisfy our obligations when due. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If that additional funding involves the sale of equity securities or convertible securities, it would result in the issuance of additional shares of our capital stock, which would result in dilution to our stockholders.

Moreover, this level of debt could have important consequences to you as an investor in our securities. For example, it could:

make it more difficult for us to satisfy our obligations with respect to payments owed to our licensors;

- limit our flexibility in planning for the development, clinical testing, approval and marketing of our products;
- place us at a competitive disadvantage compared to any of our competitors that are less leveraged than we are;
- increase our vulnerability to both general and industry-specific adverse economic conditions; and
- limit our ability to obtain additional funds.

In addition, the loan is secured by all of our assets except our intellectual property. In the event we fail to make timely payments or breach any of our representations or other obligations in the agreement, or upon any circumstance or occurrence that has a material adverse effect on the loan collateral, our business operations, properties, assets, prospects or condition, or our ability to perform our obligations under the loan agreement, Hercules can declare the loan in default. Upon an event of default, the loan principal and accrued interest would become immediately due and payable and Hercules would be entitled to enforce its security interest in our assets.

The addition of further debt to our current debt levels could make it more difficult for us to repay our indebtedness and meet our other obligations and would intensify the leverage-related risks that we now face.

If we fail to obtain additional financing, we may not be able to complete the development and commercialization of solithromycin or Taksta.

We need substantial amounts of cash to complete the clinical development of solithromycin and Taksta. Based on current assumptions and our estimates of costs and timelines for the development of solithromycin for the treatment of CABP and our existing cash and equivalents as of December 31, 2013, we expect that we have sufficient funds in hand to complete the enrollment of our two Phase 3clinical trials and to complete the two ancillary clinical studies currently expected to be necessary to support the planned NDA for solithromycin for the treatment of CABP. However, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. For example, our clinical trials may encounter technical, enrollment or other issues that could cause our development costs to increase more than we expect and we may be required to conduct additional trials requested by the FDA that could increase our costs significantly. We would also need to raise additional funds sooner if we choose to initiate clinical trials more rapidly than we presently anticipate or if we elect to conduct additional trials for alternate indications. In any event, the costs to develop solithromycin beyond our ongoing Phase 3 oral and IV-to-oral trials and Taksta beyond our ongoing Phase 2 trial will be significant and we will need to raise additional capital to continue those development activities to obtain regulatory approval of and to commercialize solithromycin and Taksta.

We may raise additional capital from the issuance of equity and/or debt securities, collaborations with third parties, outlicensing of rights to our product candidates and other means, or a combination of any of the above. Securing additional financing, however, will require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from our day-to-day activities, which may adversely affect our management's ability to conduct our day-to-day operations. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the development or commercialization of solithromycin and/or Taksta;
- seek collaborators for solithromycin and/or Taksta at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; and
- relinquish or license, potentially on unfavorable terms, our rights to solithromycin and/or Taksta that we otherwise would seek to develop or commercialize ourselves.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing discovery, development and commercialization efforts, and our ability to generate revenues and achieve or sustain profitability will be substantially harmed.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be delayed in obtaining, or may ultimately not be able to obtain, regulatory approval for or commercialize solithromycin, Taksta or any other product candidates.

We have relied, and plan to continue to rely, on various CROs to recruit patients, monitor and manage data for our on-going clinical programs for solithromycin and Taksta, as well as for the execution of our pre-clinical and non-clinical studies. We control only certain aspects of our CROs' activities; nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with the FDA's current good clinical practices, or cGCPs,

which are regulations and guidelines enforced by the FDA for all of our products in clinical development. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA may require us to perform additional clinical trials before approving our product candidates. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, to evaluate the safety and effectiveness of solithromycin and Taksta to a statistically significant degree our clinical trials will require an adequately large number of test subjects. Any clinical trial that a CRO conducts abroad on our behalf is subject to similar regulation. Accordingly, if our CROs fail to comply with these regulations or recruit a sufficient number of patients, we may have to repeat clinical trials, which would delay the regulatory approval process.

In addition, our CROs are not our employees and we cannot control whether or not they devote sufficient time and resources to our on-going clinical, non-clinical and pre-clinical programs. Our CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If our CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize solithromycin, Taksta or any other product candidates that we seek to develop. As a result, our financial results and the commercial prospects for solithromycin, Taksta or any other product candidates that we seek to develop would be harmed, our costs could increase and our ability to generate revenues could be delayed or ended.

We typically engage one or more CROs on a project-by-project basis for each study or trial. While we have developed and plan to maintain our relationships with CROs that we have previously engaged, we also expect to enter into agreements with other CROs to obtain additional resources and expertise in an attempt to accelerate our progress with regard to on-going clinical, non-clinical and pre-clinical programs and specifically, the compilation of clinical trial data for submission with an NDA for each of solithromycin and Taksta. Switching or entering into new relationships with CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Although we try to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, results of operations or prospects.

Our dependence upon third parties for the manufacture and supply of solithromycin, Taksta and any future product candidates may cause delays in, or prevent us from, successfully developing and commercializing our products.

We do not currently have nor do we plan to build the infrastructure or capability internally to manufacture solithromycin or Taksta for use in the conduct of our clinical trials. In January 2013, we entered into an agreement with Wockhardt to supply the API and commercial supply for solithromycin. Wockhardt manufactures solithromycin according to our specifications under our proprietary rights. While we have the ability to develop alternate sources for solithromycin should Wockhardt be unable to supply our needs, we may not be able to negotiate an agreement with another source on acceptable terms, if at all. Similarly, in July 2013, we contracted with Hospira Worldwide, Inc., or Hospira, to provide us with clinical and commercial supplies of the intravenous form of solithromycin. If Hospira fails to supply a specified percentage of product to us, we may seek an alternate supplier. If Hospira were unable to provide our needed supply of intravenous solithromycin, we may not be able to negotiate an agreement with another source on acceptable terms, if at all.

We employ the services of Ercros S.A., or Ercros, to produce Taksta's API and intend to utilize a third-party manufacturer to produce the finished dosing formulation of Taksta. We have a long-term exclusive supply arrangement with Ercros to produce the fusidic acid used in Taksta in which Ercros agrees to exclusively supply us with fusidic acid in the U.S., and we agree to obtain our supply of fusidic acid for commercial sale exclusively from Ercros, subject to a right to develop a second source for limited supply quantities. We believe Ercros is one of only two currently known manufacturers that can produce fusidic acid compliant with the purity required for human use. The second manufacturer is not available as a supplier to us. Fusidic acid is difficult to produce at these purity levels because of its complex fermentation process. As such, there are underlying risks associated with its manufacture, which could include cost overruns, new impurities, difficulties in scaling up or reproducing manufacturing processes and lack of timely availability of raw materials. We have yet to identify a viable second source of fusidic acid but continue to research alternatives. If Ercros cannot supply sufficient quantities of fusidic acid to make clinical supplies of Taksta, it would harm our ability to develop Taksta. We may not be able to locate a second manufacturer or, if we do, we may not be able to negotiate an agreement on favorable terms, if at all.

In addition, regulatory requirements could pose barriers to the manufacture of our API and finished product for solithromycin and Taksta. Our third-party manufacturers are required to comply with the FDA's current good manufacturing practices, or cGMP, regulations. As a result, the facilities used by Wockhardt, Ercros, and any of our future manufacturers to manufacture solithromycin

and Taksta must be approved by the FDA after we submit our NDA to the FDA and before approval of solithromycin and Taksta. Similar regulations apply to manufacturers of our products for use or sale in foreign countries. We do not control the manufacturing process of solithromycin or Taksta and are completely dependent on these third party manufacturing partners for compliance with the applicable regulatory requirements for the manufacture of solithromycin and Taksta API and their finished product. If our manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are unable to comply with the FDA's cGMP requirements, or otherwise are not approved for the commercial manufacture of solithromycin or Taksta, we may need to find alternative manufacturing facilities, which would result in significant delays of up to several years in obtaining approval for solithromycin or Taksta. In addition, our manufacturers will be subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMP regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply, and criminal prosecutions, any of which could have a material adverse impact on our business, financial condition, results of operations or prospects.

Finally, we also could experience manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us.

If Wockhardt, Hospira, Ercros, or any alternate supplier of API or finished drug product for solithromycin or Taksta experiences any significant difficulties in its respective manufacturing processes, does not comply with the terms of the agreement between us or does not devote sufficient time, energy and care to providing our manufacturing needs, we could experience significant interruptions in the supply of solithromycin or Taksta, which could impair our ability to supply solithromycin or Taksta at the levels required for our clinical trials and commercialization and prevent or delay their successful development and commercialization. On June 20, 2012, the FDA issued a Warning Letter to Ercros, citing cGMP violations at the Ercros facility that manufactures the API for Taksta. Although some of the alleged violations may be related to products other than fusidic acid, the FDA's issuance of a Warning Letter signifies Agency concerns with cGMP compliance at the Ercros facility. We believe Ercros is actively working with FDA to resolve these issues. However, if Ercros is unable to satisfactorily address the FDA's concerns in a timely manner, the FDA may take further enforcement actions that could significantly jeopardize our supply of Taksta API for use in clinical trials or later commercialization. For example, the FDA might issue an import alert, which could preclude us from importing Taksta API manufactured at the Ercros facility. Particularly in light of the unavailability of alternative suppliers for Taksta API, this could significantly impact our ability to develop and commercialize Taksta.

Similarly, one of two facilities in India at which Wockhardt produces API for solithromycin was audited by the Medicines and Healthcare Products Regulatory Agency, or MHRA, the regulatory agency of Great Britain, took issue with Wockhardt's practices at the plant and as a result the capsules of solithromycin produced at that plant could not be imported into Europe. We had product on hand and also have reformulated capsules, but the incident caused a several month delay in having drug available for our Phase 3 oral solithromycin trials in Europe, which, however, was planned to be in advance of the onset of flu season in Europe so the delay had minimal impact on the trial timeline. However, similar experiences could occur with more significant impact on our development program for solithromycin.

A substantial portion of our future revenues may be dependent upon our strategic partnerships.

Our success will depend in significant part on our ability to attract and maintain strategic partners and strategic relationships to support the development and commercialization of our product candidates. We currently expect that a substantial portion of our future revenues may be dependent upon our strategic partnership with Toyama. Under the license agreement we entered into in May 2013 with Toyama, Toyama has significant development and commercialization responsibilities with respect to solithromycin in Japan. If Toyama or any of our other strategic partners were to terminate their agreements with us, fail to meet their obligations or otherwise decrease their level of efforts, allocation of resources or other commitments under these agreements with us, our future revenues could be negatively impacted and the development and commercialization of product candidates could be interrupted. In addition, if some or any of the development, regulatory and commercial milestones are not achieved or if certain net sales thresholds are not achieved, as set forth in the Toyama agreement or any agreements with other strategic partners, we will not fully realize the expected economic benefits of those agreements. Further, the achievement of certain of the milestones under our partnership agreements will depend on factors that are outside of our control and most are not expected to be achieved for several years, if at all. Any failure to successfully maintain our strategic partnership agreements could materially and adversely affect our ability to generate revenues.

The timing of the milestone and royalty payments we are required to make to Optimer Pharmaceuticals, Inc. and The Scripps Research Institute is uncertain and could adversely affect our cash flows and results of operations.

In March 2006, we entered into a Collaborative Research and Development and License Agreement with Optimer Pharmaceuticals, Inc., or Optimer (now owned by Cubist Pharmaceuticals, Inc.), pursuant to which we acquired an exclusive license to certain patent applications and other intellectual property related to a series of compounds, including solithromycin, to develop and commercialize licensed products outside of the Association of South East Asian Nations, or ASEAN, countries (Brunei Darussalam, Cambodia, Indonesia, Laos, Malaysia, Myanmar (Burma), the Philippines, Singapore, Thailand and Vietnam). We have an obligation to make additional payments upon achievement of specified development, regulatory and commercialization milestones. The aggregate amount of such milestone payments we may need to pay is based in part on the number of products developed under the agreement. The aggregate amount (including our two milestone payments to date) would be \$27.5 million if four products are developed and gain FDA approval. Additional limited milestone payments would be due if we develop more than four products. We will also pay tiered mid-single-digit royalties based on the amount of annual net sales of solithromycin (or related licensed compounds), if and when approved by regulatory authorities. We have already paid a \$0.5 million milestone in 2010 and a \$1.0 million milestone in 2012 upon completion of our discussions with the FDA for the protocol for our pivotal Phase 3 trial for oral solithromycin. Optimer can elect to receive certain milestone payments in cash or in shares of our common stock having an equivalent fair market value. The timing of our achievement of these events and corresponding milestone payments to Optimer is subject to factors relating to the clinical and regulatory development and commercialization of solithromycin (or related licensed compounds), many of which are beyond our control. We may become obligated to make a milestone payment when we do not have the cash on hand to make such payment, which could require us to delay our clinical trials, curtail our operations, scale back our commercialization and marketing efforts or seek funds to meet these obligations on terms unfavorable to us. If we were unable to make a milestone payment, we would be in material breach of the agreement, in which event Optimer could terminate the agreement, which would result in the loss of our rights to develop and commercialize solithromycin, which would seriously harm our ability to generate revenues or achieve profitability.

We also must pay The Scripps Research Institute various milestone and annual payments, which, while significantly lower than amounts potentially due to Optimer, could become due when we do not have the cash on hand to make such payment, which could require us to delay our clinical trials, curtail our operations, scale back our commercialization and marketing efforts or seek funds to meet these obligations on terms unfavorable to us.

Our loan agreement with Hercules contains covenants that impose restrictions on our operations that may adversely impact the operation of our business.

Our loan agreement with Hercules contains customary restrictive covenants, including restrictions on our ability to incur additional debt, transfer or place a lien or security interest on our assets, including our intellectual property, merge with or acquire other companies, redeem any shares of our capital stock or pay cash dividends to our stockholders. These restrictions may inhibit our ability to conduct our business and to provide distributions to our stockholders. Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants than the Hercules loan.

The commercial success of solithromycin, Taksta and any other product candidates that we develop, if approved in the future, will depend upon attaining significant market acceptance of these products among physicians and payors.

As a company, we have never commercialized a product candidate for any indication. Even if solithromycin, Taksta or any other product candidate that we develop is approved by the appropriate regulatory authorities for marketing and sale, physicians may not prescribe our approved products, which would prevent us from generating revenues or becoming profitable. Market acceptance of solithromycin, Taksta and any other product candidates that we develop by physicians, patients and payors will depend on a number of factors, many of which are beyond our control, including:

- the clinical indications for which the product is approved;
- acceptance by physicians and payors of each product as a safe and effective treatment;
- the cost of treatment in relation to alternative treatments, including numerous generic drug products, such as azithromycin, levofloxacin and vancomycin;
- the relative convenience and ease of administration of solithromycin in the treatment of CABP and Taksta in the treatment of prosthetic joint infections;
- the availability and efficacy of competitive drugs;
- the effectiveness of our or any third party partner's sales force and marketing efforts;
- our ability to manufacture or obtain commercial quantities of our drug products;
- · our ability to deliver our products on a timely basis;

- the extent to which bacteria develop resistance to any antibiotic product candidate that we develop, thereby limiting its efficacy in treating or managing infections;
- the extent to which the product is approved for inclusion on formularies of hospitals and managed care organizations;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the availability of adequate reimbursement by third parties, such as insurance companies and other health care payors, and/or by government health care programs, including Medicare and Medicaid;
- our ability to have our products included in hospital formularies;
- limitations or warnings contained in a product's FDA-approved labeling; and
- prevalence and severity of adverse side effects.

Even if the medical community accepts that solithromycin and Taksta are safe and efficacious for their approved indications, physicians may not immediately be receptive to the use or may be slow to adopt solithromycin as an accepted treatment for CABP and Taksta as an accepted treatment for prosthetic joint infections. While we believe each of solithromycin and Taksta has significant advantages, we cannot assure you that any labeling approved by the FDA will permit us to promote solithromycin and Taksta as being superior to competing products. If either or both of solithromycin or Taksta are approved but do not achieve an adequate level of acceptance by physicians and payors, we may not generate sufficient or any revenues from these products and we may not become profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of solithromycin and Taksta may require significant resources and may never be successful.

If approved, solithromycin and Taksta will face significant competition from branded and generic antibiotics and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. If solithromycin or Taksta is approved, we will have competitors both in the U.S. and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies. Many of these companies have greater financial and other resources, such as larger research and development staffs and more experienced marketing and manufacturing organizations. As a result, these companies may obtain regulatory approval more rapidly and may be more effective in selling and marketing their products. They also may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make solithromycin, Taksta or any other product candidates that we develop obsolete. As a result, our competitors may succeed in commercializing antibiotics before we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

If approved, both solithromycin and Taksta will face competition from currently commercially available antibiotics, as well as any competing products that may be developed in the future. In July 2012, the United States Congress passed, and President Obama signed, the Food and Drug Administration Safety and Innovation Act, which included the Generating Antibiotic Incentives Now Act, or the GAIN Act. The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products. These incentives might result in more competition in the market for new antibiotics and might cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of products that could be competitive with our product candidates. Existing approved products that will compete with solithromycin include azithromycin (sold under the brand name Zithromax [®] by Pfizer Inc. and available as a generic), clarithromycin (sold under the brand name Biaxin [®] by Abbott Laboratories and available as a generic), moxifloxacin (sold under the brand name Avelox [®] by Bayer AG), levofloxacin (sold under the brand name Levaquin by Johnson & Johnson and available as a generic), linezolid (sold under the brand name Zyvox by Pfizer Inc.), ceftriaxone (sold under the brand name Rocephin® by F. Hoffman-La Roche Ltd and available as a generic) and ceftaroline (sold under the brand name Teflaro [®] by Forest Laboratories, Inc.). Existing approved products that will compete with Taksta include vancomycin (available as a generic), linezolid (sold under the brand name Zyvox by Pfizer Inc.), daptomycin (sold under the brand name Cubicin by Cubist Pharmaceuticals, Inc.), quinupristin/dalfopristin (sold under the brand name Synercid® by Sanofi-Aventis and Monarch Pharmaceuticals, Inc.), tigecycline (sold under the brand name Tygacil® by Pfizer Inc.), telavancin (sold under the brand name Vibativ ® by Theravance, Inc. and Astellas Pharma, Inc.) and ceftaroline (sold under the brand name Teflaro by Forest Laboratories, Inc.). Generic antibiotics are typically sold at lower prices than branded antibiotics and are generally preferred by managed care providers of health services.

If we are unable to demonstrate the advantages of solithromycin or Taksta over competing drugs and drug candidates, we will not be able to successfully commercialize solithromycin or Taksta and our results of operations will suffer.

Reimbursement may not be available for solithromycin, Taksta or any other product candidates that we develop, which could make it difficult for us to sell our products profitably.

Market acceptance and sales of solithromycin, Taksta or any other product candidates that we develop will depend on reimbursement policies and may be affected by health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for solithromycin, Taksta or any other product candidates that we develop. Also, we cannot be sure that the amount of reimbursement available, if any, will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize solithromycin, Taksta or any other product candidates that we develop.

Specifically, in both the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the health care system in ways that could affect our ability to sell our products profitably. In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the Medicare Modernization Act, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, we expect that there will be additional pressure to contain and reduce costs. These cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products and could seriously harm our business. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, PPACA, became law in the U.S. The goal of PPACA is to reduce the cost of health care and substantially change the way health care is financed by both governmental and private insurers. While we cannot predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically, the PPACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of solithromycin or Taksta or any future products. Earlier this year, members of the U.S. Congress and some state legislatures sought to overturn at least portions of the legislation including those on the mandatory purchase of insurance. However, on June 28, 2012, the United States Supreme Court upheld the constitutionality of these provisions. Members of the U.S. Congress have since proposed a number of legislative initiatives, including possible repeal of the PPACA. We cannot predict the outcome or impact of current proposals or whether new proposals will be made or adopted, when they may be adopted or what impact they may have on us if they are adopted.

The availability of numerous generic antibiotics at lower prices than branded antibiotics, such as solithromycin or Taksta if either were approved for commercial introduction, may also substantially reduce the likelihood of reimbursement for such products. We expect to experience pricing pressures in connection with the sale of solithromycin, Taksta and any other products that we develop, due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative proposals. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and our business will be harmed.

We currently have no marketing and sales organization and have no experience as a company in marketing drug products. If we are unable to establish our own marketing and sales capabilities, or enter into agreements with third parties, to market and sell our products after they are approved, we may not be able to generate product revenues.

We do not have a sales organization for the marketing, sales and distribution of any drug products. In order to commercialize any products, we must develop these capabilities on our own or make arrangements with third parties for the marketing, sales and distribution of our products. The establishment and development of our own sales force would be expensive and time consuming and could delay any product launch, and we cannot be certain that we would be able to successfully develop this capability. As a result, we may seek one or more licensing partners to handle some or all of the sales and marketing of solithromycin for CABP in the U.S. and elsewhere and Taksta for prosthetic joint infections in the U.S. There also may be certain markets within the U.S. for solithromycin for which we may seek a co-promotion arrangement. However, we may not be able to enter into arrangements with third parties to sell solithromycin or Taksta on favorable terms or at all. In the event we are unable to develop our own marketing and sales force or collaborate with a third-party marketing and sales organization, we would not be able to commercialize solithromycin, Taksta or any other product candidates that we develop, which would negatively impact our ability to generate product revenues. Further, whether we commercialize products on our own or rely on a third party to do so, our ability to generate revenue will be dependent on the effectiveness of the sales force. In addition, to the extent we rely on third parties to commercialize our approved products, we will likely receive less revenues than if we commercialized these products ourselves.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends in large part on our ability to attract and retain highly qualified managerial, scientific and medical personnel. In order to induce valuable employees to remain with us, we have provided stock options that vest over time. The value to employees of stock options will be significantly affected by movements in our stock price that we cannot control and may at any time be insufficient to counteract more lucrative offers from other companies.

Our scientific team has expertise in many different aspects of drug discovery and development. We conduct our operations at our facility in Chapel Hill, North Carolina, which is part of the Research Triangle consisting of Raleigh, Durham and Chapel Hill. This region is headquarters to other biopharmaceutical companies and many academic and research institutions and, as a result, at any given time there may be a shortage of experienced scientists and medical personnel. Competition for skilled personnel in our area and elsewhere in the U.S. is very intense and competition for experienced scientists may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

Despite our efforts to retain valuable employees, members of our management, scientific and medical teams may terminate their employment with us on short notice. While we have an employment agreement with our Chief Executive officer, Prabha Fernandes, we do not have employment agreements with Mark W. Hahn, our Chief Financial Officer or any other employee. As a result, all employees other than Dr. Fernandes are employed on an at-will basis, which means that any of these employees could leave our employment at any time, with or without notice, and may go to work for a competitor. Even though Dr. Fernandes has entered into an employment agreement with us, she could leave at any time, although she would be subject to that agreement's non-compete provision. The loss of the services of any of our executive officers or other key employees could potentially harm our business, operating results or financial condition. Our success also depends on our ability to continue to attract, retain and motivate highly skilled scientific and medical personnel.

Other biotechnology and pharmaceutical companies with which we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we offer. If we are unable to continue to attract and retain high quality personnel, our ability to discover, develop and commercialize drug candidates will be limited.

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

As of February 20, 2014, we had 38 employees. As our development and commercialization plans and strategies develop, we expect to expand our employee base for managerial, operational, financial and other resources and, depending on our commercialization strategy, we may further expand our employee base for sales and marketing resources. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of its attention away from their day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize solithromycin, Taksta and our other product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth in our organization.

Even if we obtain FDA approval of solithromycin, or any other product candidate, we may never obtain approval or commercialize our products outside of the U.S., which would limit our ability to realize their full market potential. If foreign approval is obtained, there are risks in conducting business in international markets.

In order to market solithromycin or any other products outside of the U.S., we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and require additional pre-clinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays.

In addition, our failure to obtain regulatory approval in the U.S. or any foreign country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in the U.S. or any foreign country and we do not have experience as a company in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in a foreign country or to obtain and maintain required approvals, our potential market for solithromycin or other products will be reduced and our ability to realize the full market potential of our products will be harmed. We do not intend to commercialize Taksta outside the U.S. because of the widespread use of fusidic acid in Europe and Australia.

If approved for commercialization in a foreign country, we intend to enter into agreements with third parties to market solithromycin whenever it may be approved and wherever we have the right to market it. Consequently, we expect that we will be subject to additional risks related to entering into international business relationships, including:

- potentially reduced protection for intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally:
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with laws for employees traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- · foreign currency fluctuations, which could result in increased operating expenses and reduced revenues;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting API and/or finished drug product supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act.

These and other risks may materially adversely affect our ability to attain or sustain revenue from international markets.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We have incurred significant operating losses since inception and anticipate that we will incur continued losses for the foreseeable future.

As of December 31, 2013, we had an accumulated deficit of approximately \$166.3 million. We have no product revenues, but do have revenue from contract research and an upfront fee paid in connection with a license agreement. We have funded our operations to date from the private sale of equity and debt securities and our IPO. We expect to incur substantial additional losses over the next several years as our research, development, pre-clinical testing, and clinical trial activities increase, especially those related to solithromycin and Taksta. In addition, we also expect to incur additional costs operating as a public company. The amount of future losses and when, if ever, we will achieve profitability are uncertain.

To raise additional funds to support our business operations, we may issue equity or debt securities. Debt securities could contain restrictive covenants that may adversely impact the operation of our business. The issuance of equity securities or convertible debt securities would result in dilution to our stockholders.

The incurrence of indebtedness would result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. For example, in August 2011, we issued 10.0% unsecured convertible notes (the "August 2011 Notes") in the aggregate principal amount of \$5,000,000. The August 2011 Notes contained restrictive covenants that prohibited us from incurring new indebtedness in excess of \$0.5 million in the aggregate and granting a security interest on any of our material assets without the consent of the holders of at least a majority of the aggregate outstanding principal amount of the August 2011 Notes. Pursuant to this authority, the holders of the August 2011 Notes approved the Hercules debt financing that we closed in December 2011. The August 2011 Notes automatically converted into shares of our common stock upon the closing of our IPO and their restrictive covenants terminated at such time. Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants than the August 2011 Notes. In addition, the sale of equity securities or convertible debt securities would result in the issuance of additional shares of our capital stock, which would result in dilution to our stockholders.

Our limited operating history makes it difficult to evaluate our business and prospects.

We began operations in 2006. Our operations to date have been limited to financing and staffing our company, conducting product development activities for solithromycin and Taksta and performing research and development with respect to our proprietary macrolide library. We have not yet demonstrated an ability as a company to obtain regulatory approval for or commercialize a product candidate. Consequently, the ability to predict our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

Risks Related to Our Industry

We are subject to extensive and costly government regulation.

Antibiotics, including those we are developing and plan to develop in the future, are subject to extensive and rigorous domestic government regulation including regulation by the FDA, the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services, the U.S. Department of Justice, state and local governments and their respective foreign equivalents. The FDA regulates the research, development, pre-clinical and clinical testing, manufacture, safety, effectiveness, record keeping, reporting, labeling, storage, approval, advertising, promotion, sale, distribution, import and export of pharmaceutical products. If any products we develop are tested or marketed abroad, they will also be subject to extensive regulation by foreign governments, whether or not we have obtained FDA approval for a given product and its uses. Such foreign regulation may be equally or more demanding than corresponding U.S. regulation. Government regulation substantially increases the cost and risk of researching, developing, manufacturing and selling products. Our failure to comply with these regulations could result in significant fines or the inability of our product candidates to obtain and maintain regulatory approval, which would have a materially adverse effect on our business, financial condition, results of operations and prospects.

Even if we obtain regulatory approval for solithromycin, Taksta or any of our future product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if regulatory approval in the U.S. is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the labeling ultimately approved for solithromycin and/or Taksta if any, may include restrictions on use. Solithromycin, Taksta or any of our other product candidates will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record keeping and reporting of safety and other post-market information. The holder of an approved NDA is subject to obligations to monitor and report adverse events and instances of the failure of a product to meet the specifications in the NDA. Application holders must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Application holders must also submit advertising and other promotional material to the FDA and report on ongoing clinical trials. Legal requirements have also been enacted to require disclosure of clinical trial results on publicly available databases.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing, requiring new warnings or other labeling changes to limit use of the drug, requiring that we conduct additional clinical trials, imposing new monitoring requirements,

or requiring that we establish a REMS. Advertising and promotional materials must comply with FDA rules in addition to other potentially applicable federal and state laws. The distribution of product samples to physicians must comply with the requirements of the Prescription Drug Marketing Act. Sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veteran's Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws. If we or our third party collaborators fail to comply with applicable regulatory requirements, a regulatory agency may:

- conduct an investigation into our practices and any alleged violation of law;
- issue warning letters or untitled letters asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements;
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall; or
- refuse to allow us to enter into supply contracts, including government contracts.

The occurrence of any event or penalty described above may force us to expend significant amounts of time and money and may significantly inhibit our ability to bring to market or continue to market our products and generate revenues. Similar regulations apply in foreign jurisdictions.

Product liability lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our products.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants, and will face an even greater risk if we commercialize solithromycin or Taksta in the U.S. or other additional jurisdictions or if we engage in the clinical testing of new product candidates or commercialize any additional products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products or product candidates that we may develop;
- loss of revenue;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize our products or product candidates; and
- a decline in our stock price.

Although we maintain general liability insurance of up to \$2.0 million in the aggregate and clinical trial liability insurance of \$5.0 million in the aggregate for each of solithromycin and Taksta, this insurance may not fully cover potential liabilities. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. In addition, inability to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims could prevent or inhibit the development and commercial production and sale of our products, which could adversely affect our business, financial condition, results of operations, and prospects.

If we use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical, biological and radioactive materials and viruses. In addition, our operations produce hazardous waste products. Federal, state and local laws and regulations in the U.S. govern the use, manufacture, storage, handling and disposal of hazardous materials. Although we believe that our procedures for use, handling, storing and disposing of these materials (all of which only occur at third-party sites operated by our contractors) comply with legally prescribed standards, we may incur significant additional costs to comply with applicable laws in the future. We also cannot predict the impact on our business of new or amended environmental laws or regulations, or any changes in the way existing and future laws and regulations are interpreted or enforced. Also, even if we are in compliance with applicable laws, we cannot completely eliminate the risk of contamination or injury resulting from hazardous materials, and we may incur liability as a result of any such contamination or injury. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources, and we do not carry liability insurance covering the use of hazardous materials. If we fail to comply with applicable requirements, we could incur substantial costs, including civil or criminal fines and penalties, clean-up costs, or capital expenditures for control equipment or operational changes necessary to achieve or maintain compliance. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which adversely affect our business, financial condition, results of operations, and prospects.

Risks Related to our Intellectual Property

Our ability to pursue the development and commercialization of solithromycin depends upon the continuation of our licenses from Optimer and TSRI.

Our agreement with Optimer (now owned by Cubist) provides us with a worldwide exclusive license to develop and sell solithromycin outside of ASEAN countries. We are obligated to use our diligent efforts to develop and commercialize products licensed from Optimer. We have other obligations to Optimer under the license related to progress reporting, payment terms and confidentiality. If we are unable to make the required milestone and royalty payments under the agreement, if we do not continue to use diligent efforts to develop and commercialize solithromycin or if we otherwise materially breach the agreement, our rights to develop and commercialize solithromycin would terminate and revert to Optimer. In addition, either we or Optimer may terminate the agreement upon the uncured material breach of the agreement. If our agreement with Optimer is terminated by Optimer, we would lose our rights to develop and commercialize solithromycin, which would adversely affect our business, financial condition, results of operations, and prospects.

Our agreement with TSRI provides us with a license to make, use, sell, and import products for human or animal therapeutic use that use or incorporate one or more macrolides as an active pharmaceutical ingredient and is covered by certain patent rights owned by TSRI claiming technology related to copper-catalysed ligation of azides and acetylenes, with exclusive rights as to the People's Republic of China (excluding Hong Kong), South Korea and Australia, and non-exclusive rights in all other countries worldwide, except the member-nations of the Association of Southeast Asian Nations (which are not included in the license with TSRI). We are obligated to use commercially reasonable efforts to develop and obtain regulatory approvals to market and sell one or more licensed products. TSRI may terminate the agreement due to our insolvency, our conviction for a felony relating to the development, manufacture, use, marketing, distribution or sale of a licensed product, or upon an uncured breach of the agreement by us, including failure to make any required payment. If our agreement with TSRI is terminated by TSRI, we could lose our rights to synthesize and/or manufacture solithromycin under the licensed TSRI technology, which could adversely affect our business, financial condition, results of operations, and prospects.

Another party could develop a fusidic acid product and achieve FDA regulatory exclusivity in the U.S. before we do, potentially preventing our ability to commercialize Taksta.

We will rely partly on FDA regulatory exclusivity to protect our proprietary rights for Taksta, our fusidic acid product, in the U.S. Fusidic acid has been approved and sold for several decades in Europe and other countries outside the U.S., but it has never been approved in the U.S. We believe this was due to the lack of regulatory exclusivity that was available for the molecule until the passage of Public Law 110-379 on October 8, 2008, which allowed old antibiotics such as fusidic acid to obtain five-year new chemical entity, or NCE, exclusivity upon NDA approval. This exclusivity will be granted to the first fusidic acid product that receives NDA approval.

During the exclusivity period, for a minimum of four years the FDA will not accept an application filed by a third party that relies on any data contained in the approved NDA. Although we are not aware of another party currently developing fusidic acid for use in the U.S. for any indication, if another party were to do so and obtain NDA approval before we do, we would not be able to obtain approval for Taksta for any disease until after any period of regulatory exclusivity if our NDA relies on data contained in the previously approved NDA. In that event, we may not be able to commercialize Taksta, which would harm our ability to generate revenue and achieve profitability.

Our competitive position may be harmed if a competitor obtains orphan drug exclusivity for the treatment of prosthetic joint infections before we do. Even if we were to obtain orphan drug exclusivity, a competitor could obtain approval of a different drug for the treatment of prosthetic joint infections or for the same drug upon a showing that its drug is clinically superior to ours, which would harm our business.

Orphan drug designation is an important element of our competitive strategy for Taksta. The company that obtains the first FDA approval for a drug that is designated as an orphan drug for a rare disease receives a type of marketing exclusivity known as "orphan drug exclusivity." Orphan drug exclusivity prevents FDA approval of applications by others for the same drug and the designated orphan disease or condition for seven years from the date of NDA approval. If the orphan indication is the first NDA approved for the drug, the drug is also eligible for the five-year Hatch-Waxman exclusivity for NCEs. Orphan and Hatch-Waxman exclusivities run concurrently.

The FDA may approve a subsequent application from another entity for the orphan indication of prosthetic joint infections if it determines that the application is for a different drug. The FDA may also approve a subsequent application for fusidic acid for an indication other than prosthetic joint infections. Orphan exclusivity does not block the same drug from being approved for another indication; however, Hatch-Waxman exclusivity could block submission for a period of at least four years after approval if the subsequent application references data in the earlier NDA.

The FDA may approve a subsequent application from another entity for the same drug for the same designated and approved orphan indication during the orphan exclusivity period if it determines that the subsequent product is clinically superior, or that the holder of the initial orphan drug approval cannot assure the availability of sufficient quantities of the drug to meet the public's need.

If we do not receive orphan exclusivity for Taksta for the treatment of prosthetic joint infections, our business would be negatively affected. In addition, even if we do obtain orphan exclusivity for Taksta, the FDA may permit other companies to market other drugs for the same condition or use. In addition, the FDA may approve another fusidic acid product for prosthetic joint infections during our period of orphan drug exclusivity if it can be demonstrated that the drug is clinically superior to our drug, or if we are unable to supply sufficient product to meet the public's need. This could create a more competitive market for us.

If our efforts to protect the proprietary nature of the intellectual property related to solithromycin, Taksta, and our other product candidates are not adequate, we may not be able to compete effectively in our market.

Our commercial success will depend in part on our ability to obtain additional patents and protect our existing patent position as well as our ability to maintain adequate protection of other intellectual property for solithromycin, Taksta and any future products in the U.S. and other countries. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. The patent positions of pharmaceutical companies are highly uncertain. The legal principles applicable to patents are in transition due to changing court precedent and legislative action and we cannot assure you that the historical legal standards surrounding questions of validity will continue to be applied or that current defenses relating to issued patents in these fields will be sufficient in the future. Changes in patent laws in the U.S. such as the America Invents Act of 2011 may affect the scope, strength and enforceability of our patent rights or the nature of proceedings which may be brought by us related to our patent rights. In addition, the laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the U.S., and we may encounter significant problems in protecting our proprietary rights in these countries. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary technologies, solithromycin, Taksta and any future products are covered by valid and enforceable patents or are effectively maintained as trade secrets.

These risks include the possibility that:

- the patent applications that we licensed or have filed on our own may fail to result in issued patents in the U.S. or in foreign countries;
- patents issued or licensed to us or our partners may be challenged, discovered to have been issued on the basis of insufficient or incorrect information and/or held to be invalid or unenforceable;
- the scope of any patent protection may be too narrow to exclude other competitors from developing or designing around these patents;

- we or our licensors were not the first to make the inventions covered by each of our issued patents and pending patent applications;
- we or our licensors were not the first to file patent applications for these inventions;
- we may fail to comply with procedural, documentary, fee payment and other similar provisions during the patent application process, which can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights;
- future product candidates may not be patentable;
- others will claim rights or ownership with regard to patents and other proprietary rights which we hold or license;
- delays in development, testing, clinical trials and regulatory review may reduce the period of time during which we could market our product candidates under patent protection; and
- we may fail to timely apply for patents on our technologies or products.

While we apply for patents covering both our technologies and potential products, including solithromycin and Taksta, as we deem appropriate, many biopharmaceutical companies and university and research institutions already have filed patent applications or have received patents in our areas of product development. These entities' applications, patents and other intellectual property rights may conflict with patent applications to which we have rights and could prevent us from obtaining patents or could call into question the validity of any of our patents, if issued, or could otherwise adversely affect our ability to develop, manufacture or commercialize antibiotic candidates. In addition, if third parties file patent applications in the technologies that also claim technology to which we have rights, we may have to participate in interference, derivation or other proceedings with the U.S. Patent and Trademark Office, or USPTO, or applicable foreign patent regulatory authorities, as applicable, to determine our rights in the invention, which may be time-consuming and expensive. Moreover, issued patents may be challenged during post-grant proceedings brought by a third party or the USPTO, or in foreign countries, or in the courts. These proceedings may result in loss of patent claims or adverse changes to the scope of the claims.

If we or our licensors or partners fail to obtain and maintain patent protection for our product candidates, or our proprietary technologies and their uses, companies may be dissuaded from collaborating with us. In such event, our ability to commercialize solithromycin, Taksta and our other product candidates may be threatened, we could lose our competitive advantage and the competition we face could increase, all of which could adversely affect on our business, financial condition, results of operations, and prospects.

If we are sued for infringing intellectual property rights of third parties, litigation will be costly and time consuming and could prevent us or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our not infringing the patents and proprietary rights of other parties and not breaching any collaboration or other agreements we have entered into with regard to our technologies and products. Numerous third-party U.S. and non-U.S. issued patents and pending applications exist in the areas of antibacterial treatment, including compounds, formulations, treatment methods and synthetic processes that may be applied towards the synthesis of antibiotics. Although no legal action has been commenced or threatened against us by a third party for infringing intellectual property rights, we cannot provide assurances that we or our partners will be free to manufacture or market our product candidates as planned, or that we or our licensors' and partners' patents will not be opposed or litigated by third parties.

There is a substantial amount of litigation involving intellectual property in the biopharmaceutical industry generally. If a third party asserts that we infringe its patents or other proprietary rights, we could face a number of risks that could adversely affect our business, financial condition, results of operations, and prospects, including:

- infringement and other intellectual property claims, which would be costly and time consuming to defend, whether or not we are ultimately successful, which in turn could delay the regulatory approval process, consume our capital and divert management's attention from our business;
- substantial damages for past infringement, which we may have to pay if a court determines that our products or technologies infringe a competitor's patent or other proprietary rights;
- a court prohibiting us from selling or licensing our technologies or future products unless the third party licenses its patents or other proprietary rights to us on commercially reasonable terms, which it is not required to do;
- if a license is available from a third party, we may have to pay substantial royalties or lump sum payments or grant cross licenses to our patents or other proprietary rights to obtain that license; and

• redesigning our products so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Although we are not currently party to any legal proceedings relating to our intellectual property, in the future, third parties may file claims asserting that our technologies, processes or products infringe on their intellectual property. We cannot predict whether third parties will assert these claims against us or our partners or against the licensors of technology licensed to us, or whether those claims will harm our business. In addition, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. If we or our partners were to face infringement claims or challenges by third parties relating to our product candidates, an adverse outcome could subject us to significant liabilities to such third parties, and force us or our partners to curtail or cease the development of some or all of our product candidates, which could adversely affect our business, financial condition, results of operations, and prospects.

We may be required to file lawsuits or take other actions to protect or enforce our patents or the patents of our licensors, which could be expensive and time consuming.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally.

In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents, or those of our licensors, do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents, or those of our licensors, at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications, or those of our licensors, at risk of not issuing. Moreover, we may not be able to prevent, alone or with our licensors, misappropriation of our proprietary rights, particularly in countries where the laws may not protect those rights as fully as in the U.S. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, if securities analysts or investors perceive public announcements of the results of hearings, motions or other interim proceedings or developments to be negative, the price of our common stock could be adversely affected. The occurrence of any of the above could adversely affect our business, financial condition, results of operations, and prospects.

The intellectual property protection for our products is dependent on third parties.

With respect to patent applications relating to solithromycin or other compounds licensed from Optimer (now owned by Cubist), Optimer retains rights in ASEAN countries. Generally, we do not have the right to prosecute and maintain any applications in those countries, unless Optimer elects not to file, prosecute or maintain any or all of such patents. Our potential future licensors also may retain the right to prosecute and maintain the patent rights that they license to us. If Optimer or other licensors fail to appropriately prosecute and maintain patent protection for any of our product candidates in those countries controlled by them, our ability to develop and commercialize those products may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products in those countries.

With respect to inventions that are jointly made by us and one of our licensors, partners or potential partners, we would need to determine, with our licensors, partners or potential partners, who would be responsible for the prosecution of patents relating to any joint inventions should they arise. In addition, we may be required to cede control of prosecution of our patents to partners or potential partners in order to consummate a partnering transaction. If any of our licensors or partners fails to appropriately prosecute and maintain patent protection for any of our product candidates in those countries controlled by them, our ability to develop and commercialize those products may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products in those countries.

If we are unable to protect the confidentiality of certain information, the value of our products and technology could be materially adversely affected.

We also rely on trade secrets, know-how and continuing technological advancement to develop and maintain our competitive position. To protect this competitive position, we regularly enter into confidentiality and proprietary information agreements with third parties, including employees, independent contractors, suppliers and collaborators. We cannot, however, ensure that these protective arrangements will be honored by third parties, and we may not have adequate remedies if these arrangements are breached. In addition, enforcement of claims that a third party has illegally obtained and is using trade secrets, know-how and technological advancements is expensive, time consuming and uncertain. Non-U.S. courts are sometimes less willing than U.S. courts to protect this information.

Moreover, our trade secrets, know-how and technological advancements may otherwise become known or be independently developed by competitors in a manner providing us with no practical recourse against the competing parties. If any such events were to occur, they could adversely affect our business, financial condition, results of operations, and prospects.

A substantial portion of our future revenues may be dependent upon our strategic partnerships.

Our success will depend in significant part on our ability to attract and maintain strategic partners and strategic relationships to support the development and commercialization of our product candidates. We currently expect that a substantial portion of our future revenues may be dependent upon our strategic partnership with Toyama. Under the license agreement we entered into in May 2013 with Toyama, Toyama has significant development and commercialization responsibilities with respect to solithromycin in Japan. If Toyama or any of our other strategic partners were to terminate their agreements with us, fail to meet their obligations or otherwise decrease their level of efforts, allocation of resources or other commitments under these agreements with us, our future revenues could be negatively impacted and the development and commercialization of product candidates could be interrupted. In addition, if some or any of the development, regulatory and commercial milestones are not achieved or if certain net sales thresholds are not achieved, as set forth in the Toyama agreement or any agreements with other strategic partners, we will not fully realize the expected economic benefits of those agreements. Further, the achievement of certain of the milestones under our partnership agreements will depend on factors that are outside of our control and most are not expected to be achieved for several years, if at all. Any failure to successfully maintain our strategic partnership agreements could materially and adversely affect our ability to generate revenues.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

We have filed an application with the USPTO for our mark "Taksta"; however, that application has not yet been examined. We cannot guarantee that the application will be allowed, nor whether the USPTO will ultimately issue a trademark registration. In addition, although we are not currently aware of any oppositions to or cancellations of our registered trademarks or pending applications, it is possible that one or more of the applications could be subject to opposition or cancellation after the marks are registered. The registrations will be subject to use and maintenance requirements. We have not yet registered all of our trademarks in all of our potential markets and there are names or symbols other than "Cempra" that may be protectable marks for which we have not sought registration. Failure to secure those registrations could adversely affect our business. We cannot assure you that opposition or cancellation proceedings will not be filed against our trademarks or that our trademarks would survive such proceedings.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Such claims may lead to material costs for us, or an inability to protect or use valuable intellectual property rights, which could adversely affect our business, financial condition, results of operations, and prospects.

Risks Related to Ownership of Our Common Stock

An active trading market for our common stock may not develop to provide our stockholders with adequate liquidity.

Prior to February 3, 2012, there had not been a public market for our common stock. Since that time, our common stock has been thinly traded. We cannot assure you that an active trading market for our common stock will develop, or if it does develop, it may not be maintained. You may not be able to sell your shares quickly or at the market price if trading in our common stock is not active.

We might not be able to maintain the listing of our common stock on the Nasdaq Global Market.

Our common stock began listing on the Nasdaq Global Market on February 3, 2012, under the symbol "CEMP." We might not be able to maintain the listing standards of that exchange. If we fail to maintain the listing requirements, our common stock might trade on the Nasdaq Capital Market, or move to the OTC Bulletin Board or in the "pink sheets" maintained by Pink OTC Markets, Inc. The OTC Bulletin Board and the "pink sheets" are generally considered to be markets that are less efficient and less broad than the Nasdaq Capital Market.

The market price of our common stock may be highly volatile, and you could lose all or part of your investment.

Our stock began trading on the Nasdaq Global Market on February 3, 2012. Between that date and February 20, 2014, it has traded between \$5.26 and \$15.39. Our stock price could be subject to wide fluctuations in response to a variety of factors, which include:

- any delay in commencement of our planned Phase 3 clinical trial for IV to oral solithromycin or our Phase 3 clinical trials for Taksta;
- adverse results or delays in clinical trials;
- any delay in filing our NDAs for solithromycin or Taksta and any adverse development or perceived adverse development with respect to the FDA's review of the NDAs, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- changes in laws or regulations applicable to our products or product candidates, including but not limited to clinical trial requirements for approvals;
- unanticipated serious safety concerns related to the use of solithromycin, Taksta or any of our other product candidates;
- a decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- the inability to obtain adequate product supply for solithromycin, Taksta or any other approved drug product, or the inability to do so at acceptable prices;
- · adverse regulatory decisions;
- the introduction of new products or technologies offered by us or our competitors;
- the effectiveness of our or our potential partners' commercialization efforts;
- the inability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- the failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- the overall performance of the U.S. equity markets and general political and economic conditions;
- · developments concerning our sources of manufacturing supply and any commercialization partners;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- adverse market reaction to any indebtedness we may incur or securities we may issue in the future;
- sales of our common stock by our stockholders in the future;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- the trading volume of our common stock;
- effects of natural or man-made catastrophic events or other business interruptions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the NASDAQ Global Market and the stock of biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

At February 20, 2014, our executive officers, directors and entities affiliated with certain of our directors beneficially owned approximately 31% of our outstanding voting common stock. Therefore, these stockholders have the ability to influence us through their ownership position. These stockholders may be able to determine the outcome of all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

The requirements of being a public company add to our operating costs and might strain our resources and distract our management.

We became a public company on February 2, 2012. As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and the NASDAQ Global Market have imposed various requirements on public companies. While we may opt to rely on certain exemptions from these requirements provided in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, our management and other personnel still need to devote a substantial amount of time to compliance initiatives. Moreover, we anticipate that compliance with certain rules and regulations will increase our legal, accounting and financial compliance costs substantially. We estimate the additional costs we may incur to respond to these requirements to range from \$0.9 million to \$1.2 million annually, although unforeseen circumstances could increase actual costs. In addition, these rules and regulations may make our activities related to legal, accounting and financial compliance more difficult, time-consuming and costly and may also place undue strain on our personnel, systems and resources. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations.

We are an "emerging growth company" and we cannot be certain if the reduced disclosure requirements applicable to emerging growth will make our common stock less attractive to investors or otherwise negatively impact the price of our stock.

The JOBS Act contains provisions that, among other things, reduce reporting requirements for qualifying companies. As an "emerging growth company", we evaluate the benefits of relying on the other reduced reporting requirements provided by the JOBS Act.

Subject to certain conditions set forth in the JOBS Act, as an emerging growth company, we have chosen to rely on these exemptions, and as a result, we are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis), and disclose executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the CEO's compensation to median employee compensation. These exemptions will apply for a period of five years following the completion of our IPO on February 8, 2012 or until we otherwise no longer satisfy the criteria to be an emerging growth company, whichever is earlier. We cannot be certain if our scaled disclosure will make our stock less attractive to investors or negatively affect the price of our stock.

If we fail to establish and maintain proper internal controls, our ability to produce accurate financial statements or comply with applicable regulations could be impaired.

SEC rules that implement Section 404 of the Sarbanes-Oxley Act require us to make a formal assessment of the effectiveness of our internal controls over financial reporting for that purpose. We first became subject to this requirement for this report. While we have concluded that our internal control over financial reporting was effective as of December 31, 2013, there can be no assurance that we will be able to so conclude in the future or that we will not identify one or more material weaknesses in our internal controls in connection with future evaluations. Additionally, we have opted to rely on the exemptions provided in the JOBS Act, and will not be required to provide our independent auditor's assessment of our internal controls over financial reporting until such time we cease to be an "emerging growth company", which, at the latest, would be for our annual report on Form 10-K for the year ending December 31, 2017. Investors may lose confidence in our operating results, our stock price could decline and we may be subject to litigation or regulatory enforcement actions if (i) in the future we are unable to conclude that our internal control over financial reporting is effective, (ii) we identify material weaknesses in our internal control over financial reporting, which could result in financial statement errors which, in turn, could require us to restate our operating results or (iii) when required, our independent auditors are unwilling or unable to provide us with an attestation report on the effectiveness of internal control over financial reporting as required by Section 404 of the Sarbanes-Oxley Act. Any of these events could cause investors to lose confidence in our operating results, our stock price could decline and we may be subject to litigation or regulatory enforcement actions. In addition, if we are unable to meet the requirements of Section 404 of the Sarbanes-Oxley Act, we may not be able to remain listed on the NASDAQ Global Market.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to decline.

Certain holders of shares of our common stock are entitled to rights with respect to the registration under the Securities Act of 1933, as amended, or the Securities Act, of shares of our common stock or shares of our common stock issuable upon the exercise of warrants held by these individuals or entities. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Sales of stock by these stockholders could have a material adverse effect on the trading price of our common stock.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. A limited number of securities and industry analysts currently publish research on our company. If one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which might cause our stock price and trading volume to decline.

Our ability to use our net operating loss carry-forwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, referred to as the Internal Revenue Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation's ability to use its pre-change net operating loss carry-forwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We believe that, with the financing transactions that have occurred over the past three years, we may have triggered an "ownership change" limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carry-forwards to offset U.S. federal taxable income may be subject to limitations, which potentially could result in increased future tax liability to us.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will be limited to the value of their stock.

In addition, pursuant to the terms of the Hercules loan, for as long as the Hercules loan is outstanding, we may not pay any cash dividends on our common stock.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if an acquisition would benefit our stockholders, and could also make it more difficult to remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by the board of directors. This provision could have the effect of discouraging, delaying or preventing someone from acquiring us or merging with us, whether or not it is desired by or beneficial to our stockholders. Any provision of our certificate of incorporation or bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease approximately 12,060 square feet of space for our headquarters in Chapel Hill, North Carolina under an agreement that expires in May 2019. We are expecting to hire additional employees during 2014 which will require us to locate additional space on commercially reasonable terms.

Item 3. Legal Proceedings

We are not a party to any legal proceedings and we are not aware of any claims or actions pending or threatened against us. In the future, we might from time to time become involved in litigation relating to claims arising from our ordinary course of business.

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

Our common stock is traded under the symbol "CEMP" and is quoted on the NASDAQ Global Market. Our common stock began trading on the NASDAQ Global Market on February 3, 2012, on a "when-issued" basis. On February 6, 2012, the first trading day after the distribution, "when-issued" trading with respect to our common stock ended and "regular way" trading began. As a result, our stock was not listed in any year prior to 2012.

On February 20, 2014, the closing price for the common stock as reported on the NASDAQ Global Market was \$13.26.

As of February 20, 2014, there were 25 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers. We believe that, when our record holders and stockholders whose shares are held in nominee or street name by brokers are combined, we have in excess of 800 stockholders.

Dividend Policy

We currently do not plan to declare dividends on shares of our common stock in the foreseeable future. We expect to retain our future earnings, if any, for use in the operation and expansion of our business. The payment of cash dividends in the future, if any, will be at the discretion of our board of directors and will depend upon such factors as earnings levels, capital requirements, our overall financial condition and any other factors our board deems relevant.

Pursuant to the terms of the Hercules loan, for as long as the Hercules loan is outstanding, we may not pay any cash dividends on our common stock.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to "Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" in this report.

Item 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and the notes thereto included elsewhere in this report.

Condensed Consolidated Statement of Operations Data

	Year Ended December 31,									
	2009		2010		(in thousands)		2012			2013
Revenue:					(111)	tiiousanus)				
Total revenue	\$	-	\$	-	\$	-	\$	-	\$	7,813
Operating expenses:										
Research and development		13,674		15,475		16,872		16,869		41,300
General and administrative		3,027		3,198		3,708		6,069		9,433
Total operating expenses		16,701		18,673		20,580		22,938		50,733
Loss from operations		(16,701)		(18,673)		(20,580)		(22,938)		(42,920)
Other income (expense), net		(1,911)		(1,002)		(641)		(1,289)		(2,114)
Net loss		(18,612)		(19,675)		(21,221)		(24,227)		(45,034)
Accretion of redeemable convertible preferred shares		(2,291)		(3,238)		(3,763)		(313)		-
Net loss attributable to common shareholders		(20,903)		(22,913)		(24,984)		(24,540)		(45,034)
Basic and diluted loss per share	\$	(42.57)	\$	(46.60)	\$	(47.53)	\$	(1.23)	\$	(1.53)
Shares used in computation of basic and diluted loss per share		491,077		491,722		525,689		19,882,585		29,449,716

Condensed Consolidated Balance Sheet Data

	As of December 31,									
	2009		2010		2011		2012		2013	
					(ın t	housands)				
Balance sheet data:										
Cash and equivalents	\$	17,264	\$	20,048	\$	15,602	\$	70,109	\$	96,503
Working capital		8,845		18,339		11,699		65,029		87,675
Total assets		17,918		20,553		16,859		70,738		99,008
Total debt		-		-		13,962		9,850		14,739
Total shareholders' equity (deficit)		(49,446)		(72,215)		(96,685)		57,770		69,658

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under "Item 1A. Risk Factors."

Overview

We are a clinical-stage pharmaceutical company focused on developing differentiated antibiotics for the acute care and community settings to meet critical medical needs in the treatment of bacterial infectious diseases, particularly respiratory tract infections and chronic staphylococcal infections. Our lead product, solithromycin (CEM-101), is in Phase 3 clinical trials. We are developing solithromycin in oral capsules, intravenous, or IV, and suspension formulations, initially for the treatment of community acquired bacterial pneumonia, or CABP, one of the most serious infections of the respiratory tract. Solithromycin is a potent new

fourth generation macrolide and the first fluoroketolide in clinical development. We have also completed a Phase 2 study of solithromycin in uncomplicated gonorrhea. Our second program is Taksta, which we are developing exclusively in the U.S. as a long term oral treatment for prosthetic joint infections caused by staphylococci, including *S. aureus and* MRSA. We are conducting a Phase 2 trial for Taksta in patients with prosthetic joint infections and have submitted a proposal for a Phase 3 trial for Taksta as a treatment for PJI, which could lead to an NDA. If we receive concurrence from the FDA on the planned Phase 3 trial, we plan to stop the Phase 2 trial and roll into the Phase 3 trial.

We acquired worldwide rights (exclusive of ASEAN countries) to a library of over 500 macrolide compounds, including solithromycin, from Optimer Pharmaceuticals, Inc., or Optimer, in March 2006. We entered into a long-term supply arrangement with Ercros, S.A. in March 2011, pursuant to which we have the exclusive right to acquire fusidic acid for the production of Taksta. We believe Ercros is one of only two currently known manufacturers that can produce fusidic acid compliant with the purity required for human use. The United States Patent and Trademark Office (USPTO) issued our patent, entitled "Fusidic Acid Dosing Regimens for Treatment of Bacterial Infections," on May 28, 2013 with claims directed to the company's novel loading dose regimen for Taksta. This patent provides protection until 2029, excluding possible patent term extensions.

Our Board of Directors approved a 1-for-9.5 reverse stock split of our common and preferred shares on January 12, 2012, which became effective on January 29, 2012. All references to common stock, common shares outstanding, average number of common shares outstanding and per share amounts in our consolidated financial statements and notes to consolidated financial statements have been restated to reflect the 1-for-9.5 reverse stock split on a retroactive basis.

Financial Overview

Revenue

To date, we have not generated revenue from the sale of any products. All of our revenue to date has been derived from (1) a government contract and (2) the receipt of up-front proceeds under our license agreement with Toyama, a portion of which has been recognized in accordance with US GAAP.

In May 2013, we entered into an agreement with the Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human Services, or BARDA, for the evaluation and development of solithromycin for the treatment of bacterial infections in pediatric populations and infections caused by bioterror threat pathogens, specifically anthrax and tularemia.

The BARDA agreement is a cost plus fixed fee development contract, with a base performance segment valued at approximately \$17.7 million, and four option work segments that BARDA may request in its sole discretion pursuant to the agreement. If all four option segments are requested, the cumulative value of the agreement would be approximately \$58 million. Three of the options are cost plus fixed fee arrangements and one option is a cost sharing arrangement for which we would be responsible for a designated portion of the costs associated with that work segment. The estimated period of performance for the base performance segment is May 24, 2013 through May 23, 2015. If all option segments are requested, this estimated period of performance would be extended until approximately May 23, 2018.

Under the contract, we are reimbursed and recognize revenue as allowable costs are incurred plus a portion of the fixed-fee earned. We consider fixed-fees under cost reimbursable contracts to be earned in proportion to the allowable costs incurred in performance of the work as compared to total estimated contract costs, with such costs incurred representing a reasonable measurement of the proportional performance of the work completed. Through December 31, 2013, we recognized \$3.5 million in revenue under this agreement.

In May 2013, Cempra Pharmaceuticals, Inc., our wholly owned subsidiary, entered into a license agreement with Toyama, whereby we licensed to Toyama the exclusive right, with the right to sublicense, to make, use and sell any product in Japan that incorporates solithromycin as its sole active pharmaceutical ingredient, or API, for human therapeutic uses, other than for ophthalmic indications or any condition, disease or affliction of the ophthalmic tissues. Toyama also has a nonexclusive license in Japan and certain other countries, with the right to sublicense, to manufacture or have manufactured API for solithromycin for use in manufacturing such products, subject to limitations and obligations of the concurrently executed supply agreement discussed below. Toyama has granted us certain rights to intellectual property generated by Toyama under the license agreement with respect to solithromycin or licensed products for use with such products outside Japan or with other solithromycin-based products inside or outside Japan.

Following execution of the agreement, we received a \$10.0 million upfront payment from Toyama. Toyama is also obligated to pay us up to an aggregate of \$60.0 million in milestone payments, depending on the achievement of various regulatory, patent, development and commercial milestones. Under the terms of the license agreement, Toyama must also pay us a royalty equal to a low-to-high first double decimal digit percentage of net sales, subject to downward adjustment in certain circumstances. Through December 31, 2013, we recognized \$4.3 million in revenue under this agreement and the remainder, which is deferred, will be recognized when earned.

As part of the license agreement, we also entered into a supply agreement with Toyama, whereby we will be the exclusive supplier (with certain limitations) to Toyama and its sublicensees of API for solithromycin for use in licensed products in Japan, as well as the exclusive supplier to Toyama and its sublicensees of finished forms of solithromycin to be used in its clinical trials in Japan. Pursuant to the supply agreement, Toyama will pay us for such clinical supply of finished product and all supplies of API for solithromycin for any purpose, other than the manufacture of products for commercial sale in Japan, at prices equal to our costs. All API for solithromycin supplied by us to Toyama for use in the manufacture of finished product for commercial sale in Japan will be ordered from us at prices determined by our manufacturing costs, and which may, depending on such costs, equal, exceed, or be less than such costs. Either party may terminate the supply agreement for uncured material breach or insolvency of the other party, with Toyama's right to terminate for our breach subject to certain further conditions in the case of our failure to supply API for solithromycin or clinical supply, but otherwise the supply agreement will continue until the expiration or termination of the license agreement.

In the future, we anticipate generating revenue from a combination of sales of our products, if approved, whether through our own or a third-party sales force, and license fees, milestone payments and royalties in connection with strategic collaborations regarding any of our product candidates. We expect that any revenue we generate will fluctuate from quarter to quarter. If we or our strategic partners fail to complete the development of solithromycin or Taksta in a timely manner or obtain regulatory approval for them, or if we fail to develop our own sales force or find one or more strategic partners for the commercialization of approved products, our ability to generate future revenue, and our financial condition and results of operations would be materially adversely affected.

Research and Development Expenses

Since our inception, we have focused our resources on our research and development activities, including conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings for our product candidates. We recognize our research and development expenses as they are incurred. Our research and development expenses consist primarily of:

- employee-related expenses, which include salaries, benefits and share compensation expense, for personnel in research and development functions;
- fees paid to consultants and clinical research organizations, or CROs, in connection with our clinical trials, and other
 related clinical trial costs, such as for investigator grants, patient screening, laboratory work and statistical compilation
 and analysis;
- costs related to acquiring and manufacturing clinical trial materials;
- costs related to compliance with regulatory requirements;
- consulting fees paid to third parties related to non-clinical research and development;
- research supplies; and
- license fees and milestone payments related to in-licensed technologies.

Our direct research and development expenses consist principally of external costs, such as fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical trials, and related clinical trial fees. Our internal resources, employees and infrastructure are not directly tied to any individual research project and are typically deployed across multiple projects. Through our clinical development programs, we are advancing solithromycin and Taksta in parallel primarily for the treatment of CABP and prosthetic joint infections, respectively, as well as for other indications. Through our pre-clinical development programs, we are seeking to develop macrolide product candidates for non-antibacterial indications.

The following table sets forth costs incurred on a program-specific basis for solithromycin and Taksta, excluding personnel-related costs. Macrolide research includes costs for discovery programs. All employee-related expenses for those employees working in research and development functions are included in "Research and development personnel cost" in the table, including salary, bonus, employee benefits and share-based compensation. We do not allocate insurance or other indirect costs related to our research and development function to specific product candidates. Those expenses are included in "Indirect research and development expense" in the table.

		Year Ended December 31,							
	2011		2012			2013			
			(in t	housands)					
Direct research and development expense by program:									
Solithromycin	\$	14,129	\$	12,786	\$	34,155			
Taksta		282		1,079		1,459			
Macrolide research		162		46		61			
Research and development personnel cost		1,865		2,657		4,887			
Total direct research and development expense		16,438		16,568		40,562			
Indirect research and development expense		434		301		738			
Total research and development expense	\$	16,872	\$	16,869	\$	41,300			

The successful development of our clinical and pre-clinical product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our clinical or pre-clinical product candidates or the period, if any, in which material net cash inflows from these product candidates may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our ongoing, as well as any additional clinical trials required and other research and development activities;
- future clinical trial results; and
- the timing of regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

We are conducting our pivotal trial program for solithromycin, including one trial with oral solithromycin and one trial with IV solithromycin progressing to oral solithromycin. Both of these trials are randomized, double-blinded studies conducted against a comparator drug agreed upon with the FDA, for which we will have to show non-inferiority from an efficacy perspective and acceptable safety and tolerability. Using feedback received from the FDA, we began the Phase 3 trial with oral solithromycin in December 2012. We finalized the overall development program for solithromycin for CABP with the FDA at our end of Phase 2 meeting for solithromycin, which occurred in May 2013, and initiated the IV-to-oral trial in the December 2013. In 2010, we successfully completed a Phase 2 clinical trial with Taksta in ABSSSI patients. In this trial, the Taksta loading dose regimen demonstrated efficacy, safety and tolerability that was comparable to linezolid. Like ABSSSI, prosthetic joint infections are often caused by *S. aureus*, including MRSA. At this time, however, we do not intend to pursue Taksta as a treatment for ABSSSI. In December 2012, we initiated a Phase 2 trial of Taksta in patients with prosthetic joint infections.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs, including share-based compensation, for employees in executive, operational, finance and human resources functions. Other significant general and administrative expenses include professional fees for accounting, legal, and information technology services, facilities costs, and expenses associated with obtaining and maintaining patents.

We expect that our general and administrative expenses will increase with the continued development and potential commercialization of our product candidates. We believe that these increases will likely include increased costs related to the hiring of additional personnel and increased fees for outside consultants, lawyers and accountants. We also expect to incur significant costs to comply with corporate governance, internal controls and similar requirements applicable to public companies.

Other Income (Expense), Net

Interest income consists of interest earned on our cash and equivalents as well as changes in fair value of warrants issued in connection with the August 2011 Notes and the Hercules loan as described below. We expect our interest income to decrease as our cash resources are used to fund the development of our programs.

Interest expense in 2011 consists of interest accrued under the August 2011 Notes and the Hercules loan as described below. Interest expense in 2012 and 2013 consists of interest accrued and paid under the Hercules loan as described below as well as changes in fair value of warrants issued in connection with the Hercules warrant agreement as described below.

In August 2011, we issued unsecured convertible notes, referred to as the August 2011 Notes, in the original aggregate principal amount of \$5.0 million. The August 2011 Notes bore interest at a rate of 10.0% per annum, originally were to mature on August 4, 2012 and precluded us from incurring any other debt in excess of \$0.5 million or granting a security interest in any of our assets without the consent of the noteholders. This restriction was revised by our shareholders in connection with the Hercules loan (discussed below) in December 2011. Also in connection with the Hercules loan, in December 2011, we and the holders of the August 2011 Notes agreed to extend the maturity dates of the August 2011 Notes to May 29, 2016. We did not record any gain or loss in connection with the extension of the maturity date of the August 2011 Notes because we determined that the extension of the maturity date of the August 2011 Notes met the criteria of a troubled debt restructuring outlined in ASC Topic 470-60, Troubled Debt Restructurings. The August 2011 Notes converted into shares of common stock in connection with the IPO completed in February 2012. Additionally, we granted warrants to the holders of the August 2011 Notes, which, after completion of the IPO in February 2012, became exercisable for shares of common stock with an exercise price equal to the IPO price of \$6.00.

In December 2011, we entered into a \$20,000,000 loan and security agreement (the "December 2011 Note") with Hercules Technology Growth Capital, Inc. ("Hercules") and borrowed \$10,000,000 upon closing. The principal amount outstanding under the \$10,000,000 borrowing bears interest at the greater of (i) 9.55%, or (ii) the sum of 9.55% plus the prime lending rate, as published by the Wall Street Journal, minus 3.25% per annum. The terms of the December 2011 Note agreement provided that we could, at any time prior to October 1, 2012, request another borrowing in the aggregate amount of \$10,000,000. We elected not to request the additional borrowing and let the option expire on September 30, 2012. In May 2013, we amended the December 2011 Note, increasing the initial loan amount to \$15,000,000, receiving an additional \$5,238,327 upon closing. We also extended the date by which it could request the additional \$10,000,000 to September 30, 2013. We elected not to request the additional borrowing and let the option expire on September 30, 2013. This amendment also provides for us to make interest only payments through June 2014. Principal and interest payments will start July 1, 2014 over a 36-month amortization period. The principal balance outstanding on the loan agreement and all accrued but unpaid interest thereunder will be due and payable on June 1, 2017. In addition, we are required to pay Hercules the following fees:

- \$400,000 on the earliest to occur of (i) December 1, 2015, (ii) the date that we prepay all of the outstanding advances and accrued interest, or (iii) the date that all of the advances and interest become due and payable.
- \$495,245 on the earliest to occur of (i) June 1, 2017, (ii) the date that we prepay all of the outstanding advances and accrued interest, or (iii) the date that all of the advances and interest become due and payable.

We granted Hercules a security interest in all of its assets, except intellectual property. Our obligations to Hercules include restrictions on borrowing, asset transfers, placing liens or security interests on our assets including our intellectual property, mergers and acquisitions and distributions to stockholders.

In connection with the initial closing of the December 2011 note, we entered into a warrant agreement with Hercules (the "First Hercules Warrant"), under which Hercules has the right to purchase 39,038 shares of our common stock. The exercise price of the First Hercules Warrant was initially \$10.25 per share, subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. In connection with the amendment to the loan agreement, the exercise price of the First Hercules Warrant was reduced to the lower of (a) \$6.11, and (b) the effective price per share of our common stock issued or issuable in any offering of our equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes. The First Hercules Warrant expires on December 20, 2021. Proceeds equal to the fair value of the First Hercules Warrant were recorded as a liability at the date of issuance and the borrowings under the December 2011 Note will be increased to equal the face amount of the borrowings plus interest through interest expense over the term of the loan using the effective interest method. Upon completion of IPO, the warrant liability was reclassified to additional paid-in capital. Since the amendment to the warrant resulted in a variable exercise price, the fair value of the warrant as of the date of the amendment was reclassified from additional paid-in capital to a warrant liability.

Additionally, in connection with the amendment of the December 2011 note, we entered into a warrant agreement with Hercules (the "Second Hercules Warrant"), under which Hercules has the right to purchase an aggregate number of shares of our common stock equal to the quotient derived by dividing \$609,533 by the exercise price then in effect, which is defined as the lower of (a) \$6.11, and

(b) the effective price per share of our common stock issued or issuable in any offering of our equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes. The exercise price is subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. The Second Hercules Warrant expires on May 31, 2023. Proceeds equal to the fair value of the Second Hercules Warrant were recorded as a liability at the date of issuance and the borrowings under the December 2011 Note will be increased to equal the face amount of the borrowings plus interest through interest expense over the term of the loan using the effective interest method.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses and the disclosure of contingent assets and liabilities in our financial statements. We evaluate our estimates and judgments, including those related to accrued expenses and share-based compensation, on an ongoing basis. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates.

Our significant accounting policies are described in more detail in the notes to our audited consolidated financial statements included in this report. We believe the following accounting policies to be most critical to the judgments and estimates used in preparation of our financial statements and such policies have been reviewed and discussed with our audit committee.

Accrued Expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable vendor personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued expenses include:

- fees paid to CROs in connection with pre-clinical or clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- milestone payments; and
- · unpaid salaries, wages and benefits.

We accrue our expenses related to clinical trials based on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. We do not currently anticipate the future settlement of existing accruals to differ materially from our estimates.

Revenue Recognition

Our revenue generally consists of research related revenue under federal contracts and licensing revenue related to non-refundable upfront fees, milestone payments and royalties earned under license agreements. Revenue is recognized when the following criteria are met: (1) persuasive evidence that an arrangement exists; (2) delivery of the products and/or services has occurred; (3) the selling price is fixed or determinable; and (4) collectability is reasonably assured.

For arrangements that involve the delivery of more than one element, each product, service and/or right to use assets is evaluated to determine whether it qualifies as a separate unit of accounting. This determination is based on whether the deliverable has "stand-alone value" to the customer. The consideration that is fixed or determinable is then allocated to each separate unit of accounting based on the relative selling prices of each deliverable. The consideration allocated to each unit of accounting is recognized as the related goods and services are delivered, limited to the consideration that is not contingent upon future deliverables.

When an arrangement is accounted for as a single unit of accounting, we determine the period over which the performance obligations will be performed and revenue recognized. Management exercises significant judgment in the determination of whether a deliverable has stand-alone value, is considered to be a separate unit of accounting, and in estimating the relative fair value of each deliverable in the arrangement.

Valuation of Financial Instruments

Liability-classified warrants

In connection with the initial \$20,000,000 loan and security agreement with Hercules under which we borrowed \$10,000,000 upon closing on December 20, 2011, we entered into the First Hercules Warrant, under which Hercules has the right to purchase up to 39,038 shares of common stock at an exercise price per share of \$10.25 subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. In connection with the amendment of the loan agreement, the exercise price of the First Hercules Warrant was reduced to the lower of (a) \$6.11, and (b) the effective price per share of our common stock issued or issuable in any offering of our equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes. The warrant expires on December 20, 2021. Proceeds equal to the fair value of the warrants were recorded as a liability at the date of issuance and the borrowings under the Hercules loan will be increased to equal the face amount of the borrowings plus interest through interest expense over the term of the loan using the effective interest method.

In May 2013, we amended the Hercules loan and security agreement increasing the initial loan amount to \$15,000,000. In connection with this amendment, we entered into the Second Hercules Warrant, under which Hercules has the right to purchase an aggregate number of shares of our common stock equal to the quotient derived by dividing \$609,533 by the exercise price then in effect, which is defined as the lower of (a) \$6.11, and (b) the effective price per share of our common stock issued or issuable in any offering of our equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes. The exercise price is subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. The warrant expires on May 31, 2023. Proceeds equal to the fair value of the warrants were recorded as a liability at the date of issuance and the borrowings under the Hercules loan will be increased to equal the face amount of the borrowings plus interest through interest expense over the term of the loan using the effective interest method.

The fair value of the First and Second Hercules Warrants is determined using a Binomial model. The valuation of warrants is subjective and is affected by changes in inputs to the valuation model including the price per share of our common stock, the historical volatility of the stock prices of our peer group, risk-free rates based on U.S. Treasury security yields, the expected term of the warrants and our dividend yield. Changes in these assumptions can materially affect the fair value estimate. We will continue to classify the estimated fair value of the First and Second Hercules Warrants as liabilities and record changes in fair value in other income (expense) until June 1, 2014 when the exercise price is no longer adjustable.

Share-Based Compensation

In accordance with FASB ASC Topic 718, *Stock Compensation*, as modified or supplemented, we measure compensation cost for share-based payment awards granted to employees and non-employee directors at fair value using the Black-Scholes option-pricing model. We recognize compensation expense on a straight-line basis over the service period for awards expected to vest. Share-based compensation cost related to share-based payment awards granted to non-employees is adjusted each reporting period for changes in the fair value of our shares until the measurement date. The measurement date is generally considered to be the date when all services have been rendered or the date that options are fully vested.

Share-based compensation expense includes options granted to employees and non-employees and has been reported in our statements of operations as follows:

		Year Ended December 31,						
	2	2011		2012		2012		2013
			(in t	housands)				
Research and development	\$	158	\$	520	\$	963		
General and administrative		286		1,149		2,249		
Total	\$	444	\$	1,669	\$	3,212		

We calculate the fair value of share-based compensation awards using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of subjective assumptions, including share price volatility, the expected life of options, risk-free interest rate and the fair value of the underlying common shares on the date of grant. In developing our assumptions, we take into account the following:

- we do not have sufficient history to estimate the volatility of our common share price. We calculate expected volatility based on reported data for selected reasonably similar publicly traded companies for which the historical information is available. For the purpose of identifying peer companies, we consider characteristics such as industry, market capitalization, length of trading history, similar vesting terms and in-the-money option status. We plan to continue to use the guideline peer group volatility information until the historical volatility of our common shares is relevant to measure expected volatility for future option grants;
- we determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant;
- the assumed dividend yield is based on our expectation of not paying dividends in the foreseeable future;
- we determine the average expected life of options based on the mid-point between the vesting date and the contractual term; and
- we estimate forfeitures based on our historical analysis of actual option forfeitures.

The assumptions used in the Black-Scholes option-pricing model for the years ended December 31, 2011, 2012, and 2013 are set forth below:

		Year Ended December 31,						
	2011	2011			2013	3		
		Non-		Non-		Non-		
	Employees	employees	Employees	employees	Employees	employees		
Volatility	73.9%	N/A	72.5%	53.5%	70.8%	69.8%		
Risk-free interest rate	2.5%	N/A	1.3%	1.6%	1.0%	2.3%		
Expected dividend yield	0.0%	N/A	0.0%	0.0%	0.0%	0.0%		
Expected life of options (in years)	6.1	N/A	5.5	9.5	5.5	9.8		

Results of Operations

Comparison of Year Ended December 31, 2012 and Year Ended December 31, 2013

The following table summarizes the results of our operations for each of the years ended December 31, 2012 and 2013, together with the changes in those items in dollars:

	 Year Ended I 2012	Decen	nber 31, 2013	Dollar Change
Revenue				
Contract research	\$ -	\$	3,478	\$ 3,478
License	 -		4,335	4,335
Total revenue	 		7,813	 7,813
Research and development expense (1)	16,869		41,300	24,431
General and administrative expense (1)	6,069		9,433	3,364
Other income (expense), net	(1,289)		(2,115)	(826)
(1) Includes the following stock-based compensation expenses:				
Research and development expense	\$ 520	\$	963	\$ 443
General and administrative expense	1,149		2,249	1,100

Contract revenue

For the twelve months ended December 31, 2013, contract research revenue increased \$3.5 million as we initiated our BARDA contract in May 2013. We expect contract research revenue to continue to increase as the base performance segment of the contract progresses.

License revenue

License revenue of \$4.3 million was recognized upon receipt of the \$10.0 million upfront payment from the execution of the Toyama license agreement in May 2013.

Research and Development Expense

For the twelve months ended December 31, 2013, our research and development expenses increased to \$41.3 million compared to \$16.9 million for the twelve months ended December 31, 2012. The increase of \$24.4 million is primarily related to the following:

- an increase in solithromycin clinical trial expenses of \$17.2 million primarily related to the ongoing Phase 3 oral study and the initiation of the Phase 3 IV to oral study;
- an increase in Taksta clinical trial expenses of \$1.0 million primarily related to the ongoing Phase 2 study;
- an increase in clinical trial supplies of \$2.7 million;
- an increase in pre-clinical studies of \$1.8 million;
- an increase in consulting expense of \$0.8 million;
- a decrease in license fee and milestone payments of \$1.4 million; and
- an increase in employee cost of \$2.3 million primarily from increased headcount and stock compensation expense.

General and Administrative Expense

For the twelve months ended December 31, 2013, our general and administrative costs increased to \$9.4 million compared to \$6.0 million for the twelve months ended December 31, 2012. The increase of \$3.4 million is related to increases in employee costs, mainly stock compensation expense, franchise tax, legal and other professional service fees.

Other Income (Expense), Net

Other income (expense), net increased by \$0.8 million in the year ended December 31, 2013 compared to the year ended December 31, 2012 as a result of a \$0.1 million increase in warrant liability fair value adjustments recorded as interest expense and a \$0.7 million increase in interest expense related to the December 2011 Notes.

Comparison of Year Ended December 31, 2011 and Year Ended December 31, 2012

The following table summarizes the results of our operations for each of the years ended December 31, 2011 and 2012, together with the changes in those items in dollars and as a percentage:

	 Year Ended 2011	Decen	nber 31, 2012	Dollar Change
Revenue	\$ -	\$	-	\$ -
Research and development expense (1)	16,872		16,869	(3)
General and administrative expense (1)	3,708		6,069	2,361
Other income (expense), net	(641)		(1,289)	(648)
(1) Includes the following stock-based compensation expenses:				
Research and development expense	\$ 158	\$	520	\$ 362
General and administrative expense	286		1,149	863

Revenue

We did not recognize any revenue for the years ended December 31, 2011 and 2012.

Research and Development Expense

For the twelve months ended December 31, 2012, our research and development expenses remained consistent compared to the twelve months ended December 31, 2011as a result of the following:

- a \$3.2 million decrease in API purchases;
- a \$3.5 million decrease in the solithromycin oral Phase 2 clinical trial expenses as the study was completed in Q4 2011;
- a \$1.4 million decrease in in pre-clinical costs;
- a \$4.5 million increase in the initiation of our Phase 3 trial for oral solithromycin;
- a \$0.8 million increase in drug development costs;

- a \$1.4 million increase in license fee and milestone payments;
- a \$0.7 million increase in the Taksta Phase 2 clinical trial expenses in Q4 2012; and
- a \$0.7 million increase in indirect expenses.

General and Administrative Expense

General and administrative expense increased \$2.3 million for the year ended December 31, 2012 compared to the year ended December 31, 2011. Financing activities in 2011 drove increases in legal, accounting and tax services that were partially offset by decreases in employee costs and information technology services from reduced headcount in business development and a change in IT service provider.

Other Income (Expense), Net

Other income (expense), net decreased by \$0.7 million in the year ended December 31, 2012 compared to the year ended December 31, 2011 as a result of a \$0.1 million increase in fair value adjustments recorded as interest income and a \$0.8 million increase in interest expense related to the August and December 2011 Notes.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception in November 2005 through December 31, 2013, we have funded our operations primarily with \$239.5 million from debt, and the sale of convertible notes, convertible preferred shares, common shares and common stock. As of December 31, 2013, we had cash and equivalents of approximately \$96.5 million.

Cash Flows

The following table sets forth the major sources and uses of cash for the periods set forth below:

	Year Ended December 31,					
	 2011	2012	2013			
		(in thousands)				
Net cash provided by (used in):						
Operating activities	\$ (18,315)	\$ (23,107)	\$ (32,441)			
Investing activities	(13)	(8)	(134)			
Financing activities	 13,882	77,622	58,969			
Net increase (decrease) in cash and equivalents	\$ (4,446)	\$ 54,507	\$ 26,394			

Operating Activities. Cash used in operating activities of \$18.3 million during the year ended December 31, 2011 was primarily a result of our \$21.2 million net loss, offset by changes in operating assets and liabilities of \$2.0 million and non-cash items of \$0.9 million. Cash used in operating activities of \$23.1 million during the year ended December 31, 2012 was primarily a result of our \$24.2 million net loss and changes in operating assets and liabilities of \$0.9 million offset by non-cash items of \$2.0 million. Cash used in operating activities of \$32.4 million during the year ended December 31, 2013 was primarily a result of our \$45.0 million net loss, offset by changes in operating assets and liabilities of \$8.5 million and non-cash items of \$4.1 million.

Investing Activities. Net cash used in investing activities was \$13,000, \$8,000 and \$134,000 for the years ended December 31, 2011, 2012 and 2013, respectively, primarily related to our purchases of equipment.

Financing Activities. Net cash provided by financing activities was \$13.9 million for the year ended December 31, 2011, \$77.6 million for the year ended December 31, 2012 and \$59.0 million for the year ended December 31, 2013. The cash provided by financing activities in the year ended December 31, 2011 consisted primarily of proceeds from the August 2011 Notes of \$5.0 million and the Hercules loan of \$10.0 million offset by issuance costs of \$1.2 million. Additionally, we received \$70,000 of proceeds from the issuance of common shares pursuant to the exercise of stock options. The cash provided by financing activities of \$77.6 million in the year ended December 31, 2012 consisted primarily of gross proceeds of \$58.0 million from the IPO and a \$25.0 million private placement, offset by underwriting discounts and offering costs of \$5.6 million. The cash provided by financing activities of \$59.0 million in the year ended December 31, 2013 consisted primarily of gross proceeds of \$57.9 million from the public offering in June 2013 offset by underwriting discounts and offering costs of \$3.7 million and \$5.2 million of proceeds from the amendment of the December 2011 Note.

Funding Requirements

To date, we have not generated any product revenue from our clinical stage product candidates or from any other source. We do not know when, or if, we will generate any product revenue. We do not expect to generate product revenue unless and until we obtain marketing approval of, and commercialize solithromycin and/or Taksta or any of our other product candidates. At the same time, we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, solithromycin and Taksta and our other product candidates. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. We will need substantial additional funding in connection with our continuing operations.

Based on current assumptions, we expect that our existing cash and equivalents, including interest thereon, will enable us to fund our operating expenses and capital expenditure requirements through 2015, which includes the completion of enrollment in our two Phase 3 clinical trials and the completion of the two ancillary clinical studies currently expected to be necessary to support the planned NDA for solithromycin for the treatment of CABP. This projection does not include any funds from future financings or partnerships beyond the Toyama relationship. We will need to obtain additional financing for the continued development of Taksta and our other product candidates and prior to the commercialization of any of our product candidates. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Due to the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development of our product candidates.

Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our ongoing oral solithromycin Phase 3 trial and Phase 3 IV-to-oral trial for solithromycin, our ongoing Taksta Phase 2 trial and any future trials for solithromycin and Taksta;
- the scope, progress costs, and results of pre-clinical development, laboratory testing and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive regulatory approval;
- Receipt of payments under the BARDA contract;
- our ability to establish collaborations on favorable terms;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- revenue if any, received from sales of our product candidates, if approved by the FDA;
- the extent to which we acquire or invest in businesses, products and technologies;
- our ability to obtain government or other third-party funding; and
- Obtaining milestone payments from Toyama.

Until we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of any securities may include liquidation or other preferences that adversely affect our stockholders' rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, such as currently imposed under the loan from Hercules. 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.

We plan to seek partners or other sources of third-party funding, including government grants, for the continued development of solithromycin and Taksta and our other product candidates. If we are unable to raise additional funds when needed, whether on favorable terms or not, we may be required to delay, limit, reduce or terminate our development of our product candidates, or our

commercialization efforts, or to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our significant contractual obligations and commercial commitments at December 31, 2013 and the effects such obligations are expected to have on our liquidity and cash flows in future periods (in thousands):

				More
		1 - 3	4 - 5	Than
	 Total	 years	 years	 5 years
Operating lease	\$ 1,350	\$ 678	\$ 553	\$ 119
The Scripps Research Institute	748	203	170	375
December 2011 Note	15,895	12,554	3,341	-
Interest on December 2011 Note	3,077	2,996	81	-
Total	\$ 21,070	\$ 16,431	\$ 4,145	\$ 494

In May 2013, we amended our operating lease agreement for office space in Chapel Hill, North Carolina. The new lease provides for aggregate lease payments of \$1.3 million paid over a 68 month term.

In December 2011, we entered into the \$20,000,000 the December 2011 Note with Hercules and borrowed \$10,000,000 upon closing. The principal amount outstanding under the \$10,000,000 borrowing bears interest at the greater of (i) 9.55%, or (ii) the sum of 9.55% plus the prime lending rate, as published by the Wall Street Journal, minus 3.25% per annum. The terms of the December 2011 Note agreement provided that we could, at any time prior to October 1, 2012, request another borrowing in the aggregate amount of \$10,000,000. We elected not to request the additional borrowing and let the option expire on September 30, 2012. In May 2013, we amended the December 2011 Note, increasing the intial loan amount to \$15,000,000, receiving an additional \$5,238,327 upon closing. We also extended the date by which we could request the additional \$10,000,000 to September 30, 2013. We elected not to request the additional borrowing and let the option expire on September 30, 2013. This amendment also provides for us to make interest only payments through June 2014. Principal and interest payments will start July 1, 2014 over a 36-month amortization period. The principal balance outstanding on the loan agreement and all accrued but unpaid interest thereunder will be due and payable on June 1, 2017. In addition, we are to pay Hercules the following fees:

- \$400,000 on the earliest to occur of (i) December 1, 2015, (ii) the date that we prepay all of the outstanding advances and accrued interest, or (iii) the date that all of the advances and interest become due and payable.
- \$495,245 on the earliest to occur of (i) June 1, 2017, (ii) the date that we prepay all of the outstanding advances and accrued interest, or (iii) the date that all of the advances and interest become due and payable

We granted Hercules a security interest in all of our assets, except intellectual property. Our obligations to Hercules include restrictions on borrowing, asset transfers, placing liens or security interests on our assets including its intellectual property, mergers and acquisitions and distributions to stockholders.

In connection with the initial closing of the December 2011 Note, we entered into a warrant agreement with Hercules, referred to as the First Hercules Warrant, under which Hercules has the right to purchase 39,038 shares of our common stock. The exercise price of the First Hercules Warrant was initially \$10.25 per share, subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. In connection with the amendment to the December 2011 Note, the exercise price of the First Hercules Warrant was reduced to the lower of (a) \$6.11, and (b) the effective price per share of our common stock issued or issuable in any offering of our equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes, The First Hercules Warrant expires on December 20, 2021.

Additionally, in connection with the amendment of the December 2011 Note, we entered into a warrant agreement with Hercules, referred to as the Second Hercules Warrant, under which Hercules has the right to purchase an aggregate number of shares of our common stock equal to the quotient derived by dividing \$609,533 by the exercise price then in effect, which is defined as the lower of (a) \$6.11, and (b) the effective price per share of the common stock issued or issuable in any offering of the our equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes. The exercise price is subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. The Second Hercules Warrant expires on May 31, 2023.

Effective June 12, 2012, Cempra Pharmaceuticals, Inc., our wholly owned subsidiary, entered into a license agreement with The Scripps Research Institute, or TSRI, whereby TSRI licensed to us rights, with rights of sublicense, to make, use, sell, and import

products for human or animal therapeutic use that use or incorporate one or more macrolides as an active pharmaceutical ingredient and is covered by certain patent rights owned by TSRI claiming technology related to copper-catalysed ligation of azides and acetylenes. The rights licensed to us are exclusive as to the People's Republic of China (excluding Hong Kong), South Korea and Australia, and are non-exclusive in all other countries worldwide, except the member-nations of the Association of Southeast Asian Nations, which are not included in the territory of the license. Under the terms of the agreement with TSRI, we paid a one-time only, non-refundable license issue fee in the amount of \$350,000. Our rights under the agreement are subject to certain customary rights of the U.S. government that arise or result from TSRI's receipt of research support from the U.S. government.

We are also obligated to pay annual maintenance fees to TSRI in the amount of (i) \$50,000 each year for the first three years (beginning on the first anniversary of the agreement), and (ii) \$85,000 each year thereafter (beginning on the fourth anniversary of the agreement). Each calendar year's annual maintenance fees will be credited against sales royalties due under the agreement for such calendar year. Under the terms of the agreement, we must pay TSRI low single-digit percentage royalties on the net sales of the products covered by the TSRI patents for the life of the TSRI patents, a low single-digit percentage of non-royalty sublicensing revenue received with respect to countries in the nonexclusive territory and a mid-single-digit percentage of sublicensing revenue received with respect to countries in the exclusive territory, with the sublicensing revenue royalty in the exclusive territory and the sales royalties subject to certain reductions under certain circumstances. TSRI is eligible to receive milestone payments of up to \$1.1 million with respect to regulatory approval in the exclusive territory and first commercial sale, in each of the exclusive territory and nonexclusive territory, of the first licensed product to achieve those milestones that is based upon each macrolide covered by the licensed patents. Each milestone is payable once per each macrolide. Each milestone payment made to TSRI with respect to a particular milestone will be creditable against any payment due to TSRI with respect to any sublicense revenues received in connection with the achievement of such milestone. Any payments made to TSRI under the TSRI license for territories subject to the Optimer agreement, discussed below, can be deducted pursuant to the terms of the license agreement we have with Optimer from any sales-based royalty payments due under the Optimer agreement up to a certain percentage reduction of the royalties due to Optimer.

Under the terms of the TSRI agreement, we are also required to pay additional fees on royalties, sublicensing and milestone payments if we, an affiliate, or a sub licensee challenges the validity or enforceability of any of the patents licensed under the agreement. Such increased payments would be required until all patent claims subject to challenge are invalidated in the particular country where such challenge was mounted.

The term of the TSRI license agreement (and the period during which we must pay royalties to TSRI in a particular country for a particular product) will end, on a country-by-country and product-by-product basis, at such time as no patent rights licensed from TSRI cover a particular product in the particular country. We have included in the table above the annual payments due TSRI, but have not included any other payments because we cannot estimate if, when or in what amounts such payments will become due under the agreement.

In March 2006, we entered into a Collaborative Research and Development and License Agreement with Optimer. Under the terms of the Optimer agreement, we acquired exclusive rights to further develop and commercialize certain Optimer technology worldwide, excluding ASEAN countries. As partial consideration for this license, during 2007 and 2006, we issued to Optimer an aggregate of 1,193,638 common shares with a total value of \$0.2 million. We also have an obligation to make additional payments upon achievement of specified development, regulatory and commercialization milestones. The aggregate amount of such milestone payments we may need to pay is based in part on the number of products developed under the agreement. The aggregate amount of such payments would be \$27.5 million if four products are developed and gain FDA approval. Additional limited milestone payments would be due if we develop more than four products. In July 2010, we made a \$0.5 million milestone payment to Optimer after our successful completion of the Phase 1 trial for oral solithromycin and in July 2012 we made a \$1.0 million milestone payment upon completion of our discussions with the FDA for the protocol for our proposed pivotal Phase 3 trial for oral solithromycin. Optimer can elect to receive certain milestone payments in cash or in shares of our common stock having an equivalent fair market value. We are also obligated to make tiered, mid-single-digit royalty payments to Optimer based on annual net sales of licensed products outside the ASEAN countries, which royalties are subject to reduction in the event additional licenses are obtained from third parties in order to practice our rights under the agreement and/or we are required to grant a compulsory license to a third party. We have not included these payments in the table above because we cannot estimate if, when or in what amounts such payments will become due under this agreement.

We enter into contracts in the normal course of business with clinical research organizations for clinical trials and clinical supply manufacturing and with vendors for pre-clinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice and therefore we believe that our non-cancelable obligations under these agreements are not material.

Net Operating Losses

As of December 31, 2013, we had federal net operating loss carryforwards of approximately \$108.1 million and state net operating loss carryforwards of approximately \$106.9 million. The net operating loss carryforwards begin to expire in 2026 and 2021 for federal and state tax purposes, respectively. We also had federal research and development credit carryforwards of approximately \$4.2 million which begin to expire in 2026 and federal charitable contribution carryforwards of approximately \$90,900 which begin to expire in 2014.

The Tax Reform Act of 1986 contains provisions which limit the ability to utilize the net operating loss carryforwards in the case of certain events including significant changes in ownership interests. If our net operating loss carryforwards are limited, and we have taxable income which exceeds the permissible yearly net operating loss carryforward, we would incur a federal income tax liability even though net operating loss carryforwards would be available in future years.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under SEC rules.

Recent Accounting Pronouncements

We have evaluated whether there are any material new accounting pronouncements applicable to the Company that have been issued but not yet adopted as of December 31, 2013 and noted none.

Cautionary Statement

We operate in a highly competitive environment that involves a number of risks, some of which are beyond our control. The following statement highlights some of these risks. For more detail, see "Item 1A. Risk Factors".

Statements contained in this Form 10-K that are not historical facts are or might constitute forward-looking statements under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Although we believe the expectations reflected in such forward-looking statements are based on reasonable assumptions, our expectations might not be attained. Forward-looking statements involve known and unknown risks that could cause actual results to differ materially from expected results. Factors that could cause actual results to differ materially from expectations expressed in the report include, among others: risks related to the costs, timing, regulatory review and results of our studies and clinical trials; our ability to obtain FDA approval of our product candidates; differences between historical studies on which we have based our planned clinical trials and actual results from our trials; our anticipated capital expenditures, our estimates regarding our capital requirements, and our need for future capital; our liquidity and working capital requirements; our expectations regarding our revenues, expenses and other results of operations; the unpredictability of the size of the markets for, and market acceptance of, any of our products; our ability to sell any approved products and the price we are able realize; our need to obtain additional funding and our ability to obtain future funding on acceptable terms; our ability to retain and hire necessary employees and to staff our operations appropriately; our ability to compete in our industry and innovation by our competitors; our ability to stay abreast of and comply with new or modified laws and regulations that currently apply or become applicable to our business; estimates and estimate methodologies used in preparing our financial statements; the future trading prices of our common stock and the impact of securities analysts' reports on these prices; and the risks set out in our filings with the SEC.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates.

We do not believe that our cash and equivalents have significant risk of default or illiquidity. While we believe our cash and equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and equivalents at one or more financial institutions that are in excess of federally insured limits.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during 2011, 2012 or 2013.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e)) are designed only to provide reasonable assurance that information to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. As of the end of the period covered by this report, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer (our principal executive officer) and Chief Financial Officer (our principal financial officer), of the effectiveness of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15(b). Based upon that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of the end of the period covered by this report to provide the reasonable assurance discussed above.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. A control system, no matter how well designed and operated, can only provide reasonable, not absolute, assurance that the objectives of the control system are met. Because of these inherent limitations, management does not expect that our internal controls over financial reporting will prevent all error and all fraud. Under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control—Integrated Framework (1992 Framework) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in Internal Control—Integrated Framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2013.

This annual report does not include an attestation report of our independent registered public accounting firm regarding our internal control over financial reporting due to an exemption provided by the JOBS Act for emerging growth companies.

Changes in Internal Control over Financial Reporting

No change to our internal control over financial reporting occurred during the last fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

We have adopted a written code of ethics and business conduct that applies to our directors, executive officers and all employees. We intend to disclose any amendments to, or waivers from, our code of ethics and business conduct that are required to be publicly disclosed pursuant to rules of the SEC by filing such amendment or waiver with the SEC. This code of ethics and business conduct can be found in the corporate governances section of our website, www.cempra.com.

Executive Officers

As of February 20, 2014, our executive officers are Dr. Prabhavathi Fernandes, our President and Chief Executive Officer and Mark W. Hahn, our Chief Financial Officer. Information for each is provided below.

Name	Age (as of 02/20/14)	Business Experience For Last Five Years
Prabhavathi Fernandes, Ph.D.	64	Dr. Fernandes, one of our founders, has been our President and Chief Executive Officer and a member of our board of directors since our founding in November 2005. Prior to that, she was President and Chief Executive Officer of several privately-held companies, including DarPharma, Inc. from 2003 to 2005, Ricerca Biosciences from 2000 to 2003 and Small Molecule Therapeutics from 1998 to 2000 Dr. Fernandes was Vice President, Drug Discovery of Bristol-Myers Squibb Company from 1988 to 1998, Senior Director of Squibb Pharmaceutical Research Institute from 1987 to 1988, Senior Project Leader of Abbott Laboratories from 198 to 1987 and Senior Microbiologist of the Squibb Institute for Medical Research, the research division of E.R. Squibb and Sons, from 1980 to 1983. During her years at Squibb, Abbott and Bristol-Meyers Squibb, she was directly involved in the development of numerous antibiotics, four of which have been approved by the FD and one achieving sales over a billion dollars. She has served on the advisory board of Optimer Pharmaceuticals, Inc. since 2004 and the supervisory board of GPC Biotech AG from 2004 to 2008. Dr. Fernandes served on the product development working group for Biodefense for the National Institute of Allergy and Infectious Diseases from 2003 to 2004 and the U.S. Congressional Panel for Assessment of Impact of Antibiotic Resistant Bacteria and the American Society for Microbiology Advisory Panel for Antibiotic Resistance from 1991 to 1995. Dr. Fernandes holds a B.S. in botany, zoology and chemistry from the University of Bangalore (India), an M.S. in microbiology from Thomas Jefferson University, Philadelphia,
Mark W. Hahn	51	Mr. Hahn has been our Executive Vice President and Chief Financial Officer since February 2010. From 2008 to 2009, Mr. Hahn was the Chief Financial Officer of Athenix Corp., an agricultural biotechnology company, leading its merger with Baye CropScience, where he served as Finance Director into 2010. Mr. Hahn has been the chief financial officer of various companies including GigaBeam Corporation, a telecommunications equipment company, from 2007 to 2008; BuildLinks, Inc., a software company, from 2002 to 2007; PerformaWorks, Inc., a software company, from 2001 to 2002; and Charles & Colvard, Ltd., a consumer products company, from 1996 to 2001. Mr. Hahn also served in various capacities, culminating in Senior Manager, at Ernst & Young and its predecessors from 1984 until 1996. Mr. Hahn

The other information required by this Item concerning our directors is incorporated by reference from the section captioned "Proposal No. 1—Election of Directors" and "Corporate Governance" contained in our proxy statement related to the 2014 Annual Meeting of Stockholders scheduled to be held on May 20, 2014 which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Carolina.

holds a B.B.A. in accounting and finance from the University of Wisconsin-Milwaukee and is a certified public accountant in the State of Maryland and North

Item 11. Executive Compensation

The information required by this Item concerning our directors is incorporated by reference from the section captioned "Director Compensation," "Executive Compensation – Summary Compensation Table" and "Executive Compensation – Outstanding Equity Awards at Fiscal Year End 2013" contained in the proxy statement.

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

The following table sets forth the indicated information as of December 31, 2013 with respect to our equity compensation plans:

Number of

	Number of securities to be issued upon exercise of outstanding options, warrants and rights	eighted-average exercise price of outstanding options, warrants and rights	securities remaining available for future issuance under equity compensation plans
Plan Category			
Equity compensation plans approved by our shareholders	1,832,851	\$ 5.26	1,984,728
Equity compensation plans not approved by our shareholders	138,797	\$ 6.11	-
Total	1,971,648		1,984,728

Our equity compensation plans consist of the Sixth Amended and Restated 2006 Stock Plan and the 2011 Equity Incentive Plan, both of which were approved by our stockholders.

The shares included in the table that were not approved by our stockholders are issuable pursuant to warrants issued to Hercules as part of the amended loan and security agreement we entered into with Hercules, pursuant to which we have borrowed \$15 million.

The other information required by this Item is incorporated by reference to the information under the section captioned "Security Ownership of Certain Beneficial Owners and Management" contained in the proxy statement.

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

The information required by this Item is incorporated by reference to the information under the section captioned "Certain Relationships and Related Transactions" and "Corporate Governance and Board Matters—Independence of Directors" contained in the proxy statement.

Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated by reference to the information under the section captioned "Audit and Audit Committee Matters" contained in the proxy statement.

PART IV

Item 15. Exhibits, Financial Statement Schedules

	Page
(a) The following documents are filed as part of this report:	
(1) Financial Statements:	
Report of Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets	F-3
Consolidated Statements of Operations	F-4
Consolidated Statements of Redeemable Preferred Shares and Shareholders' Equity (Deficit)	F-5
Consolidated Statements of Cash Flows	F-6
Notes to Consolidated Financial Statements	F-7

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The following exhibits are included herein or incorporated herein by reference:

Exhibit No.	Description	Registrant's Form	Dated	Exhibit Number	Filed Herewith
1.2	Sales Agreement dated as of March 8, 2013 by and between Cempra, Inc. and Cowen and Company, LLC	S-3	3/03/2013	1.2	
1.3	Underwriting Agreement, dated June 14, 2013 by and between Cempra, Inc. and Barclays Capital Inc., Stifel, Nicolaus & Company, Incorporated, and Cowen and Company, LLC, as representatives of the several underwriters named therein.	8-K	6/14/2013	1.2	
1.4	Amendment No. 1 to Sales Agreement, dated as of December 10, 2013 by and between Cempra, Inc. and Cowen and Company, LLC.	S-3	12/10/2013	1.4	
2.1	Form of Plan of Conversion of Cempra Holdings, LLC.	S-1	10/12/2011	2.1	
3.1	Certificate of Incorporation of Cempra, Inc.	S-1/A	1/13/2012	3.1	
3.2	Form of Bylaws of Cempra, Inc.	S-1	10/12/2011	3.2	
3.3	Certificate of Formation of Cempra Holdings, LLC dated May 16, 2008.	S-1	10/12/2011	3.3	
3.4	Cempra Holdings, LLC Second Amended and Restated Limited Liability Company Agreement dated as of May 13, 2009, as amended.	S-1	10/12/2011	3.4	
4.1	Specimen of Common Stock Certificate of Cempra, Inc.	S-1/A	11/22/2011	4.1	
4.2	Form of Registration Rights Agreement by and among Cempra, Inc. and certain of its stockholders, to be effective upon the corporate conversion.	S-1	10/12/2011	4.2	
4.3	Cempra Holdings, LLC Preferred Unit Purchase Warrant and Global Amendment thereto dated October 11, 2011.	S-1	10/12/2011	4.3	
4.4	Cempra Holdings, LLC Unsecured Convertible Promissory Note and Global Amendment thereto dated October 11, 2011.	S-1	10/12/2011	4.4	
4.5	Amended and Restated Warrant Agreement, dated as of December 20, 2011, amended and restated on May 31, 2013, between Cempra Holdings, LLC and Hercules Technology Growth Capital, Inc.	8-K	6/06/2013	4.10	

Exhibit No.	Description	Registrant's Form	Dated	Exhibit Number	Filed Herewith
4.6	Global Amendment, dated December 20, 2011, to Cempra Holdings, LLC Unsecured Convertible Promissory Note dated August 5, 2011, as amended October 11, 2011.	S-1/A	1/30/2012	4.6	
4.7	Fifth Amendment to Cempra Holdings, LLC Second Amended and Restated Limited Liability Company Agreement, effective as of January 12, 2012.	S-1/A	1/30/2012	4.7	
4.9	Warrant Agreement, dated May 31, 2013, issued to Hercules Technology Growth Capital, Inc.	8-K	6/06/2013	4.9	
10.1	Forms of Indemnification Agreements by and between Cempra, Inc. and its directors.	S-1	10/12/2011	10.1	
10.2	Cempra, Inc. Sixth Amended and Restated 2006 Stock Plan.	S-1/A	1/13/2012	10.2	
10.3	Cempra, Inc. 2011 Equity Incentive Plan and Form of Stock Option Agreement thereunder.	S-1/A	1/13/2012	10.3	
10.4*	Collaborative Research and Development and License Agreement dated March 31, 2006, by and between Cempra Pharmaceuticals, Inc. and Optimer Pharmaceuticals, Inc.	S-1	10/12/2011	10.4	
10.5*	Supply Agreement effective March 15, 2011, by and among CEM-102 Pharmaceuticals, Inc., Ercros S.A. and Gyma Laboratories of America, Inc.	S-1	10/12/2011	10.5	
10.6	Office Lease Agreement dated November 9, 2011 between Cempra Pharmaceuticals, Inc. and Property Reserve, Inc.	S-1/A	11/22/2011	10.6	
10.7	Loan and Security Agreement dated December 20, 2011 between Cempra Holdings, LLC and Hercules Technology Growth Capital, Inc.	S-1/A	12/22/2011	10.7	
10.8	Secured Promissory Note dated December 20, 2011, issued by Cempra Holdings, LLC to Hercules Technology Growth Capital, Inc.	S-1/A	12/22/2011	10.8	
10.9*	License Agreement, effective June 12, 2012, between The Scripps Research Institute and Cempra Pharmaceuticals, Inc.	10-Q	8/08/2012	10.9	
10.11*	API Manufacturing and Supply Agreement, dated as of January 30, 2013, by and between Wockhardt Ltd. and Cempra Pharmaceuticals, Inc.	10-K	3/07/2013	10.11	
10.12	2011 Equity Incentive Plan, as amended May 23, 2013.	10-Q	7/31/2013	10.3	
10.13*	Exclusive License and Development Agreement by and between Cempra Pharmaceuticals, Inc. and Toyama Chemical Co., Ltd., dated May 8, 2013.	10-Q	7/31/2013	10.13	
10.14*	Supply Agreement by and between Cempra Pharmaceuticals, Inc. and Toyama Chemical Co., Ltd., dated May 8, 2013.	10-Q	7/31/2013	10.14	
10.15*	Contract by and between Cempra, Inc. and the Biomedical Advanced Research and Development Authority, dated May 24, 2013.	10-Q	7/31/2013	10.15	
10.16*	Development and Supply Agreement by and between Cempra Pharmaceuticals, Inc. and Hospira Worldwide, Inc. effective as of July 1, 2013.	10-Q/A	11/08/2013	10.18	
10.17	Amendment No. 1, effective as of September 26, 2013 to Exclusive License And Development Agreement by and between Cempra Pharmaceuticals, Inc. and Toyama Chemical Co., Ltd, dated May 8, 2013.	10-Q	10/29/2013	10.19	

Exhibit No.	Description	Registrant's Form	Dated	Exhibit Number	Filed Herewith
10.18	Amendment No. 2 to Loan and Security Agreement, dated May 31, 2013, by and among Cempra, Inc., and each of its subsidiaries signatory thereto, and Hercules Capital Funding Trust 2012-1, as a lender and Hercules Technology Growth Capital, Inc., as a lender and as an agent for the lenders.	8-K	6/06/2013	10.12	
10.19	Form of Employment Agreement by and between Cempra, Inc. and Prabhavathi B. Fernandes, Ph.D.	8-K	8/13/2013	10.16	
10.20	Form of Change in Control Severance Agreement by and between Cempra, Inc. and Prabhavathi B. Fernandes, Ph.D.	8-K	8/13/2013	10.17	
10.21	First Amendment, dated May 17, 2013, to Office Lease Agreement dated November 9, 2011 between Cempra Pharmaceuticals, Inc., and Property Reserve, Inc.				X
10.22	Second Amendment, dated August 13, 2013, to Office Lease Agreement dated November 9, 2011 between Cempra Pharmaceuticals, Inc., and Property Reserve, Inc.				X
21.1	List of subsidiaries of Cempra Holdings, LLC. (5)	S-1	10/12/2011	21.1	
23.1	Consent of Independent Registered Public Accounting Firm				X
31.1	Certification of the Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of the Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1	Certification of the Chief Executive Officer Pursuant to 18 U.S. C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
32.2	Certification of the Chief Financial Officer Pursuant to 18 U.S. C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101	Financials in XBRL format.				X

^{*} The Registrant has received confidential treatment with respect to portions of this exhibit. Those portions have been omitted and filed separately with the Securities and Exchange Commission pursuant to a confidential treatment request.

SIGNATURES

Pursuant to the requirements of the Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

CEMPRA, INC.

By: /s/ Prabhavathi Fernandes, Ph.D.

Prabhavathi Fernandes, Ph.D.

President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this Form 10-K has been signed by the following persons on behalf of the Registrant and on the dates indicated.

Signature	Title	Date
/s/ Prabhavathi Fernandes, Ph.D. Prabhavathi Fernandes, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2014
/s/ Mark W. Hahn Mark W. Hahn	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 28, 2014
/s/ Shane M. Barton Shane M. Barton	Controller and Chief Accounting Officer (Principal Accounting Officer)	February 28, 2014
/s/ Garheng Kong, M.D., Ph.D. Garheng Kong, M.D., Ph.D.	Chairman of the Board	February 28, 2014
/s/ Dov Goldstein, M.D. Dov Goldstein, M.D.	Director	February 28, 2014
/s/ John H. Johnson John H. Johnson	Director	February 28, 2014
/s/ Richard Kent, M.D.	Director	February 28, 2014
Richard Kent, M.D. /s/ P. Sherrill Neff P. Sherrill Neff	Director	February 28, 2014
/s/ Michael R. Dougherty	Director	February 28, 2014
/s/ David N. Gill David N. Gill	Director	February 28, 2014

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CONSOLIDATED FINANCIAL STATEMENTS CEMPRA, INC.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Cempra, Inc.:

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of redeemable preferred shares and shareholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Cempra, Inc. and its subsidiaries at December 31, 2013 and 2012, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2013 in conformity with accounting principles generally accepted in the United States of America. 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 of these statements 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, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Raleigh, North Carolina February 27, 2014

CEMPRA, INC. Consolidated Balance Sheets

		December 31, 2012	_	December 31, 2013
Assets				
Current assets				
Cash and equivalents	\$	70,108,754	\$	96,502,918
Receivables		-		1,626,237
Prepaid expenses		264,981		407,911
Total current assets		70,373,735		98,537,066
Furniture, fixtures and equipment, net		43,217		137,721
Deposits		321,394		333,031
Total assets	\$	70,738,346	\$	99,007,818
Liabilities				
Current liabilities				
Accounts payable	\$	2,171,633	\$	6,273,602
Accrued expenses		341,918		391,657
Accrued payroll and benefits		604,548		1,043,247
Deferred revenue		-		31,988
Warrant liability		-		920,174
Current portion of long-term debt		2,226,610		2,200,922
Total current liabilities		5,344,709		10,861,590
Deferred revenue		_		5,632,600
Long-term debt		7,623,285		12,538,238
Total liabilities		12,967,994		29,032,428
Commitments and Contingencies (Notes 4 and 9)				_
Shareholders' Equity				
Preferred stock; \$.001 par value; 5,000,000 shares authorized; no shares issued or outstanding at December 31, 2012 and December 31, 2013		-		-
Common stock; \$.001 par value; 80,000,000 shares authorized; 24,903,774 and 33,200,341 issued				
and outstanding at December 31, 2012 and December 31, 2013, respectively		24,904		33,200
Additional paid-in capital		178,970,975		236,202,423
Accumulated deficit	_(121,225,527)		(166,260,233)
Total shareholders' equity		57,770,352		69,975,390
Total liabilities and shareholders' equity	\$	70,738,346	\$	99,007,818

CEMPRA, INC. Consolidated Statements of Operations

	Year	Years Ended December 31,				
	2011	2012	2013			
Revenue						
Contract research	\$ -	\$ -	\$ 3,477,554			
License	<u> </u>	<u> </u>	4,335,412			
Total revenue		_	7,812,966			
Operating expenses						
Research and development	16,871,825	16,869,078	41,299,695			
General and administrative	3,707,563	6,068,457	9,433,447			
Total costs and expenses	20,579,388	22,937,535	50,733,142			
Loss from operations	(20,579,388)	(22,937,535)	(42,920,176)			
Other income (expenses)						
Interest income	81,063	107,564	17,693			
Interest expense	(722,454)	(1,396,818)	(2,132,223)			
Other income (expense), net	(641,391)	(1,289,254)	(2,114,530)			
Net loss and comprehensive loss	(21,220,779)	(24,226,789)	(45,034,706)			
Accretion of redeemable convertible preferred shares	(3,763,061)	(313,588)	-			
Net loss attributable to common shareholders	\$(24,983,840)	\$(24,540,377)	\$(45,034,706)			
Basic and diluted net loss attributable to common shareholders per share	\$ (47.53)	\$ (1.23)	\$ (1.53)			
Basic and diluted weighted average shares outstanding	525,689	19,882,585	29,449,716			

Consolidated Statements of Redeemable Preferred Shares and Shareholders' Equity (Deficit) CEMPRA, INC.

	Redeemab Preferi	Redeemable Convertible Preferred Shares	Common Shares	Shares	Сот	Common Stock	Additional Paid-In	Accumulated	Total Shareholders'
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	Deficit
Balance as of December 31, 2010	7,591,058	\$ 90,750,975	495,024	·	1	· ·	·	\$ (72,215,027)	\$ (72,215,027)
Issuance of common shares upon			0						
exercise of options			38,815			'	69,932		69,932
Accretion of redeemable convertible preferred shares	ı	3,763,061	1	ı	ı	1	(513,717)	(3,249,344)	(3,763,061)
Share-based compensation	ı	ı	ı	1	ı	1	443,785	ı	443,785
Net loss	1	1	1	1	ı	1	1	(21,220,779)	(21,220,779)
Balance as of December 31, 2011	7,591,058	94,514,036	533,839		1	1	1	(96,685,150)	(96,685,150)
Issuance of common shares upon exercise of options	,				10.351	10	34.498	1	34.508
Issuance of common stock, net of offering costs of \$4.7 million	,		,		000,099,6	099.6	53.184.681		53,194,341
Issuance of common stock, net of offering costs of \$1.6 million		,			3,864,461	3,865	23,508,098	•	23,511,963
Conversion of common shares to common stock	,	,	(533,839)		533,839	534	(534)	,	1
Accretion of redeemable convertible preferred shares	ı	313,588		ı		ī		(313,588)	(313,588)
Conversion of preferred shares to common stock upon initial public offering	(7,591,058)	(94,827,624)	1		9,958,502	6,959	94,817,665		94,827,624
Conversion of notes payable to common stock upon initial public offering	•	į	·		876,621	876	4,723,658	,	4,724,534
Reclassification of warrant liability to additional paid-in capital	ı	1	ı	1	ı	I	1,033,647	1	1,033,647
Share-based compensation	•	ı	٠	1	•	1	1,669,262	1 000	1,669,262
Net loss Balance as of December 31 2012			1 1	. .	24 903 774	24 904	570 070 871	(121 225 527)	(24,226,789)
Share-based compensation					1,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	- 1	3,211,802	- (17,677,171)	3,211,802
Issuance of common shares upon exercise of options and warrants	•	1			22,629	22	61,843		61,865
Issuance of common stock, net of offering costs of \$3.7 million	1		ı	1	8,273,938	8,274	54,199,390	1	54,207,664
Reclassification of additional paid-in capital to warrant liability							(241,587)		(241,587)
Net loss	'	1	1	1	'	1	1	(45,034,706)	(45,034,706)
Balance as of December 31, 2013	1	· ·	1	·	33,200,341	\$ 33,200	\$ 236,202,423	\$ (166,260,233)	\$ 69,975,390

CEMPRA, INC. Consolidated Statements of Cash Flows

Year ended December 31, 2011 2012 2013 **Operating activities** Net loss (21,220,779)(24,226,789)(45,034,706)\$ Adjustments to reconcile net loss to net cash used in operating activities Depreciation 75,141 47,140 39.622 Share-based compensation 443,785 1,669,262 3,211,802 Change in fair value of warrant liabilities (4,730)(87,204)217,443 Amortization of debt issuance costs 394,300 355,663 650,780 Changes in operating assets and liabilities Receivables (1,626,237)Prepaid expenses 4,231 19,059 (142,930)**Deposits** 43,642 (311,524)(11,637)Accounts payable 1,434,696 (809,245)4,101,969 Accrued expenses 413,103 53,564 49,739 Accrued payroll and benefits 101,975 438,699 183,447 Deferred revenue 5,664,588 (18,314,636)Net cash used in operating activities (23,106,627)(32,440,868)**Investing activities** Purchases of furniture, fixtures and equipment (13,389)(8,437)(134,125)Net cash used in investing activities (13,389)(8,437)(134,125)Financing activities 5,000,000 Proceeds from borrowing on convertible promissory notes Proceeds from borrowing on long-term debt 10,000,000 5,238,327 Payment of long-term debt (238,327)Proceeds from exercise of stock options and warrants 69,932 34,508 61,865 Proceeds from issuance of common stock, net of underwriting discounts 78,289,762 54,407,814 Payment of offering costs (880,742)(702,716)(200,150)Payment of debt issuance costs (306,898)(300,372)Net cash provided by financing activities 13,882,292 77,621,554 58,969,157 Net change in cash and equivalents (4,445,733)54,506,490 26,394,164 Cash and equivalents at beginning of the period 20,047,997 15,602,264 70,108,754 Cash and equivalents at end of the period 15,602,264 \$ 70,108,754 \$ 96,502,918 Supplemental cash flow information \$ Cash paid for interest \$ 920,514 \$ 1,208,526 Non-cash investing and financing activities Accretion of redeemable convertible preferred shares \$ 3,763,061 \$ 313,558 \$ Allocation of the convertible note proceeds to warrant \$ 852,485 \$ \$ Allocation of the long-term debt proceeds to warrant \$ 273,094 \$ \$ 461,144 Conversion of convertible notes payable and accrued interest into common \$ \$ \$ 4,724,534 Conversion of redeemable convertible preferred shares into common stock \$ \$ 94,827,625 \$ \$ \$ 1,033,647 \$ Reclassification of warrant liability to additional paid-in capital Reclassification of additional paid-in capital to warrant liability \$ \$ 241,587 \$

CEMPRA, INC. December 31, 2013

Notes to Consolidated Financial Statements

1. Description of Business

Cempra, Inc. (the "Company" or "Cempra", previously known as Cempra Holdings, LLC) is the successor entity of Cempra Pharmaceuticals, Inc. which was incorporated on November 18, 2005 and commenced operations in January 2006. Cempra is located in Chapel Hill, North Carolina, and is a pharmaceutical company developing medicines to treat drug-resistant bacterial infections in the community and hospital.

On February 2, 2012, Cempra Holdings, LLC converted from a Delaware limited liability company to a Delaware corporation and was renamed Cempra, Inc. As a result of the corporate conversion, the holders of both common and preferred shares of Cempra Holdings, LLC became holders of shares of common stock of Cempra, Inc. Holders of options to purchase common shares of Cempra Holdings, LLC became holders of options to purchase shares of common stock of Cempra, Inc. Holders of notes convertible into preferred shares of Cempra Holdings, LLC and associated warrants exercisable for preferred shares of Cempra Holdings, LLC became holders of shares of common stock and warrants to purchase shares of common stock of Cempra, Inc.

From inception through the year ended December 31, 2012, the Company was in the development stage as defined by the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 915, *Development Stage Entities*. The Company's activities since inception have consisted principally of acquiring product and technology rights, raising capital and performing research and development activities. In May 2013, the Company entered into its first revenue-generating collaboration agreement and its first cost plus fixed fee development contract both of which are consistent with the Company's business objectives. The Company emerged from the development stage due to the execution of these contracts and resulting revenue generated from its planned principal operations. Therefore, development stage reporting is no longer required.

There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations and financial condition. The Company expects to continue to incur losses and require additional financial resources to advance its products to either commercial stage or liquidity events.

Our Board of Directors approved a 1-for-9.5 reverse stock split of our common and preferred shares on January 12, 2012, which became effective on January 29, 2012. All references to common stock, common shares outstanding, average number of common shares outstanding and per share amounts in our consolidated financial statements and notes to consolidated financial statements have been restated to reflect the 1-for-9.5 reverse stock split on a retroactive basis.

2. Basis of Presentation

Principles of Consolidation and Basis of Presentation

The accompanying consolidated financial statements include the accounts and results of operations of Cempra and its wholly owned subsidiaries. The consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of these consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash Equivalents and Concentrations of Risks

The Company considers all highly liquid investments purchased with an original maturity of three months or less at the date of purchase to be cash equivalents. Cash deposits are all in financial institutions in the U.S. The Company maintains cash in accounts which are in excess of federally insured limits.

Receivables

Receivables consist of amounts billed and amounts earned but unbilled under the Company's contract with the Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human Services ("BARDA"). Receivables under the BARDA contract are recorded as qualifying research activities are conducted and invoices from the Company's vendors are received. Unbilled receivables are also recorded based upon work estimated to be complete for which the Company has not received vendor invoices. The Company carries its accounts receivable at cost less an allowance for doubtful accounts. On a periodic basis, the Company evaluates its accounts receivable and establishes an allowance based on its history of collections and write-offs and the current status of all receivables. The Company does not accrue interest on trade receivables. If accounts become uncollectible, they will be written off through a charge to the allowance for doubtful accounts. The Company has not recorded an allowance for doubtful accounts as management believes all receivables are fully collectible.

Furniture, Fixtures and Equipment

Furniture, fixtures and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Furniture, fixtures and leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to income. Repairs and maintenance costs are expensed as incurred.

Furniture, fixtures and equipment are reviewed for impairment when events or changes in circumstances indicate the carrying amount of an asset may not be recoverable. If there is an impairment, a loss is recognized.

Deferred Offering Costs

Deferred public offering costs represent legal, accounting and other direct costs related to the Company's efforts to raise capital through a public sale of the Company's common stock. Costs related to the Company's initial public offering ("IPO") activities were deferred until the completion of the IPO, at which time they were reclassified to additional paid-in capital as a reduction of the IPO proceeds.

Income Taxes

Income taxes are computed using the asset and liability approach that requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's financial statements. In estimating future tax consequences, the Company considers all expected future events other than enactment of changes in tax laws or rates. A valuation allowance is recorded, if necessary, to reduce net deferred tax assets to their realizable values if management does not believe it is more likely than not that the net deferred tax assets will be realized.

Segment and Geographic Information

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company operates and manages its business as one operating segment and all of the Company's operations are in North America.

Intellectual Property

The Company's policy is to file patent applications to protect technology, inventions and improvements that are considered important to the development of its business. The patent positions of technology companies, including the Company, are uncertain and involve complex legal and factual questions for which important legal principles are largely unresolved. The Company accounts for its intellectual property under the guidance of FASB ASC Topic 350, *Intangibles—Goodwill and Other*. Patent costs since inception have been expensed as incurred.

Research and Development Expenses

Research and development ("R&D") expenses include direct and indirect R&D costs. Direct R&D consists principally of external costs, such as fees paid to investigators, consultants, central laboratories and clinical research organizations, including costs incurred in connection with clinical trials, and related clinical trial fees and all employee-related expenses for those employees working in research and development functions, including stock-based compensation for R&D personnel. Indirect R&D costs include insurance or other indirect costs related to the Company's research and development function to specific product candidates. R&D costs are expensed as incurred.

Clinical Trial Accruals

As part of the process of preparing financial statements, the Company is required to estimate its expenses resulting from its obligation under contracts with vendors and consultants and clinical site agreements in connection with conducting clinical trials. 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 and efforts are expended. The Company accounts for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. The Company determines accrual estimates through discussion with applicable personnel and outside service providers as to the progress of trials, or the services completed. During the course of a clinical trial, the Company adjusts its rate of clinical trial expense recognition if actual results differ from its estimates. The Company makes estimates of its accrued expenses as of each balance sheet date in its financial statements based on facts and circumstances known at that time. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of status and timing of services performed relative to the actual status and timing of services performed may vary and may result in the Company reporting amounts that are too high or too low for any particular period. The Company's clinical trial accrual is dependent upon the timely and accurate reporting of fee billings and passthrough expenses from contract research organizations and other third-party vendors as well as the timely processing of any change orders from the contract research organizations.

Revenue Recognition

The Company's revenue generally consists of research related revenue under federal contracts and licensing revenue related to non-refundable upfront fees, milestone payments and royalties earned under license agreements. Revenue is recognized when the following criteria are met: (1) persuasive evidence that an arrangement exists; (2) delivery of the products and/or services has occurred; (3) the selling price is fixed or determinable; and (4) collectability is reasonably assured.

For arrangements that involve the delivery of more than one element, each product, service and/or right to use assets is evaluated to determine whether it qualifies as a separate unit of accounting. This determination is based on whether the deliverable has "stand-alone value" to the customer. The consideration that is fixed or determinable is then allocated to each separate unit of accounting based on the relative selling prices of each deliverable. The consideration allocated to each unit of accounting is recognized as the related goods and services are delivered, limited to the consideration that is not contingent upon future deliverables. When an arrangement is accounted for as a single unit of accounting, the Company determines the period over which the performance obligations will be performed and revenue recognized.

Redeemable Convertible Preferred Shares

The Company accounted for its mandatorily redeemable preferred shares under the requirements of FASB ASC Topic 480, *Distinguishing Liabilities from Equity*, which establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. The carrying value of redeemable convertible preferred shares is increased by periodic accretions so that the carrying amount will equal the redemption amount at the redemption date. These increases are effected through charges against additional paid-in capital, to the extent it is available, or the deficit accumulated during the development stage. The convertible shares were converted to common stock upon completion of the IPO on February 2, 2012.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss attributable to common shareholders by the weighted average number of common stock shares outstanding during the period. Diluted loss per share is computed by dividing the net loss attributable to common shareholders by the weighted average number of common stock shares adjusted for the dilutive effect of common stock equivalent shares outstanding during the period. Common stock equivalents consist of convertible senior notes (using the "as if converted" method), stock options, restricted stock shares and stock warrants. Common equivalent shares are excluded from the computation in periods in which they have an anti-dilutive effect on earnings per share.

Share-Based Compensation

The Company accounts for share-based compensation following the provisions of FASB ASC Topic 718, *Stock Compensation*. The Company measures compensation cost for share-based payment awards granted to employees and non-employee directors at fair value using the Black-Scholes option-pricing model. The Company recognizes compensation expense on a straight-line basis over the service period for awards expected to vest. Compensation cost related to share-based payment awards granted to non-employees is adjusted each reporting period for changes in the fair value of the Company's shares until the measurement date. The measurement date is generally considered to be the date when all services have been rendered or the date on which options are fully vested.

The Company recorded the following share-based compensation expense in accordance with ASC Topic 718:

		Ye	ar Ei	nded December	31,	
	2011 2012				2013	
Research and development	\$	158,102	\$	519,717	\$	962,443
General and administrative		285,683	_	1,149,545	_	2,249,359
Total	\$	443,785	\$	1,669,262	\$	3,211,802

Allocations to research and development and general and administrative expense are based upon the department to which the associated employee reported. No related tax benefits of the share-based compensation expense have been recognized.

All employee stock options issued during 2012 and before December 8, 2010 were granted at an exercise price equal to or above the fair value of the stock at the date of grant; therefore, there was no intrinsic value.

For the year ended December 31, 2011, for financial reporting purposes, the Company determined that options granted on December 8, 2010 and March 11, 2011 were granted at an amount less than fair market value. Compensation expense associated with these options was recorded in 2011.

Valuation Assumptions for Stock Option Plans

The employee share-based compensation expense recognized was determined using the Black-Scholes option-pricing model. Option-pricing models require the input of subjective assumptions and these assumptions can vary over time.

The weighted-average assumptions used to determine the fair value of each option grant are as follows:

		201	1	20)12		201	13
			Non-			Non-		Non-
	Emplo	yees	Employees	Employees	En	nployees	Employees	Employees
Estimated dividend yield		0.0%	N/A	0.0%	o	0.0%	0.0%	0.0%
Expected share price volatility	7	73.9%	N/A	72.5%	6	53.5%	70.8%	69.8%
Risk-free interest rate		2.5%	N/A	1.3%	6	1.6%	1.0%	2.3%
Expected life of option (in years)		6.1	N/A	5.5		9.5	5.5	9.8
Weighted-average fair value per share	\$ (0.16	N/A	\$ 4.65	\$	3.86	\$ 4.26	\$ 7.80

Expected stock price volatility is based on an average of several peer public companies due to the Company's limited history. For purposes of identifying peer companies, the Company considered characteristics such as industry, market capitalization, length of trading history, similar vesting terms and in-the-money option status. The risk-free rate is based on the U.S. Treasury yield curve during the expected life of the option. The dividend yield percentage is zero because the Company neither currently pays dividends nor intends to do so during the expected option term. The expected term represents the average time that options are expected to be outstanding. Due to a lack of term length data, the Company elected to use the mid-point between the vesting date and the contractual term as the expected term for employee options and contractual life for non-employees options. This is in accordance with the simplified method prescribed in SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, as the options meet the criteria of "plain-vanilla" options.

3. Fair Value of Financial Instruments

The carrying values of cash equivalents, receivables, prepaid expenses, and accounts payable at December 31, 2013 approximated their fair values due to the short-term nature of these items.

The Company's valuation of financial instruments is based on a three-tiered approach, which requires that fair value measurements be classified and disclosed in one of three tiers. These tiers are: Level 1, defined as quoted prices in active markets for identical assets or liabilities; Level 2, defined as valuations based on observable inputs other than those included in Level 1, such as quoted prices for similar assets and liabilities in active markets, or other inputs that are observable or can be corroborated by observable input data; and Level 3, defined as valuations based on unobservable inputs reflecting the Company's own assumptions, consistent with reasonably available assumptions made by other market participants.

At December 31, 2012 and December 31, 2013, financial instruments and respective fair values have been classified as follows:

	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Balance at December 31, 2012	
Assets:					
Money Market Funds	\$ 67,783,021	\$ -	\$ -	\$ 67,783,021	
Total assets at fair value:	\$ 67,783,021	\$ -	\$ -	\$ 67,783,021	
	Quoted Prices	Significant		Balance at December 31, 2013	
A	in Active Markets for Identical Assets (Level 1)	Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	December 31,	
Assets:	Markets for Identical Assets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)	December 31, 2013	
Money Market Funds	Markets for Identical Assets (Level 1) \$ 91,165,448	Observable Inputs (Level 2)	Unobservable Inputs	December 31, 2013 \$ 91,165,448	
	Markets for Identical Assets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)	December 31, 2013	
Money Market Funds	Markets for Identical Assets (Level 1) \$ 91,165,448	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)	December 31, 2013 \$ 91,165,448	
Money Market Funds Total assets at fair value:	Markets for Identical Assets (Level 1) \$ 91,165,448	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)	December 31, 2013 \$ 91,165,448	

The change in the fair value measurement using significant unobservable inputs (Level 3) is summarized below:

Balance at December 31, 2011	\$ 1,120,849
Change in fair value recorded as interest expense	17,461
Change in fair value recorded as interest income	(104,663)
Reclassification of August 2011 Warrant to additional paid-in capital	(865,216)
Reclassification of Hercules Warrant to additional paid-in capital	(168,431)
Balance at December 31, 2012	\$ -
Allocation of long-term debt proceeds to warrant	461,144
Reclassification of additional paid-in-capital to warrant	241,587
Change in fair value recorded as interest income	(14,355)
Change in fair value recorded as interest expense	231,798
Balance at December 31, 2013	\$ 920,174

The warrant liability represents the Company's allocation of a portion of the proceeds from the August 2011 Notes and the December 2011 Note (both as defined in Note 8). The allocation of the proceeds from the August 2011 Notes and the December 2011 Note was based on the fair value of the warrant liability on the dates of grant. The Company accounted for the warrant liability in accordance with ASC Topic 480, *Distinguishing Liabilities from Equity*, which requires that a purchase option to acquire redeemable equity (either puttable or mandatorily redeemable) be reported as liabilities. The Company measured the fair value of the warrant liability based upon contemporaneous valuations. The August 2011 Warrants (as defined in Note 8) utilized the Black-Scholes pricing model while the Hercules Warrant (as defined in Note 8) utilized the Binomial model at each balance sheet date. The Company recorded changes in the fair value of the warrant liability as interest expense or interest income, as applicable.

The August 2011 Warrant liability and Hercules Warrant liability were reclassified to additional paid-in-capital upon the conversion of warrants to purchase preferred stock into warrants to purchase common stock, in connection with the Company's IPO. The May 2013 amendment to the warrant agreement with Hercules required the First Hercules Warrant and the Second Hercules Warrant (as defined in Note 8) to be classified as a liability and be marked to market at each reporting period.

The Company used significant assumptions in estimating the fair value of the warrant liability including the estimated volatility, risk free interest rate, estimated fair value of the preferred shares in relation to the August 2011 Warrant liability and current market value of common stock for the December 2011 Warrant liability. These assumptions were used to establish an expected set of cash flows which were probability-weighted and discounted to present value to determine a fair value.

The Company calculated the fair value of the Hercules Warrants using a Binomial model. For the year ended December 31, 2013, the Company applied the following assumptions:

	Year Ended Decen	nber 31, 2013
		Second
	First Hercules	Hercules
	<u>Warrant</u>	Warrant
Estimated dividend yield	-	-
Volatility	86.9%	85.3%
Risk-free interest rate	2.7%	2.8%
Expected life of warrant (in years)	8.0	9.4

The August 2011 Notes were converted to common stock in February 2012 when the Company completed its IPO.

The December 2011 Note, which is classified as a level 2 liability (see Note 8) has a variable interest rate and, accordingly, its carrying value approximates its fair value. At December 31, 2013, the carrying value was \$14.7 million. There were no transfers between levels of the fair value hierarchy for any assets or liabilities measured at fair value in the twelve months ended December 31, 2013.

4. Significant Agreements and Contracts

License Agreements

Optimer Pharmaceuticals, Inc.

In March 2006, the Company, through its wholly owned subsidiary, Cempra Pharmaceuticals, Inc., entered into a Collaborative Research and Development and License Agreement ("Optimer Agreement") with Optimer Pharmaceuticals, Inc. ("Optimer"). Under the terms of the Optimer Agreement, the Company acquired exclusive rights to further develop and commercialize certain Optimer technology worldwide, excluding member nations of the Association of Southeast Asian Nations. Optimer was acquired by Cubist Pharmaceuticals, Inc. in October 2013.

In exchange for this license, during 2006 and 2007, the Company issued an aggregate of 125,646 common shares with a total fair value of \$190,418 to Optimer. These issuances to Optimer were expensed as incurred in research and development expense.

In July 2010, the Company paid a \$500,000 milestone payment to Optimer after the successful completion of its first solithromycin Phase 1 program. In July 2012, the Company paid a \$1,000,000 milestone after the successful completion of its first solithromycin Phase 2 program. Both milestones were expensed as incurred in research and development expense. Under the terms of the Optimer Agreement, the Company will owe Optimer additional payments, contingent upon the achievement of various development, regulatory and commercialization milestone events. The aggregate amount of such milestone payments the Company may need to pay is based in part on the number of products developed under the agreement and would total \$27,500,000 (including payments made to date) if four products are developed through FDA approval. The Company will also pay tiered mid-single-digit royalties based on the amount of annual net sales of its approved products.

The Scripps Research Institute

In June 2012, the Company entered into a license agreement with The Scripps Research Institute ("TSRI"), whereby TSRI licensed to the Company rights, with rights of sublicense, to make, use, sell, and import products for human or animal therapeutic use that use or incorporate one or more macrolides as an active pharmaceutical ingredient and is covered by certain patent rights owned by TSRI claiming technology related to copper-catalysed ligation of azides and acetylenes. The rights licensed to the Company are exclusive as to the People's Republic of China (excluding Hong Kong), South Korea and Australia, and are non-exclusive in all other countries worldwide, except the member-nations of the Association of Southeast Asian Nations, which are not included in the territory of the license. Under the terms of the agreement with TSRI, the Company paid a one-time only, non-refundable license issue fee in the amount of \$350,000 which was charged to research and development expense in the second quarter of 2012.

The Company is also obligated to pay annual maintenance fees to TSRI in the amount of (i) \$50,000 each year for the first three years (beginning on the first anniversary of the agreement), and (ii) \$85,000 each year thereafter (beginning on the fourth anniversary of the agreement). Each calendar year's annual maintenance fees will be credited against sales royalties due under the agreement for such calendar year. Under the terms of the agreement, the Company must pay TSRI low single-digit percentage royalties on the net sales of the products covered by the TSRI patents for the life of the TSRI patents, a low single-digit percentage of non-royalty sublicensing revenue received with respect to countries in the nonexclusive territory and a mid-single-digit percentage of sublicensing revenue received with respect to countries in the exclusive territory, with the sublicensing revenue royalty in the exclusive territory

and the sales royalties subject to certain reductions under certain circumstances. TSRI is eligible to receive milestone payments of up to \$1.1 million with respect to regulatory approval in the exclusive territory and first commercial sale, in each of the exclusive territory and nonexclusive territory, of the first licensed product to achieve those milestones that is based upon each macrolide covered by the licensed patents. Each milestone is payable once per each macrolide. Each milestone payment made to TSRI with respect to a particular milestone will be creditable against any payment due to TSRI with respect to any sublicense revenues received in connection with the achievement of such milestone. Pursuant to the terms of the Optimer Agreement, any payments made to TSRI under this license for territories subject to the Optimer Agreement can be deducted from any sales-based royalty payments due under the Optimer Agreement up to a certain percentage reduction of the royalties due to Optimer.

Under the terms of the agreement, the Company is also required to pay additional fees on royalties, sublicensing and milestone payments if the Company, an affiliate with TSRI, or a sub licensee challenges the validity or enforceability of any of the patents licensed under the agreement. Such increased payments would be required until all patent claims subject to challenge are invalidated in the particular country where such challenge was mounted.

Biomedical Advanced Research and Development Authority

In May 2013, the Company entered into an agreement with BARDA, for the evaluation and development of the Company's lead product candidate solithromycin for the treatment of bacterial infections in pediatric populations and infections caused by bioterror threat pathogens.

The agreement is a cost plus fixed fee development contract, with a base performance segment valued at approximately \$17.7 million, and four option work segments that BARDA may request at its sole discretion pursuant to the agreement. If all four option segments are requested, the cumulative value of the agreement would be approximately \$58 million. Three of the options are cost plus fixed fee arrangements and one option is a cost sharing arrangement for which the Company would be responsible for a designated portion of the costs associated with that work segment. The estimated period of performance for the base performance segment is May 24, 2013 through May 23, 2015. If all option segments are requested, this estimated period of performance would be extended until approximately May 23, 2018.

Under the agreement, the Company is reimbursed and recognizes revenue as allowable costs are incurred plus a portion of the fixed-fee earned. The Company considers fixed-fees under cost reimbursable agreements to be earned in proportion to the allowable costs incurred in performance of the work as compared to total estimated agreement costs, with such costs incurred representing a reasonable measurement of the proportional performance of the work completed. For the twelve-month period ended December 31, 2013, the Company recognized \$3.4 million in revenue under this agreement.

The agreement provides the U.S. government the ability to terminate the agreement for convenience or to terminate for default if the Company fails to meet its obligations as set forth in the statement of work. The Company believes that if the government were to terminate the agreement for convenience, the costs incurred through the effective date of such termination and any settlement costs resulting from such termination would be allowable costs.

Toyama Chemical Co., Ltd.

In May 2013, Cempra Pharmaceuticals, Inc., the Company's wholly owned subsidiary, entered into a license agreement with Toyama Chemical Co., Ltd. ("Toyama"), whereby the Company licensed to Toyama the exclusive right, with the right to sublicense, to make, use and sell any product in Japan that incorporates solithromycin, the Company's lead compound, as its sole active pharmaceutical ingredient, or API, for human therapeutic uses, other than for ophthalmic indications or any condition, disease or affliction of the ophthalmic tissues. Toyama also has a nonexclusive license in Japan and certain other countries, with the right to sublicense, to manufacture or have manufactured API for solithromycin for use in manufacturing such products, subject to limitations and obligations of the concurrently executed supply agreement discussed below. Toyama granted the Company certain rights to intellectual property generated by Toyama under the license agreement with respect to solithromycin or licensed products for use with such products outside Japan or with other solithromycin-based products inside or outside Japan.

Following execution of the agreement, the Company received a \$10.0 million upfront payment from Toyama. Toyama is also obligated to pay the Company up to an aggregate of \$60.0 million in milestone payments, depending on the achievement of various regulatory, patent, development and commercial milestones. Under the terms of the license agreement, Toyama must also pay the Company a royalty equal to a low-to-high first double decimal digit percentage of net sales, subject to downward adjustment in certain circumstances.

As part of the license agreement, Toyama and the Company also entered into a supply agreement, whereby the Company will be the exclusive supplier (with certain limitations) to Toyama and its sublicensees of API for solithromycin for use in licensed products in Japan, as well as the exclusive supplier to Toyama and its sublicensees of finished forms of solithromycin to be used in Phase 1 and Phase 2 clinical trials in Japan. Pursuant to the supply agreement, which is an exhibit to the license agreement, Toyama will pay the Company for such clinical supply of finished product and all supplies of API for solithromycin for any purpose, other than the manufacture of products for commercial sale in Japan, at prices equal to the Company's cost. All API for solithromycin supplied by the Company to Toyama for use in the manufacture of finished product for commercial sale in Japan will be ordered from the Company at prices determined by the Company's manufacturing costs, and which may, depending on such costs, equal, exceed, or be less than such costs. Either party may terminate the supply agreement for uncured material breach or insolvency of the other party, with Toyama's right to terminate for the Company's breach subject to certain further conditions in the case of the Company's failure to supply API for solithromycin or clinical supply, but otherwise the supply agreement will continue until the expiration or termination of the license agreement.

The Company has determined that there are six deliverables under this agreement including (1) the license to develop and commercialize solithromycin in Japan, (2) the obligation of the Company to conduct Phase 3 studies and obtain regulatory approval in the United States and one other territory, (3) participation in a Joint Development Committee, or JDC, (4) participation in a Joint Commercialization Committee, or JCC, (5) the right to use the Company's trademark, and (6) a supply agreement. The amounts received under the license agreement have been allocated to the deliverables based on their relative fair values and will be recognized into income when the revenue recognition criteria have been achieved. As of December 31, 2013, the license is the only unit of accounting that has been delivered. The Company has recognized \$4.3 million in revenue associated with the delivery of the license. The Company has recorded \$5.7 million as deferred revenue at December 31, 2013 which will be recorded as revenue when the revenue recognition criteria of each deliverable have been met.

Milestone payments are recognized when earned, provided that (i) the milestone event is substantive; (ii) there is no ongoing performance obligation related to the achievement of the milestone earned; and (iii) it would result in additional payments. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment is non-refundable; achievement of the milestone was not reasonably assured at the inception of the arrangement; substantive effort is involved to achieve the milestone; and the amount of the milestone appears reasonable in relation to the effort expended, the other milestones in the arrangement, and the related risk associated with the achievement of the milestone. Contingent-based payments the Company may receive under a license agreement will be recognized when received.

Royalties are recorded as earned in accordance with the contract terms when third party sales can be reliably measured and collectability is reasonably assured.

5. Receivables

Receivables consist of billed and unbilled amounts that have been earned under the Company's licensing agreements or its contract with BARDA. At December 31, 2013, the Company's receivables consisted primarily of earned but unbilled receivables under the BARDA agreement.

6. Furniture, Fixtures and Equipment

Furniture, fixtures and equipment consist of the following as of:

	Useful Life (years)	 December 31,					
		 2012		2013			
Computer equipment	2	\$ 191,889	\$	207,795			
Software	2	46,594		41,842			
Furniture	5	38,792		74,499			
Leasehold improvements	3	4,809		11,936			
Total furniture, fixtures and equipment		282,084		336,072			
Less accumulated depreciation		 (238,867)		(198,351)			
Furniture, fixtures and equipment, net		\$ 43,217	\$	137,721			

Depreciation expense for the years ended December 31, 2011, 2012 and 2013 was \$75,142, \$47,140 and \$39,622, respectively.

7. Accrued Expenses

Accrued expenses are comprised of the following as of:

	 Decem	ber 31,		
	2012		2013	
Accrued professional fees	\$ 238,179	\$	153,689	
Other accrued fees	-		55,046	
Accrued interest	82,236		123,354	
Deferred rent	21,503		59,568	
Total accrued expenses	\$ 341,918	\$	391,657	

8. Long-term Debt & Unsecured Convertible Promissory Note

9.55% Long-term Debt

In December 2011, the Company entered into a \$20,000,000 loan and security agreement (the "December 2011 Note") with Hercules Technology Growth Capital, Inc. ("Hercules") and borrowed \$10,000,000 upon closing. The principal amount outstanding under the \$10,000,000 borrowing bears interest at the greater of (i) 9.55%, or (ii) the sum of 9.55% plus the prime lending rate, as published by the Wall Street Journal, minus 3.25% per annum. The terms of the December 2011 Note agreement provided that the Company could, at any time prior to October 1, 2012, request another borrowing in the aggregate amount of \$10,000,000. The Company elected not to request the additional borrowing and let the option expire on September 30, 2012. In May 2013, the Company amended its December 2011 Note, increasing the initial loan amount to \$15,000,000, and receiving an additional \$5,238,327 upon closing. The Company also extended the date by which it could request the additional \$10,000,000 to September 30, 2013. The Company elected not to request the additional borrowing and let the option expire on September 30, 2013. This amendment also provides for the Company to make interest only payments through June 2014. Principal and interest payments will start July 1, 2014 over a 36-month amortization period. The principal balance outstanding on the loan agreement and all accrued but unpaid interest thereunder will be due and payable on June 1, 2017. In addition, the Company is to pay Hercules the following fees:

- \$400,000 on the earliest to occur of (i) December 1, 2015, (ii) the date that the Company prepays all of the outstanding advances and accrued interest, or (iii) the date that all of the advances and interest become due and payable.
- \$495,245 on the earliest to occur of (i) June 1, 2017, (ii) the date that the Company prepays all of the outstanding advances and accrued interest, or (iii) the date that all of the advances and interest become due and payable.

The Company granted Hercules a security interest in all of its assets, except intellectual property. The Company's obligations to Hercules include restrictions on borrowing, asset transfers, placing liens or security interests on the Company's assets including its intellectual property, mergers and acquisitions and distributions to stockholders.

In connection with the initial closing of the December 2011 Note, the Company entered into a warrant agreement with Hercules (the "First Hercules Warrant"), under which Hercules has the right to purchase 39,038 shares of the Company's common stock. The exercise price of the First Hercules Warrant was initially \$10.25 per share, subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. In connection with the amendment to the loan agreement, the exercise price of the First Hercules Warrant was reduced to the lower of (a) \$6.11, and (b) the effective price per share of the Company's common stock issued or issuable in any offering of the Company's equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes. The First Hercules Warrant expires on December 20, 2021. Proceeds equal to the fair value of the Hercules Warrant were recorded as a liability at the date of issuance and the borrowings under the December 2011 Note will be increased to equal the face amount of the borrowings plus interest through interest expense over the term of the loan using the effective interest method. Upon completion of the Company's IPO on February 2, 2012, the warrant liability was reclassified to additional paid-in capital. Since the amendment to the warrant in May 2013 resulted in a variable exercise price, the fair value of the warrant as of the date of the amendment was reclassified from additional paid-in capital to a warrant liability.

Additionally, in connection with the amendment of the December 2011 note, the Company entered into a warrant agreement with Hercules (the "Second Hercules Warrant"), under which Hercules has the right to purchase an aggregate number of shares of the Company's common stock equal to the quotient derived by dividing \$609,533 by the exercise price then in effect, which is defined as the lower of (a) \$6.11, and (b) the effective price per share of the Company's common stock issued or issuable in any offering of the Company's equity or equity-linked securities that occurs prior to June 1, 2014, provided that such offering is effected principally for equity or debt-financing purposes. The exercise price is subject to adjustment in the event of a merger, reclassification, subdivision or combination of shares or stock dividend and subject also to antidilution protection. The Second Hercules Warrant expires on May 31, 2023. Proceeds equal to the fair value of the Second Hercules Warrant were recorded as a liability at the date of issuance and the

borrowings under the December 2011 Note will be increased to equal the face amount of the borrowings plus interest through interest expense over the term of the loan using the effective interest method.

10% Unsecured Convertible Promissory Note

In August 2011, the Company issued 10.0% unsecured convertible notes (the "August 2011 Notes") in the original aggregate principal amount of \$5,000,000.

Upon completion of the IPO, the August 2011 Notes and accrued interest of \$5.3 million converted into 876,621 shares of common stock.

In connection with the issuance of the August 2011 Notes, the Company issued warrants (the "August 2011 Warrants") that have a term of seven years. The August 2011 Warrants gave holders the right to purchase a certain number of Company shares or securities at a specified exercise price with respect to the first to occur of several scenarios. Upon completion of the IPO, the warrants became exercisable for an aggregate of 208,332 shares of the Company's common stock at an exercise price of \$6.00 per share and the related warrant liability was reclassified to additional paid-in capital.

Scheduled Maturities:

Scheduled maturities of long-term debt are as follows:

Year Ending December 31:	
2014	

2014	\$ 2,200,922
$2015^{(1)}$	5,137,766
2016	5,215,360
$2017^{(2)}$	3,341,197
Total	15,895,245
Less: Unamortized discount	(1,156,085)
Less: Current portion of long-term debt	(2,200,922)
Long-term debt	\$ 12,538,238

- (1) On the date that all of the principal and interest of the December 2011 Note was originally due and payable, the Company must pay Hercules an end of term fee of \$400,000, which is represented in year 2015 of the table above.
- (2) On the date that all of the principal and interest of the December 2011 Note become due and payable as amended, the Company must pay Hercules an end of term fee of \$495,245, which is represented in year 2017 of the table above.

9. Commitments and Contingencies

Future minimum lease payments required under non-cancellable operating leases as of December 31, 2013 are as follows:

	Operating
	 Leases
2014	\$ 157,428
2015	256,557
2016	264,253
2017	272,181
2018	280,347
Thereafter	 119,420
Total minimum lease payments	\$ 1,350,186

Rent expense for the years ended December 31, 2011, 2012 and 2013 was \$125,969, \$114,642 and \$145,549, respectively.

See Note 4—Significant Agreements and Contracts for contingencies related to the Optimer Agreement and the TSRI agreement.

10. Shareholders' Equity (Deficit)

Common Stock

In connection with the IPO, all of the Company's outstanding common and preferred shares, including accrued yield of \$13.7 million, automatically converted into a total of 10,492,341 shares of its common stock and the preferred stock warrant liability was reclassified to additional paid-in capital upon the conversion of warrants to purchase preferred stock into warrants to purchase common stock. In addition, the Company's August 2011 Notes and related accrued interest converted into 876,621 shares of common stock.

During 2013, the Company issued 13,685 shares of common stock at a weighted average exercise price of \$0.60 per share for the exercise of option grants and 8,944 shares of common stock at a weighted average exercise price of \$6.00 per share for the exercise of warrants.

During June 2013, the Company completed a public offering issuing 8,273,938 shares of common stock, at a price of \$7.00 per share, resulting in net proceeds to the Company of approximately \$54.2 million after deducting underwriting discounts of \$3.5 million and offering costs of \$0.2 million.

During 2012, the Company issued 10,351 shares of common stock at a weighted average price of \$3.33 per share for the exercise of share option grants.

During October 2012, the Company sold 3,864,461 shares of its common stock at \$6.50 per share to certain institutional accredited investors in a private placement financing, raising an aggregate of \$25,118,997 before sales agency fees and offering costs of approximately \$1.7 million. In connection with this financing, the Company entered into a registration rights agreement, pursuant to which it agreed to register the resale of the shares of common stock issued in the financing.

During February 2012, the Company completed its IPO issuing 9,660,000 shares of common stock, at a price of \$6.00 per share, resulting in net proceeds to the Company of approximately \$53.2 million after deducting underwriting discounts of \$3.2 million and offering costs of \$1.6 million.

During 2011, the Company issued 38,815 common shares at a weighted average price of \$1.81 per share for the exercise of option grants.

The following table presents common stock reserved for future issuance for the following equity instruments as of December 31, 2013:

Warrants to purchase common stock	338,185
Options:	
Outstanding under the 2006 Stock Plan	688,500
Outstanding under the 2011 Equity Incentive Plan	1,144,351
Available for future grants under the 2011 Equity Incentive Plan	1,984,728
Total common stock reserved for future issuance	4,155,764

11. Stock Option Plans

The Company adopted the 2006 Stock Plan in January 2006 ("the 2006 Plan"). The 2006 Plan provided for the granting of incentive share options, nonqualified share options and restricted shares to Company employees, representatives and consultants. As of December 31, 2013, there were options for an aggregate of 688,500 shares issued and outstanding under the 2006 Plan.

The Company's board of directors adopted the 2011 Equity Incentive Plan in October 2011 (the "2011 Plan"), which authorizes the issuance of up to 3,131,579 shares under the 2011 Plan. As of December 31, 2013, there were 1,984,728 options shares available under the 2011 Plan.

Upon adoption of the 2011 Plan, the Company eliminated the authorization for any unissued shares previously reserved under the Company's 2006 Plan. The stock awards previously issued under the 2006 Plan remain in effect in accordance with the terms of the 2006 Plan.

The following table summarizes the Company's 2006 and 2011 Plan activity:

	Number of		Weighted Average Exercise	Weighted Average Contractual	Aggregate Intrinsic
Outstanding December 21 2010	Options 756 517	Φ.	Price	Term (in years)	Value (1)
Outstanding - December 31, 2010	756,517	\$	2.00		
Granted	101,772		2.28		
Exercised	(38,815)		1.81		
Forfeited	(84,153)		2.19		
Expired	(19,510)		2.09		
Outstanding - December 31, 2011	715,811		2.00		
Granted	475,417		7.45		
Exercised	(10,351)		3.33		
Forfeited	(18,275)		5.86		
Expired	-		-		
Outstanding - December 31, 2012	1,162,602	\$	4.18		
Granted	758,374		7.03		
Exercised	(13,685)		0.60		
Forfeited	(74,440)		7.16		
Expired	-		-		
Outstanding - December 31, 2013	1,832,851		5.26	7.66	\$ 13,068,577
Exercisable - December 31, 2013	1,521,275		4.97	7.43	11,290,022
Vested and expected to vest at December 31, 2013 (2)	1,801,693	\$	5.24	7.64	\$ 12,890,721

⁽¹⁾ Intrinsic value is the excess of the fair value of the underlying common shares as of December 31, 2013 over the weighted-average exercise price.

The following table summarizes certain information about all options outstanding as of December 31, 2013:

	Options O	utstanding	Options E	xercisable
		Weighted		Weighted
		Average		Average
	Name have of	Remaining	Number of	Remaining
Exercise Price	Number of Options	Contractual Term (in years)	Number of Options	Contractual Term (in years)
\$0.48 - \$1.71	85,056	2.73	85,056	2.73
\$1.72 - \$2.94	603,444	6.10	543,867	6.00
\$5.40 - \$7.86	1,104,351	8.82	892,144	8.75
\$7.87 - \$12.66	40,000	9.93	208	9.90
	1,832,851		1,521,275	

During the year ended December 31, 2011, 2012 and 2013, the Company recorded \$443,785, \$1,669,262, and \$3,211,802 in share-based compensation expense, respectively. As of December 31, 2013, approximately \$1,238,000 of total unrecognized compensation cost related to unvested share options is expected to be recognized over a weighted-average period of 2.70 years.

⁽²⁾ The number of stock options expected to vest takes into account an estimate of expected forfeitures.

12. Income Taxes

No provision for U.S. Federal or state income taxes has been recorded as the Company has incurred net operating losses since inception.

Significant components of the Company's deferred income tax assets as of December 31, 2012 and 2013 consist of the following:

	2012	2013		
Current				
Deferred income tax assets				
Other current assets	\$ 26,400	\$	22,200	
Total net deferred income taxes, current	26,400		22,200	
Less valuation allowance	 (26,400)		(22,200)	
Total net deferred income taxes, current	\$ <u>-</u>	\$	<u>-</u>	
Non-current				
Deferred income tax assets				
Tax loss carryforwards	\$ 26,382,100	\$	40,193,200	
Contribution carryforwards	25,800		30,900	
Tax credits	2,498,800		4,230,300	
Start-up costs	6,599,200		6,871,600	
Share-based compensation	679,000		1,080,200	
Other assets	 134,600		429,900	
Total net deferred income taxes, non-current	36,319,500		52,836,100	
Less valuation allowance	 (36,319,500)		(52,836,100)	
Total net deferred income tax	\$ -	\$	-	

At December 31, 2012 and 2013, the Company provided a full valuation allowance against its net deferred tax assets since at that time, the Company could not assert that it was more likely than not that these deferred tax assets would be realized. There was an increase in the valuation allowance in the current year in the amount of \$16,512,400, all of which was allocable to current operating activities.

The table below summarizes changes in the deferred tax valuation allowance:

	 2011 2012		2012	 2013
Balance at beginning of year	\$ 19,109,500	\$	27,419,700	\$ 36,345,900
Charges to costs and expenses	8,310,200		8,926,200	16,512,400
Write-offs	 <u>-</u>		<u>-</u>	
Balance at end of year	\$ 27,419,700	\$	36,345,900	\$ 52,858,300

As of December 31, 2013, the Company had federal net operating loss carryforwards of approximately \$108,130,800 and state net operating loss carryforwards of approximately \$106,897,800. The net operating loss carryforwards begin to expire in 2026 and 2021 for federal and state tax purposes, respectively. The Company's federal and state net operating loss carryforwards include approximately \$122,200 of excess tax benefits related to deductions from the exercise of stock options. The tax benefit of these deductions has not been recognized in deferred tax assets. If utilized, the benefits from these deductions will be recorded as adjustments to additional paid-in capital. The Company also had federal research and development credit carryforwards of approximately \$4,150,000 which begin to expire in 2026, federal orphan drug credits carryforwards of approximately \$80,200 which begin to expire in 2033, and federal charitable contribution carryforwards of approximately \$90,900 which begin to expire in 2014.

The Tax Reform Act of 1986 contains provisions which limit the ability to utilize the net operating loss carryforwards in the case of certain events including significant changes in ownership interests. If the Company's net operating loss carryforwards are limited, and the Company has taxable income which exceeds the permissible yearly net operating loss carryforward, the Company would incur a federal income tax liability even though net operating loss carryforwards would be available in future years.

The reasons for the difference between actual income tax expense (benefit) for the years ended December 31, 2011, 2012 and 2013 and the amount computed by applying the statutory federal income tax rate to losses before income tax (benefit) are as follows:

	2011		2012		2012			
		% of Pretax		% of Pretax		% of Pretax		
	Amount	<u>Earnings</u>	Amount	<u>Earnings</u>	Amount	Earnings		
United States federal tax at statutory rate	\$(7,215,100)	34%	\$(8,237,100)	34%	\$(15,311,800)	34%		
State taxes (net of federal benefit)	(957,100)	5%	(1,092,600)	5%	(1,463,600)	3%		
Nondeductible expenses	12,700	0%	342,300	(1%)	901,900	(2%)		
Loss from pass-through entity	468,700	(2%)	58,700	0%	-	0%		
Credits	(557,500)	3%	-	0%	(1,731,500)	4%		
Adjustment for state rate change	-	0%	-	0%	1,092,000	(2%)		
Other, net	(61,900)	0%	2,500	0%	600	0%		
Change in valuation allowance	8,310,200	(39%)	8,926,200	(37%)	16,512,400	(37%)		
Provision for income taxes	\$ -	0%	\$ -	0%	\$ -	0%		

The research and development credit, which had previously expired on December 31, 2011, was reinstated as part of the American Taxpayer Relief Act of 2012 enacted on January 2, 2013. This legislation retroactively reinstated and extended the credit from the previous expiration date through December 31, 2013. As a result, the Company adjusted its deferred tax assets in 2013 for the 2013 and 2012 research and development credits, which resulted in an increase to the deferred tax assets and a corresponding increase to the valuation allowance of approximately \$1,256,800 and \$394,500, respectively.

On July 23, 2013, North Carolina enacted House Bill 998, which reduced the corporate income tax rate from 6.9% in 2013 to 6% in 2014 and to 5% in 2015. As a result of the new enacted tax rate, the Company adjusted its deferred tax assets in 2013 by applying the lower rate, which resulted in a decrease to the deferred tax assets and a corresponding decrease to the valuation allowance of approximately \$1,092,000.

As of December 31, 2012 and 2013, the Company had no unrecognized tax benefits. The Company's policy is to recognize interest and penalties related to uncertain tax positions in the provision for income taxes. At the adoption date of January 1, 2007 and as of December 31, 2013, the Company had no accrued interest or penalties related to uncertain tax positions.

The Company has analyzed its filing positions in all significant federal and state jurisdictions where it is required to file income tax returns, as well as open tax years in these jurisdictions. With few exceptions, the Company is no longer subject to United States Federal, state, and local tax examinations by tax authorities for years before 2010 although carryforward attributes that were generated prior to 2010 may still be adjusted upon examination by the taxing authorities if they either have been or will be used in a future period. No income tax returns are currently under examination by taxing authorities.

13. Net Loss Per Share

Basic and diluted net loss per common share was determined by dividing net loss attributable to common shareholders by the weighted average common shares outstanding during the period. The Company's potentially dilutive shares, which include redeemable convertible preferred shares, convertible debt, warrants and common share options, have not been included in the computation of diluted net loss per share for all periods as the result would be antidilutive.

The following potentially dilutive securities have been excluded from the computation of diluted weighted average shares outstanding, as they would be antidilutive:

	December 31,			
	2011	2012	2013	
Redeemable convertible preferred share	7,670,733	691,623	-	
Convertible debt	200,942	44,682	-	
Warrants outstanding	45,869	239,021	301,938	
Stock options outstanding	755,467	1,049,660	1,726,918	
	8,673,011	2,024,986	2,028,856	

14. Selected Quarterly Data (unaudited, in thousands, except for loss per share data)

	Quarter Ended				
	March 31, 2013		June 30, 2013	September 30, 2013	December 31, 2013
Revenue					
Contract research	\$	- \$	232	\$ 1,172	\$ 2,073
License		<u>-</u> _	4,335	<u>-</u>	
Total revenue	\$	- \$	4,567	\$ 1,172	\$ 2,073
Operating expenses					
Research and development		7,371	6,327	11,919	15,683
General and administrative		2,647	2,081	2,167	2,538
Loss from operations		(10,018)	(3,841)	(12,914)	(16,148)
Interest income		1	12	3	2
Interest expense		(328)	(384)	(736)	(684)
Net loss attributable to common shareholders	\$	(10,345) \$	(4,213)	\$ (13,647)	\$ (16,830)
Net loss per share - basic and diluted	\$	(0.42) \$	(0.16)	\$ (0.41)	\$ (0.51)
Shares used in calculating basic and diluted net loss per share		24,904	26,382	33,184	33,197

	Quarter Ended				
	March 31, 2012		June 30,	September 30,	December 31,
			2012	2012	2012
Operating expenses					
Research and development	\$	1,876 \$	7,424	\$ 3,156	\$ 4,413
General and administrative		972	1,777	1,495	1,825
Loss from operations		(2,848)	(9,201)	(4,651)	(6,238)
Interest income		105	1	1	1
Interest expense		(407)	(328)	(331)	(331)
Net Loss	\$	(3,150) \$	(9,528)	\$ (4,981)	\$ (6,568)
Accretion of redeemable convertible preferred shares		(314)	_	_	
Net loss attributable to common shareholders	\$	(3,464) \$	(9,528)	\$ (4,981)	\$ (6,568)
Net loss per share - basic and diluted	\$	(0.26) \$	(0.45)	\$ (0.24)	\$ (0.27)
Shares used in calculating basic and diluted net loss per share		13,251	21,035	21,038	24,147

CORPORATE INFORMATION

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Stock Listing

Cempra, Inc. common stock is listed on the Nasdaq Global Market and quoted under the symbol "CEMP"

