Zacks Equity Research

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# Trius Therapeutics (TSRX-NASDAQ)

***TSRX: Initiating Coverage: Torezolid Poised To Be Best-In-Class Antibiotic For MRSA. Rating Outperform / $10 Target.***

| | |
|---|---|
| **Current Recommendation** | **Outperform** |
| Prior Recommendation | N/A |
| Date of Last Change | 01/24/2011 |
| Current Price (01/24/11) | $3.92 |
| **Target Price** | **$10.00** |

## INITIATION

We are initiating coverage of Trius Inc. with an Outperform rating and $10 price target. We believe the company's phase III candidate, Torezolid, for acute bacterial skin and skin structure infections (ABSSSI) and methicillin-resistant *Staphylococcus aureus* (MRSA)

Accordingly, by any measure of valuation we've selected, the stock looks sizably undervalued at today's price. We have performed a discounted cash flow (DCF) analysis based on forecasting $750 million in worldwide sales of Torezolid in 2020, looked at comparative deals for late-stage antibiotics, and looked at Trius compared to its two closest competitors. Under all three metrics we see the stock at significant upside.

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$5.47** |
| **52-Week Low** | **$3.02** |
| **One-Year Return (%)** | **N/A** |
| **Beta** | **-0.10** |
| **Average Daily Volume (sh)** | **23,939** |
| **Shares Outstanding (mil)** | **24** |
| **Market Capitalization ($mil)** | **$97** |
| **Short Interest Ratio (days)** | **0.26** |
| **Institutional Ownership (%)** | **0** |
| **Insider Ownership (%)** | **N/A** |
| **Annual Cash Dividend** | **$0.00** |
| **Dividend Yield (%)** | **0.00** |
| **5-Yr. Historical Growth Rates** | |
| **Sales (%)** | **N/A** |
| **Earnings Per Share (%)** | **N/A** |
| **Dividend (%)** | **N/A** |
| **P/E using TTM EPS** | **N/A** |
| **P/E using 2010 Estimate** | **N/A** |
| **P/E using 2011 Estimate** | **N/A** |
| **Zacks Rank** | |

| | |
|---|---|
| **Risk Level** | **Above Average** |
| **Type of Stock** | **Small-Growth** |
| **Industry** | **Med-Biomed/Gene** |
| **Zacks Rank in Industry** | **23 of 161** |

## ZACKS ESTIMATES

**Revenue**
(In millions of $)

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2009 | 1.1 A | 1.2 A | 1.7 A | 1.0 A | 5.0 A |
| 2010 | 1.5 A | 2.1 A | 1.9 A | 1.8 E | 7.3 E |
| 2011 | 1.8 E | 1.8 E | 2.0 E | 2.0 E | 7.5 E |
| 2012 | | | | | 7.5 E |

**Earnings per Share**
(EPS is operating earnings before non-recurring items)

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2010 | -$5.08 A | -$2.69 A | -$0.57 A | -$0.39 E | -$2.47 E |
| 2011 | -$0.41 E | -$0.43 E | -$0.40 E | -$0.36 E | -$1.60 E |
| 2012 | | | | | -$1.37 E |
| 2013 | | | | | -$1.01 E |

Zacks Projected EPS Growth Rate - Next 4 Years % **N/A**

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## INVESTMENT THESIS

**Initiating Coverage of Trius Therapeutics**

We are initiating coverage of Trius Inc. with an Outperform rating and $10 price target. By any measure of valuation we've selected, the stock looks sizably undervalued at today's price. We have performed a discounted cash flow (DCF) analysis based on forecasting $750 million in worldwide sales of Torezolid in 2020, looked at comparative deals for late-stage antibiotics, and looked at Trius compared to its two closest competitors. Under all three metrics we see the stock as having significant upside.

***…Torezolid Poised To Be Best-In-Class…***

Trius lead pipeline candidate is Torezolid, a second generation oxazolidinone being developed for the treatment of serious gram-positive infections, including MRSA. Based on clinical data from phase I and phase II studies, Torezolid offers several key advantages over the market leading product in Pfizer's Zyvox (linezolid), a first-generation oxazolidinone with worldwide sales over $1.1 billion in 2010. These advantages include far more rapid bacteriocidal onset, far more convenient once-daily dosing, a shorter course of therapy at only 6 days vs. the 10 to 14 days recommended wit h Zyvox, and superior cure rates in difficult-to-treat MRSA infections. Additionally, Trius plans to make Torezolid available in both an oral and IV formulation, providing an advantage to Pfizer's Tygacil and Cubist's Cubicin. These three products generated sales of over $1.4 billion in the U.S. alone in 2010, gaining sizable market share as the therapeutic window on generic vancomycin is rapidly closes. We believe physicians will quickly convert the next leap forward in the treatment of acute bacterial skin and skin structure infections (ABSSSI) and methicillin-resistant *Staphylococcus aureus* (MRSA) in Torezolid.

Trius is currently conducting a phase III trial testing 200mg once-daily (QD) Torezolid head-to-head in a non-inferiority study to 600mg twice-daily (BID) Zyvox (linezolid). The program began enrollment in August 2010, and based on conversations with management, enrollment is proceeding very well. We anticipate the trial to complete enrollment later this year and offer data early in 2012. Trius will conduct a second IV-to-oral step-down phase III trial also testing non-inferiority to Zyvox prior to filing the new drug application (NDA), which we model in 2014. We are expecting results from a phase I lung pharmacokinetic (pk) study to offer data later this quarter. If positive, this could provide even further differentiation from competitors such as Tygacil and Cubicin.

Besides Torezolid, Trius is working on two preclinical antibiotic programs both funded by government grants. The first program is funded by a $28 million grant through the National Institute of Allergy and Infectious Diseases (NIAID) to support development of antibacterial agents targeting bacterial enzymes DNA gyrase and Topoisomerase IV. The second program is funded by a $29.5 million grant through the Defense Threat Reduction Agency (DTRA). Trius is using these funds to identify targets of antibacterial for biodefense applications.

## OVERVIEW

Trius Therapeutics is a biopharmaceutical company focused on the discovery, development and commercialization of innovative antibiotics for serious, life-threatening infections. The company is currently conducting phase III trials for torezolid phosphate (TR-701), an IV and orally administered second generation oxazolidinone, for the treatment of serious gram-positive bacterial infections, including those caused by methicillin-resistant *Staphylococcus aureus* (MRSA). With the continuous increase in bacterial resistance to currently marketed drugs, serious infections are becoming more difficult, if not impossible to treat, and this has led to a clear need for novel therapeutics to treat multi-drug resistant bacterial infections. Trius is headquartered in San Diego, California and has built a strong management team with significant discovery, development and regulatory experience. The senior management team collectively has over 90 years of experience in the development and approval of antibiotics.



**Bacterial Infections**

Bacteria are microscopic, single-celled organisms found in every conceivable environment all over the world. There are thousands of different kinds of bacteria, many of which reside harmlessly in the human body. Under certain circumstances, bacteria that normally reside harmlessly in the body become pathogenic (cause disease). Bacteria can cause disease by producing harmful substances (toxins), invading tissues, or doing both. Bacteria may be classified by the color they turn after a certain chemical stain, known as the Gram stain, when it is applied. Gram-positive bacteria stain blue, whereas gram-negative stain pink. Bacteria stain differently because of differences in their cell wall structure. Gram-positive and gram-negative bacteria also cause different types of infections, and different types of antibiotics may be effective against them.

Most pathogenic bacteria in humans are gram-positive. These include the cocci (spheres) *Staphylococcus* and *Streptococcus*, and the bacilli (rods) *Corynebacterium, Listeria, Bacillus,* and *Clostridium,* the latter two of which are spore-forming anaerobes. The *Staphylococcus* genus of Gram-positive bacteria includes at least 40 species, most of which are harmless and reside normally in the skin and mucous membranes of humans and other organisms. Similarly, there are roughly 30 species of *Streptococcus* bacteria, many of which are harmless. However, there are a number of potentially also harmful *Staphylococcus* and *Streptococcus* bacteria. Under instances when an infection occurs with a potentially dangerous bacterium, it is necessary to treat with an antibiotic.

For the past several decades, the U.S. FDA has classified bacterial skin infections under two categories: 1) uncomplicated skin and skin structure infections (uSSSI) and 2) complicated skin and skin structure infections (cSSSI). Recently, the FDA has reclassified cSSSI and referred these infections as Acute Bacterial Skin and Skin Structure Infections (ABSSSI) and has defined their classification by syndrome, and the description of the types of infections that can occur:



Cellulitis / erysipelas: A diffuse skin infection characterized by spreading area of redness, edema, and/or induration of minimum surface area of 75 cm2 (e.g., length of 15 cm and width of 5 cm), accompanied by lymph node enlargement or systemic symptoms such as fever greater than or equal to 38 degrees Celsius. Bacteria for cellulitis infections can be difficult to culture since there is typically no break in skin. Diabetics are more susceptible to cellulitis than the general population due to an impaired immune system and poor glucose control. Infections can be initiated by scratches, abrasions, insect bites, tattoos, or injections.



Wound infection: An infection characterized by purulent drainage from a wound with surrounding redness, edema, and/or induration (hardness) of a minimum surface area of 75 $cm^2$, accompanied by lymph node enlargement or systemic symptoms such as fever greater than or equal to 38 degrees Celsius. Wound infections initiate when opportunistic bacteria find their way under the skin into the body through an open sore, puncture, laceration, break, or incisions usually resulting from an external trauma. In the most severe forms of the infection can penetrate to the underlying bone.



Major cutaneous abscess: An infection characterized by a collection of pus within the dermis or deeper that is accompanied by redness, edema, and/or induration of a minimum surface area of 75 $cm^2$, accompanied by lymph node enlargement or systemic symptoms such as fever greater than or equal to 38 degrees Celsius. An abscess usually results from introduction of pathogenic bacteria into the skin by way of a wound or pre-existing skin lesion. In the most severe infections the abscess formation can extend into the fat or fascial layers.



Burn infections: An infection characterized by purulent drainage, redness, edema, and/or induration of a minimum surface area of 75 $cm^2$, accompanied by lymph node enlargement or systemic symptoms such as fever greater than or equal to 38 degrees Celsius. There are approximately 500,000 persons in the U.S. each year that seek medical treatment for severe burns. Given the open and moist skin, along with reduced T-cell activity resulting for tissue damage, burn sites are highly susceptible to acute bacterial skin and skin structure infections.

**MRSA – A Growing Problem**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is gram-positive pathogen that can cause serious or life-threatening infections. MRSA infections are difficult-to-treat given their resistance to commonly used beta-lactam antibiotics including penicillin derivatives, monobactams, and carbapenems, or by antibiotics in the quinolone or macrolide classes. Beta-Lactam antibiotics are bacteriocidal, and act by inhibiting the synthesis of the peptidoglycan layer of bacterial cell walls. The peptidoglycan layer is important for cell wall structural integrity, especially in gram-positive organisms. The antibiotic binds to structures on the cell wall known as penicillin-binding proteins (PBPs). The effectiveness of the antibiotic relies on its ability to reach the PBP intact and successfully bind to the active site. This irreversible binding inhibits production of the peptidoglycan layer, disrupting cell wall synthesis, leading to cell death. Unfortunately, beta-lactam antibiotics are subject to growing resistance through two separate mechanism of action. The first is when the bacteria produces an enzyme, beta-lactamase (penicillinase) that breaks open the beta-lactam ring, rendering the antibiotic ineffective. The second is when the bacteria alter the structure of the PBP so that the binding becomes less efficient or reversible.

As a result of the growing resistance to beta-lactam antibiotics, MRSA infections have become a major problem around the world. An article published in *The Lancet* in 2006 notes that 2 billion individuals worldwide are healthy carriers the *S. aureus* bacteria. In the U.S., roughly 5% of the population is colonized. Studies show roughly 40% of *S. aureus* bacteria show some level of antibiotic resistance. This has become a major problem in hospitals where patients may have open wounds or compromised immune systems. According to the CDC, 2.5% of patients admitted to the hospitals in the U.S. will contract a MRSA infection. *S aureus* infections can progress rapidly in the first 24 to 48 hours after the initial symptoms. By 72 hours *Staphylococcus* can spread rapidly and metastasize throughout the body to produce deep seated, difficult to treat, infections.



**MRSA**

In 2009, there were an estimated 1.3 million incidences of MRSA infections. This creates significant healthcare concern, especially in elderly or immuno-compromised patients. An in-hospital patient with a MRSA infection is 7-times more likely to die according to MRSAinfection.org. The average hospital stay is extended by an average of 6 days due to a MRSA infection. This costs the average patient an additional $10,000 in medical bills, or $8 billion in total healthcare costs in the U.S. alone. The number of MRSA infection deaths each year is estimated between 20,000 and 40,000, or about 2% to 4% of those infected. Based on statistics from the CDC, this is greater than the number of patients per year that die from HIV/AIDS in one year. There are two types of MRSA infections:

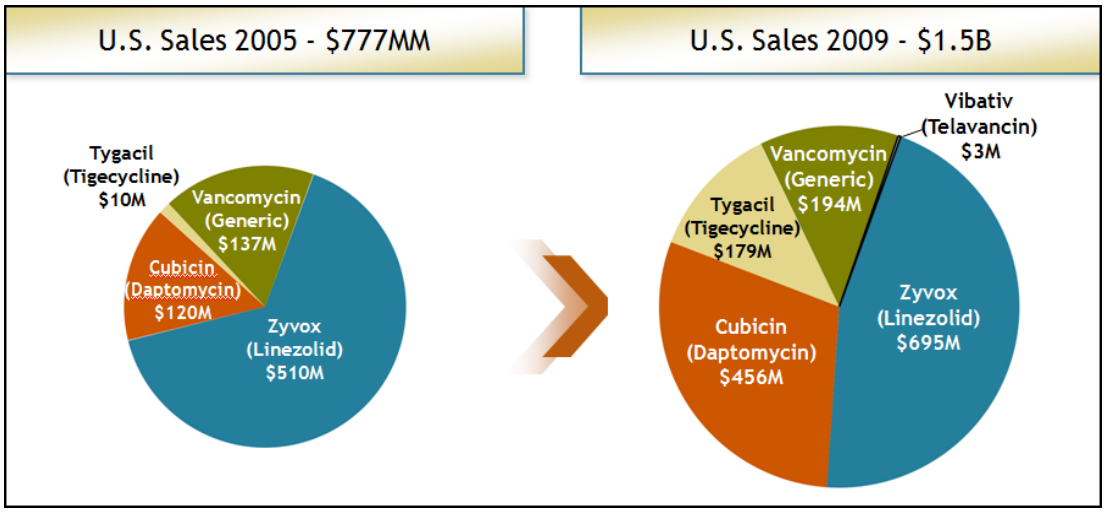
- Community-Associated (CA)-MRSA: CA-MRSA is often associated with dermatological conditions, diabetes, burns, wounds, or IV drug use, but may also occur in otherwise healthy individuals. About 75% of all CA-MRSA infections are localized to the skin and soft tissue. Transmission is person to person and the *S. aureus* growth rate is fast, but CA-MRSA infections are usually treatable with non beta-lactam antibiotics, most commonly IV vancomycin or clindamycin. CA-MRSA infections account for roughly 60% of all MRSA infections in the U.S.

- Hospital-Associated (HA)-MRSA: HA-MRSA is usually associated with an at-risk population, which includes the elderly or immuno-compromised, in the hospital or long-term care facility setting. Infection can take hold through surgery, percutaneous medical devices, catheters, ICU exposure, or prolonged antibiotic use for a concurrent infection. The infection can diffuse systemically, resulting in severe sepsis or toxic shock syndrome. The *S. aureus* growth rate is usually slower than CA-MRSA, but resistance to antibiotics is usually greater and includes, fluoroquinolones, clindamycin, and sulfamethoxazole. HA-MRSA infections account for roughly 40% of all MRSA infections in the U.S.

MRSA infections are a significant problem both in the U.S. and around the world. Besides hospitals and long-term care facilities, prison, livestock facilities, and health and fitness centers have become significant areas of growing MRSA outbreaks in the past decade. Screening procedures to indentify MRSA infections have been instituted in the U.S. and Europe as a result. A study conducted by the L.A. County Jail system in 2001 showed that >70% of all infections in the county's prisons were the result of MRSA. Since 2001 the MRSA infection rate has continued to soar. A study conducted by the Federal Bureau of Prisons in 2007 concluded that the *S. aureus* infection rate among prisoners is an astonishing 75%. MRSA is also a significant problem in livestock. *S. aureus* can infect poultry and cattle, where the infection can then be transmitted to humans. Finally, a study conducted by the Texas State Department of Health, and published in the NEJM, concluded that MRSA infection rates among high school football players was 16-times the national average for high school students

**The Current Treatment Paradigm**

Both CA-MRSA and HA-MRSA are typically resistant to traditional anti-staphylococcal beta-lactam antibiotics such as penicillin, cephalosporins, monobactams, and carbapenems. CA-MRSA infections are susceptible to a wider spectrum of antimicrobials drugs, the most commonly used of which is vancomycin. HA-MRSA is more difficult to treat, having developed low-level resistance to vancomycin. As a result, new drugs such as linezolid, sold by Pfizer as Zyvox and daptomycin, sold by Cubist Pharmaceuticals as Cubicin, are increasingly used. The introduction of new antibiotic drugs such as Zyvox and Cubicin, and most recently Tygacil (tigecycline), has greatly expanded the market for MRSA antibiotics over the past decade. The market for MRSA antibiotics stood at $1.5 billion in 2009, double in size from the $777 million only four years earlier in 2009. In 2011 we estimate this market will grow to approximately $1.7 billion. The pie charts below show the growing use of these drugs:




The growth in these drugs above represents at 20% CAGR for the branded molecules, Zyvox, Cubicin, and Tygacil, and a 9% CAGR for generic vancomycin. As the effectiveness of generic vancomycin continues to diminish, the market has rapidly shifted to new more effective branded drugs. In fact, new evolutions of MRSA bacteria are being referred to as vancomycin intermediate-resistant *Staphylococcus aureus* (VISA).

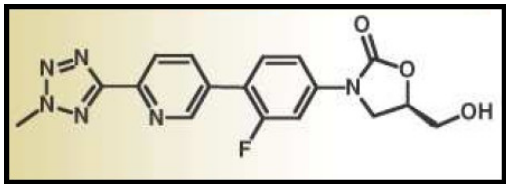
This is a key point for investors to understand. Unlike generic ace-inhibitors or statins that compete effectively with similar branded medications, antibiotics have a useful life and physicians are quick to turn to new branded products, despite the significant higher cost, based on effectiveness and desire to prevent serious systemic infections. This presents a unique opportunity for next-generation branded antibiotics to gain sizable market share when drugs like linezolid and daptomycin begin to show diminishing efficacy regardless of the patent exclusivity or cost, just like what happened with vancomycin.

Despite the rapid growth in new antibiotics such as Cubicin and Tygacil, we believe there is significant room for improvement in the treatment paradigm. There are certain key attributes we believe represent the ideal product. Those include having both an oral and IV option, the ability to administer once daily with a short course of therapy thanks to rapid onset of activity. And finally, the drug should be effective in lung infections.

| | Zyvox (linezolid) | Cubicin (daptomycin) | "Ideal" |
|---|---|---|---|
| IV & Oral Formulation | YES | NO | YES |
| Rapid Efficacy Onset | NO | YES | YES |
| Active In Lung Infections | YES | NO | YES |
| Once Daily Dosing | NO | YES | YES |
| Short Course of Therapy | NO | NO | YES |

**Trius Torezolid Poised To Be Best-In-Class**

Trius Therapeutics is working on Torezolid phosphate (TR-701), a second generation oxazolidinone being developed for the treatment of serious gram-positive infections, including MRSA. Pfizer's Zyvox (linezolid) is a first-generation oxazolidinone that posted sales over $700 million in the U.S. alone in 2010. Torezolid phosphate is a novel prodrug that once cleaved in the blood stream releases the active compound, Torezolid.




**Torezolid**

Trius Therapeutics acquired the exclusive worldwide right to Torezolid (ex-Korea) from Dong-A Pharmaceutical Co., Ltd. in January 2007. The company has been granted intellectual property (IP) protection through composition of matter patents in the U.S (issued 10/19/2010), Australia (issued 7/9/2009), New Zealand (issued 9/10/2009), India (issued 11/25/2009), and Russia (granted 8/16/2010). The company is in the process of filing applications around Europe, Canada, Brazil, China, Japan, and Mexico. This core IP will protect Torezolid through 2026, with the potential to expand the protection through dimer-molecules, manufacturing process, and crystalline forms into 2030.

***…Preclinical & Phase I Data…***

Trius acquired Torezolid from Dong-A Pharma in January 2007 because management believed the drug has the potential to be the best-in-class, first-line bacteriocidal agent for serious gram-positive infections. Preclinical data demonstrates that Torezolid offers:

- ✓ Great Potency → *In Vitro* data suggest that Torezolid offers potency 4- to 8-times greater than linezolid against linezolid-susceptible strains and up to 16-times greater potency against linezolid-resistant strains of Gram-positive bacteria. This increase potency is suggestive of shorter treatment duration and faster pathogen eradication, resulting in quicker discharge from the hospital.

- ✓ Dosing Compliance → Pharmacokinetic data suggests Torezolid can be effectively dosed once daily (QD) for 5 to 7 days for the treatment of acute bacterial skin and skin structure infections (ABSSS) infections. This compares favorably to the twice daily (BID) 10 to 14 days for Zyvox (linezolid). A shorter treatment duration and QD dosing should greatly improve compliance, resulting in better clinical outcomes.

- ✓ Effective Targeting → Torezolid, unlike linezolid, concentrates to a high extent inside certain white blood cells, which engulf pathogenic bacteria and concentrate at the site of infection. This is suggestive of Torezolid contributing to I*n Vivo* bactericidal activity, resulting in a higher degree of efficacy and faster eradication of the pathogenic bacteria.

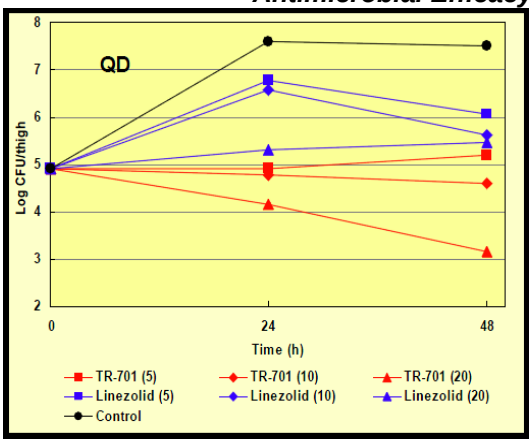
- ✓ Applicability → Preclinical data supports the strong efficacy of Torezolid against all clinically relevant gram-positive bacteria tested, including those noted to be linezolid-resistant, *Legionella* and *Chlamydia*. This supports potential use as a first-line therapy, even in difficult to treat lower respiratory infections.

- ✓ Low Risk of Resistance → Preclinical data demonstrates the frequency at which MRSA evolves resistance to Torezolid is 16-times less than linezolid. We believe that this strengthens the competitive positioning of the product vs. first-generation molecules and generics such as vancomycin.

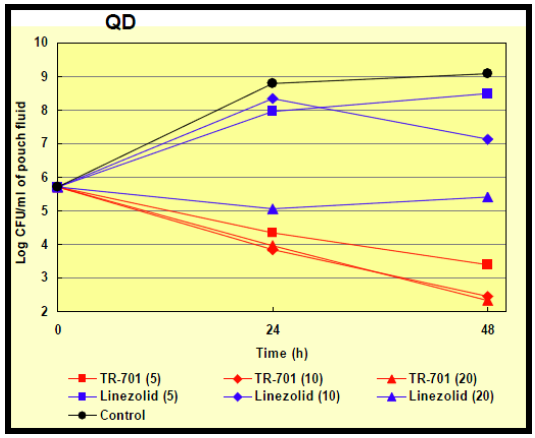
- ✓ Safety → Pharmacokinetic data support a predictable efficacy and safety profile across different patient populations when compared to linezolid. And, unlike linezolid, Torezolid has not been shown to induce higher blood pressure and faster hear rate in the presence of tyramine, contained in food, drugs such as vasoconstrictors and other pharmaceutical products such as SSRI antidepressants. Data from a 21-day comparative phase I study with 200mg QD Torezolid showed no meaningful impact on hematological parameters indicative of myelosuppression unlike what is seen with the approved dose of linezolid (600mg BID). This supports potential use of Torezolid as a safer alternative to (off-label) linezolid in indications that require longer-term dosing regimens such as bacteremia and osteomyelitis.

The data below as presented as a poster presentation 2007 (#F1-1691) at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). The data demonstrates Torezolid to be of superior potency to Linezolid in skin and soft tissue models of infection.

***Antimicrobial Efficacy of TR-701 – Torezolid vs. Linezolid***




**Thigh Infection Model**




**Air Pouch Model**

In December 2010, Trius published a paper online in Antimicrobial Agents and Chemotherapy (ACC) titled, Comparative in vitro Activities of Torezolid (TR-700, DA-7157) against Clinical Isolates of Aerobic and Anaerobic Bacteria in Korea. The results show the minimum concentration required to inhibit the growth of 90% (MIC90) of gram-positive bacterial isolates for Torezolid was ≤0.5 µg/ml. This is far superior to the MIC90 for linezolid (MIC90 of 4.0 µg/ml) or vancomycin (MIC90 of 1.0 µg/ml).

The data below is from the company's phase Ib, 21-day multiple ascending oral dose study designed to show the relative safety profile of Torezolid vs. linezolid for potential longer-term use in serious gram-positive infections such as bacteremia and osteomyelitis. This data was presented as a poster presentation at the 2008 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) conference (#F1-2069a).

***Phase Ib Comparative Safety Analysis***

| | Placebo (n=8) | 200mg BID Torezolid (n=8) | 600mg BID Linezolid (n=8) |
|---|---|---|---|
| Any AE | 5 (63%) | 5 (63%) | 4 (50%) |
| Mild-to-Moderate AE | 6 (75%) | 5 (63%) | 5 (63%) |
| Severe or Serious AE | - | - | - |
| Treatment-Related AE (Day-21) | 4 (50%) | 4 (50%) | 4 (50%) |
| Treatment-Related AE (Day-7) | 2 (25%) | - | 2 (25%) |
| Study Discontinuation | - | 1 (13%) | 1 (13%) |
| Nervous System Disorders | 2 (25%) | 1 (13%) | 4 (50%) |
| Gastrointestinal Disorders | 1 (13%) | - | 2 (25%) |
| Skin & Subcutaneous Disorders | 3 (38%) | - | 1 (13%) |
| Eye Disorders | - | 1 (13%) | - |
| Application Site Disorders | 1 (13%) | - | 2 (25%) |

Over 21days, multiple doses of 200mg Torezolid proved to be well tolerated. Management noted that 400mg Torezolid demonstrated higher incidence of mild-to-moderate adverse events compared to the 200mg dose. Exposure at day-7 was well tolerated for the 200mg dose. There were no significant changes for findings in physical or neurological examinations, or vital sign measurements. There were no QTc prolongation issues and no remarkable changes from baseline in any ophthalmologic examinations. In our view, this is a generally a safe and well-tolerated drug with a comparable, if not superior safety profile to Pfizer's blockbuster Zyvox.

***Highly Differentiated Key Attributes***

| | | 1st Generation (Pfizer) | 2nd Generation (Trius Therapeutics) | |
|---|---|---|---|---|
| | **Attribute** | **Linezolid** | **Torezolid** | **The Torezolid Advantage** |
| EFFICACY | *in vivo* Activity | Bacteriostatic | Bactericidal | Faster Acting = Expanded Applications |
| | MRSA $MIC_{90}$ µg/mL | 4.0 | 0.5 | More Potent |
| | $Lin^r$ MRSA (Cfr) $MIC_{90}$ µg/mL | 16.0 | 0.5 | Active Against Resistant MRSA |
| | Frequency of Resistance | $3 \times 10^{-9}$ | $2 \times 10^{-10}$ | Lower Resistance Acquisition |
| SAFETY | Tyramine / SSRI Interactions | Yes | No | Fewer Drug Interactions |
| | Impact on Blood Cells | 100% of subjects above LLN | 25% of subjects below LLN | Safer for LT Dosing |
| COST EFFECTIVENESS | Course of Therapy | 10-14 Day | 6 Day | Fewer Pills Shorter Time to Cure, Shorter Hospitals Stays |
| CONVENIENCE | Dosing Duration Compliance | 600 mg BID | 200 mg QD | |

***…Phase II Data…***

In 2009, Trius initiated double-blind phase II study that evaluated three oral doses of Torezolid (200, 300, or 400mg) QD over 5-7 days for complicated skin and skin structure infections (cSSSI). Patients 18-75 years with cSSSI suspected or confirmed gram-positive pathogens were randomized 1:1:1. Of 188 treated patients, 76.6% had major abscesses, 17.6% had extensive cellulitis, and 5.9% had wound infections. *S. aureus*, the most common pathogen, was isolated in 90% of patients (139/154) with a baseline pathogen; 81% were MRSA.

The primary endpoint was anti-bacterial response as assessed by the investigator at 7 to 14 days post end of treatment. Investigators also assessed early response rates at days 2, 3, and 5, as well as infection relapse rate at test of cure (TOC). The data demonstrate strong efficacy on the primary endpoint of cure rate:

| **Cure Rate** | **200mg** | **300mg** | **400mg** |
|---|---|---|---|
| Clinically Evaluable (CE)[1] | 98% | 94% | 94% |
| Microbiologically Evaluable (ME)[2] | 100% | 93% | 96% |
| MRSA + Infections | 100% | 93% | 97% |

CE: Patients that were enrolled, completed the study, and returned for final assessment
ME: Patients that yielded a Gram-positive culture

| | | | |
|---|---|---|---|
| Nausea | 14% | 19% | 16% |
| Diarrhea | 11% | 5% | 10% |
| Vomiting | 6% | 6% | 6% |
| Headache | 5% | 9% | 5% |
| Discontinuations | - | - | - |

The efficacy data from the 200mg Torezolid cohort looks very impressive in our view. The dose provides the optimal benefit-risk profile, with outstanding efficacy with the lowest potential for adverse events, even though all events during the program were designated to be mild-or-moderate with no discontinuations. The once-daily (QD) 5 to 7 day dosing schedule presents both patients and physicians with a high compliance and highly effective treatment for complicated skin and skin structure infections (cSSSI) and MRSA, regardless of infection type, presence of systemic signs of infections, and lesion size.

| Cure Rate | Infection Type | | | | Lesion Size | | |
|---|---|---|---|---|---|---|---|
| | Abscess | Wounds | Cellulitis | Systemic | 5-10cm | 10-20cm | >20cm |
| CE Population | 96% | 90% | 97% | 96% | 96% | 97% | 94% |
| ME Population | 96% | 88% | 100% | 96% | 95% | 97% | 96% |

This data was presented at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in April 2010, as well as published in the American Society of Microbiology's journal, the Antimicrobial Agents and Chemotherapy (doi:10.1128/AAC.00076-10) titled, "A Phase 2 Randomized, Double-Blind, Dose-Ranging Study Evaluating the Safety, Tolerability, Population Pharmacokinetics, and Efficacy of Oral Torezolid Phosphate in Patients with Complicated Skin and Skin Structure Infections (cSSSI)."

***...FDA Updated Draft Guidelines…***

In August 2010, the U.S. FDA updated the Draft Guidelines for development of pharmaceutical products designed to treat acute bacterial skin and skin structure infections (ABSSSI). The new guidelines are designed to provide a road-map for the endpoints necessary to gain approval in ABSSSI, impetigo, and minor cutaneous abscesses. The new guidelines can be found here:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071185.pdf

The new endpoints provide a big advantage to Trius in our view, as they call for more rapid acting drugs with clearly defined objective primary and secondary efficacy endpoints. Trius will have the opportunity to better demonstrate the benefits of Torezolid vs. Zyvox. This presents the high potential for differentiation of Torezolid if approved under the new standard vs. older-generation molecules that were approved under less rigorous and vague standards.

| | |
|---|---|
| **Primary Efficacy Endpoint** | Response: Cessation of the spread of the redness, edema, and/or induration of the lesion or reduction in the size (length, width, and area) of redness, edema, and/or induration at 48 to 72 hours after enrollment and resolution (absence) of fever. |
| | Failure: Death; continued fever; increase in the size of redness, edema, and/or induration of the lesion; or administration of rescue antibacterial drug therapy or administration of non-trial antibacterial drug therapy for treatment of ABSSSI before the primary efficacy assessment |

| | |
|---|---|
| **Secondary Efficacy Endpoint** | Response: Cessation of the spread of the lesion at 48 to 72 hours, and resolution of the infection at 10 days post-randomization and at additional follow-up visits following completion of therapy |
| | Failure: All-cause mortality, post-randomization incision and drainage of ABSSSI, persistent purulent drainage from wound infection, initiation of rescue antibacterial medication or non-trial antibacterial drug therapy for treatment of ABSSSI before the final assessment. |

A summary of the new guidelines can be found in the chart below:

| | Prior Criteria | New Criteria |
|---|---|---|
| Indication | cSSSI | ABSSSI |
| Infection Type | Large Abscess, Wound, Cellulitis | Large Abscess, Wound, Cellulitis |
| Infection Severity | Intermediate/Severe | Severe |
| Primary Endpoints | **Subjective** (Clinicians Assessment at 7-14 Days After EOT) | **Objective** (Cessation of Lesion Spread & Fever at 48-72 hrs) |
| Secondary Endpoints | Varied<br><br>**Low Potential for Differentiation** | • Primary Endpoint Sustained to EOT<br>• Clinician's Assessment at EOT<br>• Superiority of Primary Endpoint<br><br>**High Potential for Differentiation** |

Following the FDA publishing the new updated draft guidelines, Trius performed a retrospective analysis the phase II study using the new endpoints specified in the draft guidelines. The charts below demonstrate that Torezolid would have met the primary and secondary outcome for approval of a new antibacterial agent designed to treat acute bacterial skin and skin structure infections (ABSSSI) under the new draft guidelines on both: 1) Cessation of the spread of the lesion (Chart-1), and 2) Reduction in fever (Chart-2):

**Chart-1**

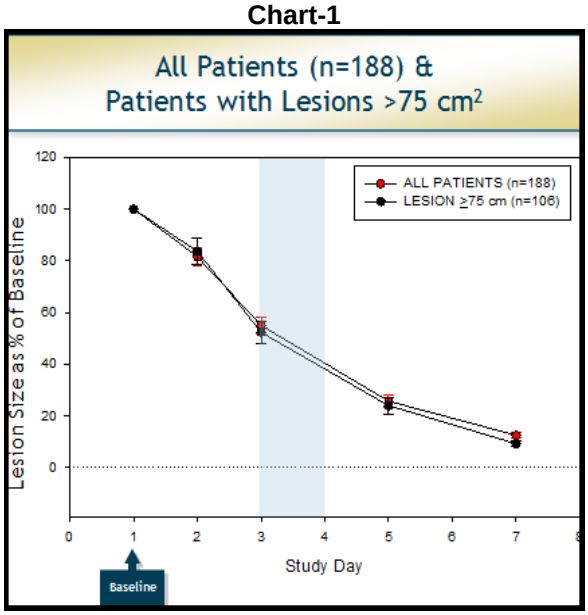
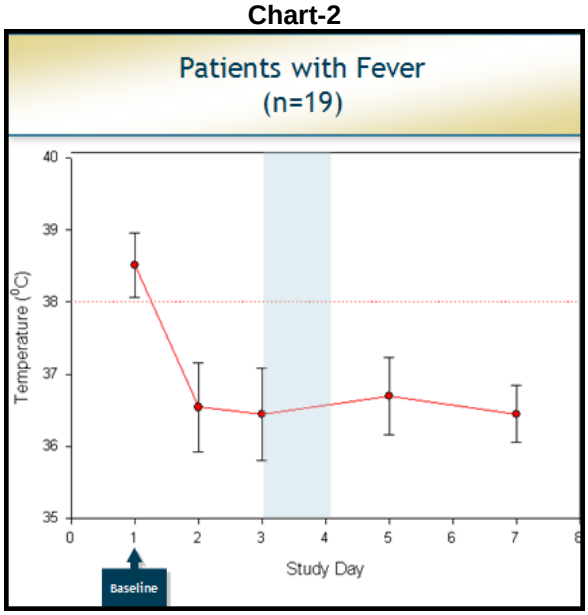



**Chart-2**

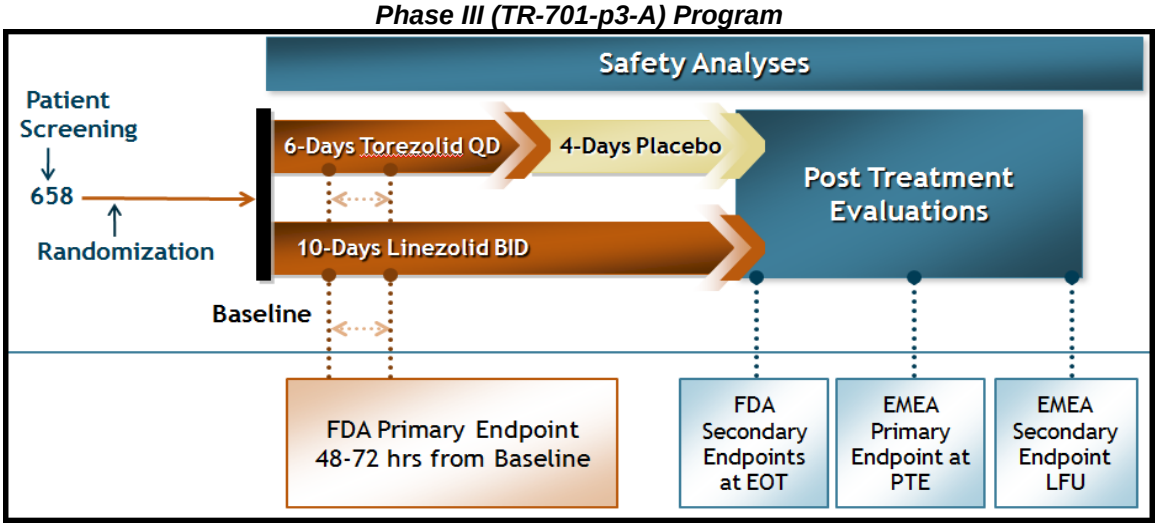



***…Phase III…***

To gain approval for Torezolid, Trius will conduct 2 phase III comparison studies looking to prove non-inferiority to Zyvox (linezolid). The first program began enrolling patients in August 2010. The second has yet to begin.

The first phase III trial is operating under a special protocol assessment (SPA) with the U.S. FDA. The trial began enrolling patients in late August 2010. The trial will study 200mg QD oral Torezolid vs. 600mg BID oral Zyvox (linezolid) in a 1:1 randomization with a target enrollment of 658-patients at over 100+ clinical sites around the world. Management plans to expand to sites in Europe and Latin American shortly to speed enrollment shortly. As of early 2011, enrollment is proceeding on plan. In fact, we have found that interest in the trial is high among clinicians and enrollment is actually proceeding ahead of schedule. The objective is to complete the study during the fourth quarter 2011 and report results early 2012. The trial employs both the new U.S. FDA guidelines and the old guidelines still in use for approval by the European EMEA.

***Phase III (TR-701-p3-A) Program***



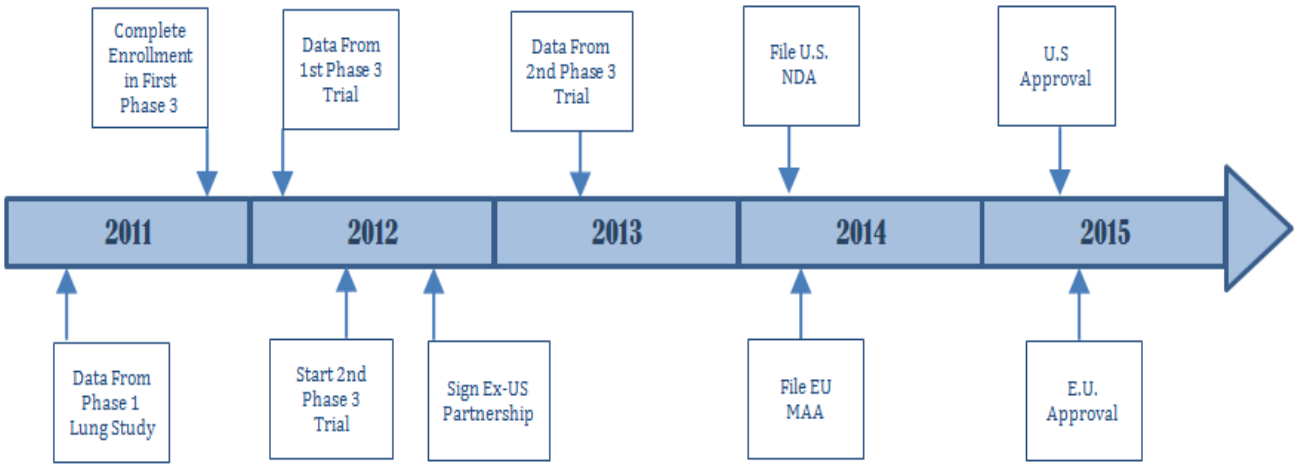
We are confident in the design and outcome of the first phase III study. Based on data from the previous phase II program, we are expecting cure rates >90% for the Torezolid arm. We have gone back and looked at previous phase III and IV data presented by Pfizer on Zyvox, assessed under the former guidelines and concluded that a cure rate of 70% to 80% for linezolid is expected. We encourage investors to go back and view this phase III data on Zyvox, which was presented at the AAC meeting in December 2000 (#3408-3413), the ICACC meeting in June 2005 (#2260-2266), and most recently in a briefing document provided by the FDA Anti-Infective Drugs Advisory Committee meeting in November 2008. The cure rate for Zyvox noted in this briefing document for a phase IV (n=195) trial was approximately 77%. The document can be found here:

http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4394b3-03-ARPIDA.pdf

Trius will also conduct a second phase III study of similar design, only patients will start with IV therapy and transition to oral medication at the discretion of the investigator. Hospitalized patients with severe infection typically start out on IV vancomycin or IV Zyvox and stay on IV therapy for as long as 4 to 5 days. Based on phase I pharmacokinetic data conducted by Trius, which the company presented data on in March 2010, we believe patients will be able to transition off IV therapy to oral therapy in as little as 2 to 3 days. Additionally, the oral bioavailability of Torezolid was determined to be approximately 92% when compared to IV dosing. This means that no dose adjustment will be necessary for Torezolid whether administered via either IV or oral routes. This is a big convenience benefit for the physicians. The same 200 mg dose may be used for both the company's planned IV-to-oral step-down phase III clinical trial. We estimate this trial will start in 2012. Management is currently in the process of securing another special protocol assessment (SPA) for this second phase III study.

***…File In 2014…***

If the timelines hold for the phase III program, the company should be in position to file for approval of Torezolid in 2013. This puts potential U.S. FDA action in 2014. We assume a similar timeframe for filing and approval in the EU. The company is also conducting a phase I lung pk study looking to assess proof-of-concept of Torezolid to treat lung infections. We anticipate that data will become available in March 2011.




Management's goal is to enter an Ex-U.S. commercialization partnership for Torezolid. We think the company will be in a better position to realize greater value from the drug following the release of the data from first phase III study in early 2012. A deal should provide funding for the initiation of the second phase III IV-to-oral step-down program, as well as allow management to start pre-commercialization efforts in the U.S. Based on the phase II data, we believe Torezolid has potential for best-in-class characteristics. The chart to the right shows that Torezolid has all the key attributes to make it a significant market share gainer for *S. aureus* infection and MRSA. The opportunity exists to expand the label into Hospital-Acquired Pneumonia (HAP) and Ventilator-Acquired Pneumonia (VAP), and Bacteremia as well.

| | Torezolid |
|---|---|
| IV & Oral Formulation | YES |
| Rapid Efficacy Onset | YES |
| Active In Lung Infections | YES |
| Once Daily Dosing | YES |
| Short Course of Therapy | YES |

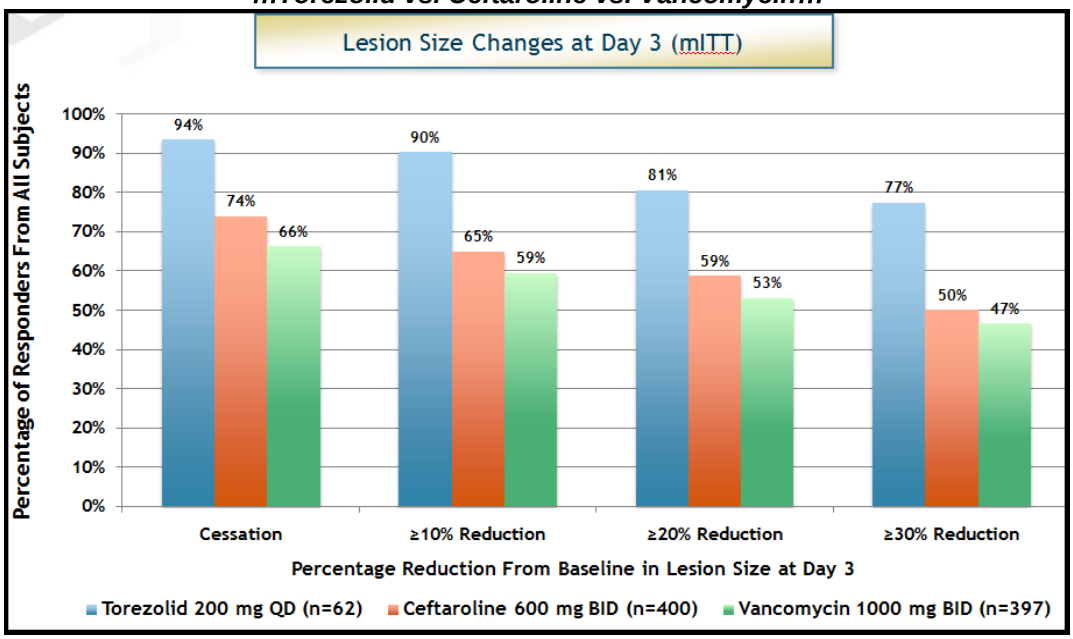
***…Competition…***

Torezolid will enter a highly competitive market in 2015. Besides generic vancomycin, which is generating roughly $200 million in sales annually, Pfizer's Zyvox (linezolid) will turn generic in May 2015. We expect rapid cannibalization of the branded Zyvox to the cheaper generic version after the patent expires. However, as noted above with generic vancomycin, the therapeutic window for these drugs is rapidly closing. As antibiotic resistance continues to grow for both vancomycin and linezolid, physicians will actively seek out newer, more effective molecules. This is clearly evidenced by the fact that branded Zyvox, Cubicin, and Tygacil posted a 20% CAGR in sales from 2005 to 2009, taking sizable market share from generic vancomycin. The MRSA market is not one where generics are a significant threat to new entrants. Typically, by the time an antibiotic goes generic its effectiveness is already waning and the market is seeking out alternatives.

Potential new competitors to Torezolid between now and 2015 include Forest Labs' Teflaro (ceftaroline). Ceftaroline is a fifth-generation cephalosporin antibiotic with positive phase III data in the treatment of infections cause by gram-positive bacteria and MRSA. Forest, under license from Takeda, conducted four phase III studies with ceftaroline, two in cSSSI and two in community-acquire bacterial pneumonia (CABP). The FDA approved the drug in October 2010 under the new guidelines for ABSSSI and CABP. Cure rates in the phase III program were superior to linezolid at around 92%. The potential issue with Teflaro, however, is limited efficacy vs. gram-positive bacteria other than *Staphylococcus or Streptococcus* such as enterococci, and direct competition from other cephalosporin molecules under development, including J&J's ceftobiprole and generic ceftazidime. Teflaro is administered via a twice-daily 600mg IV infusion, inconvenient when compared to the once-daily oral Torezolid. The recommended dosing schedule for Teflaro is 5 to 14 days, longer than we expect for Torezolid at 6 days.

The chart below shows the comparison of phase II data on Torezolid vs. phase III data taken from the FDA briefing document for the review of ceftaroline. This shows the relative efficacy of Torezolid vs. both ceftaroline and vancomycin for the treatment of skin infections. We think it is interesting to note that the FDA voted unanimously (21-0) to approval ceftaroline in August 2010 based on, among others, this head-to-head data against vancomycin. Seeing how Torezolid stacks up against both drugs clearly has management optimistic.

***…Torezolid vs. Ceftaroline vs. Vancomycin…***




Forest Labs acquired Cerexa, the developer of Teflaro (ceftaroline) for nearly $500 million in 2007 when the drug was entering phase III studies. The Teflaro (ceftaroline) patent expires in December 2018. This is certainly a good sign for Trius, currently trading with a market capitalization of ~$100 million. We find it interesting that Forest Labs is now looking at combining Teflaro with another beta-lactamase antibiotic in mid-stage development, NXL-104. Is Forest concerned about the efficacy of their drug when compared to new molecules under development? Forest acquired the rights to NXL-104 when it was in phase II development from Novexel in January 2008 for $95 million upfront and another $95 million in potential milestones. At the time, Novexel was also working on NXL-103, an oral streptogramin antibiotic in phase II. Novexel was acquired by AstraZeneca for $505 million in late December 2009.

Two phase III candidates could present competition to Torezolid around the time of approval in 2015. They are Paratek Pharma's PTK-0796 and Cempra's Taksta (sodium fusidic), both in phase III for MRSA. We discuss these candiates below:

- Paratek's PTK-0796 is an interesting molecule that could present direction competition to Torezolid. The drug is the only other once-daily IV and oral molecule in phase III. PTK-0796 is an aminomethylcycline (AMC) molecule derived from tetracycline. Phase II data demonstrated an impressive 98% cure rate vs. 93% for Zyvox (not statistically given the small size of the study). Potential issues with PTK-0796 that lead us to believe that Torezolid is superior include the potential liver toxicity issues with tetracycline analogues and the poor bioavailability of the oral PTK-0796 molecule compared to the IV – only 50%. This means that physicians will need to adjust the dose on IV-to-oral step down therapies or it could present infection issues in the lower GI track. Despite these potential limitations, Paratek was able to sign a worldwide licensing agreement with Novartis for PTK-0796 in October 2008 for payments up to $485 million. Novartis had plans to move into phase III during the second half of 2010, but put those plans on hold to redesign the study under the new FDA guidelines. We expect the new phase III PTK-0796 program in ABSSSI will begin shortly.

- Cempra's Taksta (sodium fusidic) is antibiotic used in several countries outside the U.S. for use in MRSA. The drug has shown a potential for resistance and drug-drug interactions, with a broad spectrum of efficacy so far. Taksta also offers only twice daily oral dosing, no IV step-down therapy. This is not as convenient as Torezolid. Plus, phase II data on Taksta yielded efficacy data comparable to linezolid. There seems to be no real advantage to the drug over older-generation molecules. We believe that Cempra must conduct a phase III study under the new FDA guidelines if it were to push forward with Taksta.

Based on the above deals for Teflaro (ceftaroline), NXL-104, and PTK-0796, we believe Trius has the potential to either out-license the entire Torezolid molecule, potentially for as much as $400 million all-in, or out-license the Ex-U.S. rights for potentially as much as $100-200 million. These deals could bring as much as 20% upfront, with potential backend milestone for approval and launch targets, along with royalties on sales. For Trius, a company with a market capitalization of only ~$100 million, the potential to sign a deal for $50 million upfront is encouraging.

***…HAP/VAP & Bacteremia…***

Trius is evaluating phase III trials with Torezolid in two additional indications, 1) Community-Acquire Bacterial Pneumonia (CABP), Hospital-Acquired Pneumonia (HAP) and Ventilator-Acquired Pneumonia (VAP), and 2) Bacteremia. The opportunity exists to expand the label further into osteomyelitis. HAP is the second most common nosocomial infection. In fact, it has the highest mortality among nosocomial infections, at around 20% of all infected. It is a major problem for patients in hospitals and long-term care facilities. HAP is a substantial burden on the U.S. healthcare system to prolonged hospitalization and high mortality rate. An indication for CABP would allow Torezolid to equal the labels for both Tygacil and Zyvox. The phase I lung pk data Trius plans to present in lung infections during the first half of 2011 will be key in gauging the opportunity here. The ideal drug for CABP is one that offers a rapid onset of efficacy with a short course of treatment.

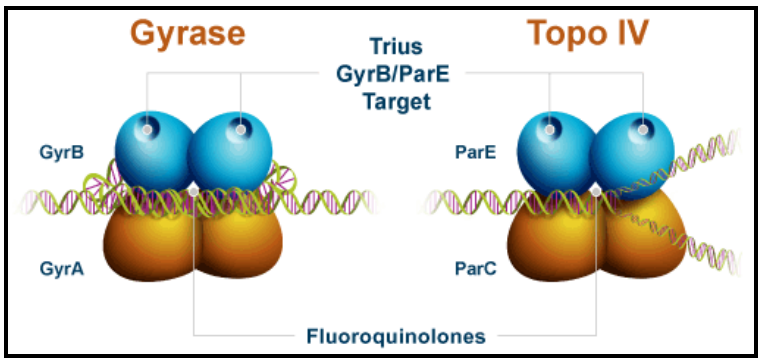
Bacteremia is caused by the presence of bacteria in the blood. The bacteria usually enter the blood stream through open wounds or cuts, deep seeded infections, or during surgery. It is a major problem in newborns, infants, and adults with compromised immune-systems. Patients with lung cancer, emphysema, or cystic fibrosis are highly susceptible to CABP. This is an excellent opportunity for Torezolid in our view. Approval and label expansion allows the Trius sales force to promote the drug as the first-line choice broad-spectrum antibiotic for serious infections. Approval in these indications also allows management to bake-in additional milestones beyond the upfront payment and sales-related milestone for Torezolid in ABSSSI or MRSA.

## PIPELINE

**Government Work Continues**

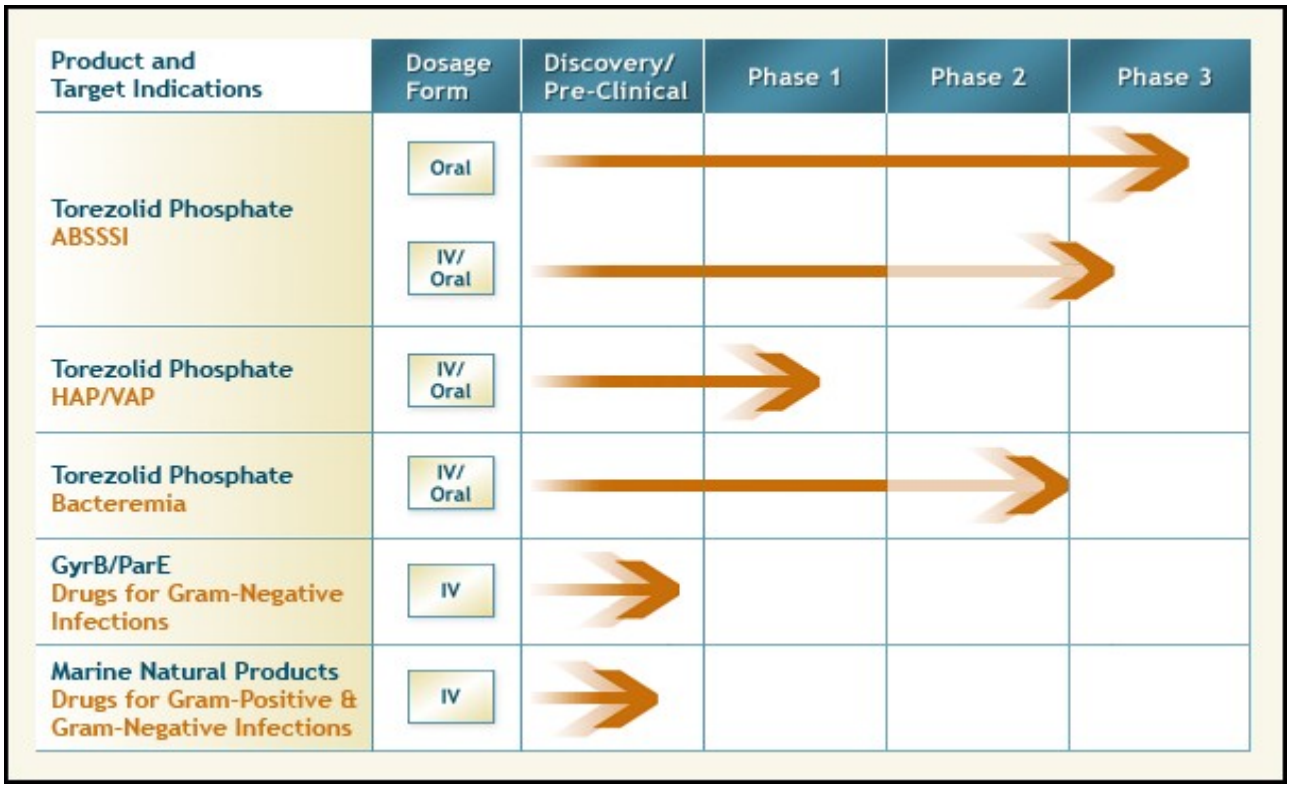
Trius has two preclinical programs ongoing, both funded by large government contracts. The first preclinical program is directed against the enzyme targets GyrB and ParE to treat infections caused by gram-negative bacteria. In September 2008, the company was awarded up to $27.7 million to support this program through a procurement contract of up to 5 years with the National Institute of Allergy and Infectious Diseases (NIAID). NIAID is part of the U.S. NIH. The contract supports development of the company's novel dual-target antibacterial agents as therapeutics for the treatment for biodefense applications. The scope of the contract includes preclinical, nonclinical and clinical IND- and/or NDA-enabling activities. Pursuant to this NIAID contract, Trius retains worldwide non-exclusive royalty-free license rights for each invention to which NIAID obtains title. Additionally, the U.S. government retains certain march-in rights with respect to our inventions developed under the NIAID contract. The NIAID contract supports the GyrB/ParE program for biodefense purposes through phase I clinical trials, subject to the achievement of program milestones.

Trius is focused on identifying and developing antibacterial agents targeting bacterial enzymes DNA gyrase, consisting of GyrA and GyrB, and Topoisomerase IV, consisting of ParC and ParE, required for the replication of bacterial cells. GyrA and ParC are the targets of the fluoroquinolone class of antibacterial agents. One such agent is ciprofloxacin (Cipro). GyrB is the target of the natural product novobiocin. The advantage here is that there currently are no approved antibacterial therapeutics in clinical use that inhibit both GyrB and ParE. This could present a meaningful step-forward in the treatment paradigm through lower bacterial resistance and increased potency, as well as broad spectrum use.




Trius second preclinical program targets antibacterial compounds from marine natural products libraries to treat infections caused by both gram-negative and gram-positive bacteria. In April 2010, the company was awarded up to $29.5 million to support this program through a 4.5 year contract with the Defense Threat Reduction Agency (DTRA). DTRA is part of the U.S. Department of Defense (DoD). Trius is using these funds to identify targets of antibacterial compounds from The Regents of the University of California, or UCSD, and to apply structure based drug design and development capabilities to optimize promising antibacterial compounds for activity against both gram-negative and gram-positive bacteria, including multiple biodefense pathogens. Pursuant to the DTRA contract, Trius retain a worldwide nonexclusive royalty-free license for each invention to which DTRA obtains title, and the United States government retains certain march-in rights with respect to these same inventions.

**PIPELINE CHART**



## MANAGEMENT

Trius Therapeutics has assembled an experienced management team highly capable of delivering on the potential for Torezolid in our view.

- Chief Executive Officer (CEO), Jeffrey Stein, Ph.D., has been with the company since 2005. Dr. Stein served as executive vice president, chief scientific officer and a member of the board of directors of Quorex Pharmaceuticals, an anti-infectives company he founded in 1999, which was acquired by Pfizer in 2005. Dr. Stein also served on the Director of Venture Development for the University of California.

- Chief Medical Officer (CMO), Philippe Prokocimer, Ph.D., has been with the company since 2007. Dr. Prokocimer served as a vice president, clinical research at Johnson & Johnson prior to joining Trius. Dr. Prokocimer also served as vice president of anti-infectives clinical research at Aventis Pharmaceuticals, Inc. and as medical director for Abbott Laboratories.

- Chief Commercial Officer, Craig Thompson joined Trius in January 2011. Mr. Thompson previously served as Vice President of Marketing for Pfizer's Specialty Care Business Unit where he was directly responsible for the U.S. commercial strategy for Zyvox, Tygacil, Vfend, Eraxis, Rapammune and Relistor. Prior to Pfizer, Mr. Thompson served in marketing activities at Merck.

- Chief Development Officer, Kenneth Bartizal, Ph.D. joined Trius in 2007. Dr. Bartizal served as executive director and head of infectious disease research at Merck & Co., Inc. and as a research scientist at Pfizer Inc.

- Chief Financial Officer (CFO), John P. Schmid, joined the company in 2004 and is a co-founder. Previously Mr. Schmid served as CFO for GeneFormatics, Inc., and Endonetics, Inc.

- Chief Scientific Officer (CSO), Dr. John Finn, Ph.D., joined the company in 2004 and is a co-founder. He previously served as the firm's President. Dr. Finn previously served as the vice president of drug discovery at Elitra Pharmaceuticals Inc. Dr. Finn also served as the senior director of lead discovery and optimization at Cubist Pharmaceuticals, Inc.

- V.P. Regulatory Affairs, Karen E. Potts, Ph.D., joined the company in 2009. Dr. Potts previously worked as a senior director of regulatory policy at Allergan, Inc. Dr. Potts also served previously with Pfizer, Inc. as an associate director for regulatory affairs.

| Management Team | Previous Experience | | |
|---|---|---|---|
| **Jeffrey Stein, Ph.D.**<br>*President and CEO* | QUOREX PHARMACEUTICALS | Diversa | Agouron |
| **Philippe Prokocimer, M.D.**<br>*Chief Medical Officer* | Johnson & Johnson | Aventis | Abbott |
| **Ken Bartizal, Ph.D.**<br>*Chief Development Officer* | MERCK | Pfizer | |
| **Craig Thompson**<br>*Chief Commercial Officer* | Pfizer | MERCK | |
| **Karen Potts, Ph.D.**<br>*VP Regulatory Affairs* | ALLERGAN | Pfizer | ISIS PHARMACEUTICALS |
| **John Finn, Ph.D.**<br>*Chief Scientific Officer* | Elitra Pharmaceuticals | CUBIST | |
| **John Schmid**<br>*Chief Financial Officer* | GeneFormatics | Endonetics | |

## VALUATION & RECOMMENDATION

**Trius Undervalued By Any Measure**

We see Torezolid as having significant market potential based on a clear superior profile to the two market-leading products in Pfizer's Zyvox (linezolid) and Cubist's Cubicin (daptomycin). Torezolid offers rapid efficacy onset, convenient once-daily dosing, a short course of therapy, and powerful efficacy. Pfizer's Zyvox will post worldwide sales over $1.1 billion in 2010 despite its limitations. We believe that Trius' phase III program will prove that 6 once-daily 200mg Torezolid pills are superior to 10 twice-daily (20 total) 600mg Zyvox pills.

***…On Future Cash Flow…***

Once approved, we believe the market will rapidly convert to Trius' Torezolid product. There is clear precedence that backs-up our belief. The market rapidly shifted from generic vancomycin to the more effective Zyvox a decade ago, and newer products such as Cubicin and Tygacil are gaining share on Zyvox now. Assuming FDA and EMEA approvals in 2015, we are modeling Torezolid worldwide sales of $750 million by 2020.

Assuming Trius seeks to commercialize Torezolid in the U.S. on its own and partners in EU, we see net income in 2020 of $230 million, with EPS of $5.75. Based on our discounted cash flow (DCF) analysis, we see Trius fairly valued at market capitalization of roughly $250 to $275 million based on these projections.

***…By Comparative Deal Analysis…***

Future cash flow is traditionally the best way to value a company. But what if Trius never even makes it to 2015 as an independent company? Anti-infectants have been an area where we have seen significant deal activity over the past decade. Accordingly, we see an excellent way to value Trius by looking at previous deals between larger pharmaceutical organizations and small companies with late-stage antibiotics for serious gram-positive infections.

| Comparative Deals For Late-Stage Antibiotics | Total Deal Value[1] |
|---|---|
| In April 2005, Johnson & Johnson acquired Peninsula Pharmaceuticals. Peninsula was in phase III studies with doripenem, a broad-spectrum antibiotic under U.S. FDA Fast Track designation for VAP. | $245 Million |
| In July 2005, Pfizer acquired Vicuron Pharmaceuticals. Vicuron was in phase III development for dalbavancin, a broad-spectrum antibiotic for cSSSI, and under U.S. FDA review with anidulafungin (Eraxis), a powerful anti-fungal agent. | $1.9 Billion |
| In November 2005, Astellas entered into a licensing agreement with Theravance. Theravance was just entering phase III development with telavancin for cSSSI. Telavancin, a bactericidal lipoglycopeptide, is now sold as branded Vibativ. | $231 Million |
| In December 2006, Forest Labs acquired Cerexa Inc. Cerexa was just entering phase III trials for ceftaroline, a cephalosporin for MRSA and other serious gram-positive cSSSI. | $580 Million |
| In October 2008, Novartis entered into a licensing agreement with Paratek. Paratek was in phase III development with PTK-0796 for cSSSI and MRSA. PTK-0796 is a broad-spectrum aminomethylcycline oral & IV antibiotic. | $485 Million |
| In January 2009, The Medicines Company acquired Targanta Therapeutics. Targanta was in phase III for oritavancin, a broad-spectrum antibiotic for cSSSI and HA-MRSA. | $138 Million |
| In December 2009, Forest Labs expanded its licensing agreement with Novexel. The agreement expanded Forest's interest in a NLX-104 / ceftazidime combination product for the treatment of cSSSI and MRSA. NLX-104 is a beta-lactamase inhibitor. | $305 Million |
| In December 2009, Cubist Pharmaceuticals acquired Calixa Therapeutics. Calixa was in phase II trials with CXA-201, a cephalosporin / tazobactam combination, | $403 Million |

1 – Includes potential backend milestones

The chart above clearly shows the interest of big pharma in this area. Pfizer, J&J, Astellas, Novartis, and Forest Labs are all major players, along with specialty pharma names such as Cubist. If we ascribe 65% of the value of Pfizer's acquisition of Vicuron to anidulafungin, which was under FDA review at the time, we still arrive at a deal value for dalbavancin north of $650 million. That puts the average deal value, all-in, at nearly $400 million for a late-stage antibiotic for cSSSI/ABSSSI or MRSA. Even the two smallest deals, Astellas' in-licensing of telavancin for $231 million and The Medicines Company acquisition of Targanta and oritavancin for $138 million, would still represent a 130% and 40% increase in market capitalization for Trius based on Torezolid alone, and this ignores the $57+ million in government contracts Trius has with the NIAID and DTRA.

In our view, Trius is worth $300 to $400 million on a take-out in 2013/2014 around the NDA filing.

***…Vs. The Competition…***

| Direct Competitors | Market Capitalization |
|---|---|
| Cubist Pharmaceuticals: 1 FDA approved product in Cubicin (daptomycin) with $625 Million in sales worldwide, and 2 phase II products in CXA-201 (gram-negative bactericide) and CB-315 (gram-positive bactericide).<br>2010 Revs: $636 million. 2010 Est. Net Income: $60 million. | $885 Million |
| Optimer Pharmaceuticals: 2 products under FDA review in fidaxomicin for *C. difficile* infection and prulifloxacin for infectious diarrhea. Also working on new indications and an oral formulation for fidaxomicin.<br>2010 Est. Revs: $1.5 million. 2010 Est. Net Income: -$50 million. | $425 Million |

Cubist and Optimer are the most directly comparable companies to Trius. We see Cubist as the model company for Trius to follow. In our view, Torezolid has similar market potential 4 to 5 years after launch to where Cubicin is right now. By the time Torezolid is under FDA review in 2014, we expect the preclinical programs currently funded by NIAID and DTRA to be in mid-to-late stage trials. Cubist's market capitalization of roughly 9-times that of Trius seems to overly discount this future potential. The market is valuing Optimer at over 4-times the value of Trius, despite that we see Torezolid as having significantly greater sales potential to fidaxomicin and prulifloxacin.

We see Trius following closely in the footsteps of both Cubist and Optimer. In our view, we see a market capitalization of $200 to $250 million more fairly valuing the company in relation to its two closest peers.

**Rating Outperform / Target of $10**

We are initiating coverage of Trius Inc. with an Outperform rating and price target of $10 per share. We are confident in the outcome of the company's ongoing phase III trial testing Torezolid vs. Pfizer's Zyvox (linezolid) for the treatment of acute bacterial skin and skin structure infections (ABSSSI). We see significant market share gains for Torezolid over the three market leading products, Zyvox, Cubicin, and Tygacil. The current market cap of only ~$100 million vastly undervalues the story in our view.

Based on a combination of three valuation methods, DCF, comparative deal analysis, and comparison to peer group, we see the company fairly valued at a market capitalization of roughly $250 million.

| Valuation Method | Projected Market Cap. |
|---|---|
| Discounted Cash Flow | $250-275 Million |
| Take-Out Value / Comparative Deals | $300-400 Million |
| Peer-Group Analysis | $200-250 Million |
| Estimated Fair Value | ~$250 Million |

This equates to a target price of $10 per share. This would be 13X our projected 2020 EPS forecast of $5.75, discounted to present day at an aggressive rate of 25%.

## PROJECTED FINANCIALS

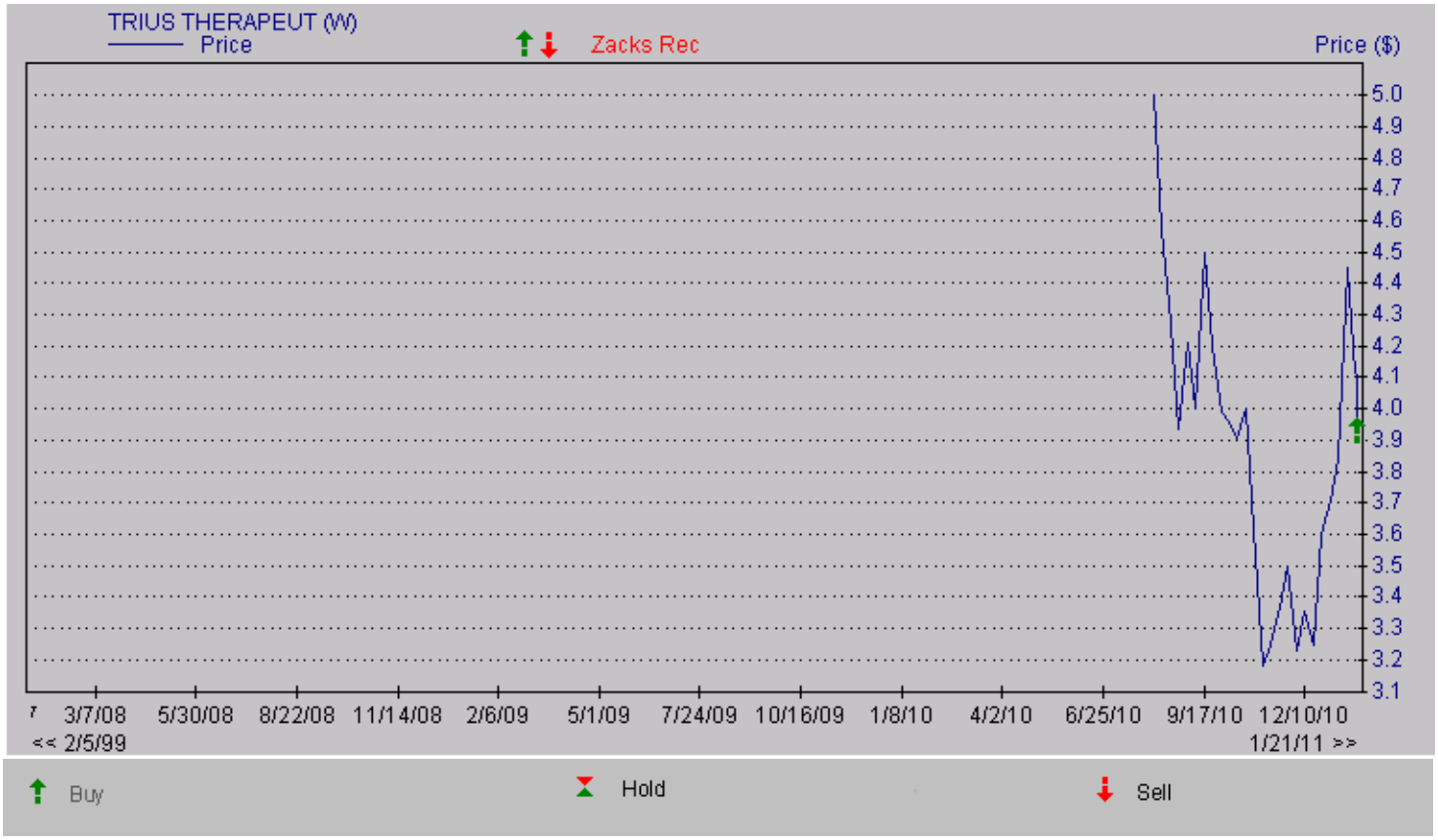
**Trius Therapeutics, Inc.**
Income Statement

| | 2009 A | Q1 A | Q2 A | Q3 A | Q4 E | 2010 E | 2011 E | 2012 E | 2013 E | 2014 E |
|---|---|---|---|---|---|---|---|---|---|---|
| Torezolid (N.A. Sales) | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 |
| *YOY Growth* | - | - | - | - | - | - | - | - | - | - |
| Torezolid (Ex-N.A. Sales) | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 |
| *YOY Growth* | - | - | - | - | - | - | - | - | - | - |
| **Total Torezolid Revs** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** |
| *YOY Growth* | - | - | - | - | - | - | - | - | - | - |
| **Contracts & Collaborations** | **$5.0** | **$1.5** | **$2.1** | **$1.9** | **$1.8** | **$7.3** | **$7.5** | **$7.5** | **$10.0** | **$15.0** |
| *YOY Growth* | - | - | - | - | - | - | *100.0%* | *0.0%* | *33.3%* | *50.0%* |
| **Total Revenues** | **$5.0** | **$1.5** | **$2.1** | **$1.9** | **$1.8** | **$7.3** | **$7.5** | **$7.5** | **$10.0** | **$15.0** |
| *YOY Growth* | - | - | - | - | - | - | *100.0%* | *0.0%* | *33.3%* | *50.0%* |
| CoGS | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 |
| *Product Gross Margin* | *0%* | - | - | - | - | *0.0%* | *0.0%* | *0%* | *0%* | *0%* |
| R&D | $23.0 | $4.2 | $3.5 | $6.0 | $9.5 | $23.2 | $39.5 | $35.0 | $30.0 | $30.0 |
| *% R&D* | - | - | - | - | - | - | - | *466.7%* | *300.0%* | *200.0%* |
| SG&A | $4.1 | $1.2 | $1.0 | $1.3 | $1.5 | $5.0 | $6.7 | $7.5 | $8.0 | $10.0 |
| *% SG&A* | - | - | - | - | - | - | *89.3%* | *100.0%* | *80.0%* | *66.7%* |
| Operating Income | ($22.2) | ($3.9) | ($2.4) | ($5.4) | ($9.2) | ($20.9) | ($38.7) | ($35.0) | ($28.0) | ($25.0) |
| *Operating Margin* | *0%* | - | - | - | - | *0.0%* | *-516.0%* | *-466.7%* | *-280.0%* | *-166.7%* |
| Interest & Other Income | ($0.5) | ($0.4) | $0.1 | ($3.1) | ($0.1) | ($3.5) | ($0.4) | ($0.5) | ($0.4) | ($0.2) |
| Pre-Tax Income | ($22.7) | ($4.3) | ($2.3) | ($8.5) | ($9.3) | ($24.4) | ($39.1) | ($35.5) | ($28.4) | ($25.2) |
| Taxes & Other | $0 | $0 | $0 | $0 | $0 | $0 | $0 | | | |
| *Tax Rate* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* |
| Net Income | ($22.7) | ($4.3) | ($2.3) | ($8.5) | ($9.3) | ($24.4) | ($39.1) | ($35.5) | ($28.4) | ($25.2) |
| *Net Margin* | *0%* | - | - | - | - | *0.0%* | *-521.6%* | *-473.3%* | *-284.0%* | *-168.0%* |
| **Reported EPS** | **($31.09)** | **($5.08)** | **($2.69)** | **($0.57)** | **($0.39)** | **($2.41)** | **($1.60)** | **($1.37)** | **($1.01)** | **($0.84)** |
| *YOY Growth* | - | - | - | - | - | *-92.2%* | *-33.7%* | *-14.5%* | *-25.7%* | *-17.2%* |
| Basic Shares Outstanding | 0.7 | 0.8 | 0.9 | 14.8 | 24.0 | 10.1 | 24.5 | 26.0 | 28.0 | 30.0 |

*Source: Zacks Investment Research, Inc.* *Jason Napodano, CFA*

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## HISTORICAL ZACKS RECOMMENDATIONS




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