Zacks Equity Research

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# Zalicus Inc.

## (ZLCS-NASDAQ)

***ZLCS: Sum Of Parts Shows Zalicus Is Under-Valued. Maintain Outperform Rating.***

## FULL REPORT

We are reiterating our Outperform rating and $3 price target on Zalicus Inc. (ZLCS). Based on our sum-of-parts analysis, Zalicus is significantly undervalued at today's price. We believe the company is well positioned from an existing and new product development, financial, and management standpoint.

Zalicus is engaged in the discovery, development, and commercialization of novel therapeutics that are combinations of approved drugs. Zalicus has identified several product candidates that target multiple diseases like immuno-inflammatory diseases, chronic pain, topical dermatoses, metabolic disease and oncology.

| | |
|---|---|
| **Current Recommendation** | **Outperform** |
| Prior Recommendation | N/A |
| Date of Last Change | 09/13/2010 |
| Current Price (11/10/10) | $1.18 |
| **Six- Month Target Price** | **$3.00** |

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$1.85** |
| **52-Week Low** | **$0.78** |
| **One-Year Return (%)** | **-24.00** |
| **Beta** | **1.64** |
| **Average Daily Volume (sh)** | **657,147** |
| **Shares Outstanding (mil)** | **89** |
| **Market Capitalization ($mil)** | **$118** |
| **Short Interest Ratio (days)** | **5.16** |
| **Institutional Ownership (%)** | **14** |
| **Insider Ownership (%)** | **3** |
| **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** | **3** |

| | |
|---|---|
| **Risk Level** | **Above Average** |
| **Type of Stock** | **Small-Blend** |
| **Industry** | **Med-Biomed/Gene** |
| **Zacks Rank in Industry** | **50 of 140** |

## ZACKS ESTIMATES

### Revenue

(In millions of $)

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2009 | 3.0 A | 3.3 A | 4.7 A | 8.6 A | 17.3 A |
| 2010 | 41.3 A | 2.9 A | 1.2 A | 2.0 E | 47.4 E |
| 2011 | | | | | 19.8 E |
| 2012 | | | | | 31.1 E |

### Earnings per Share

(EPS is operating earnings before non-recurring items)

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2009 | -$0.27 A | $0.23 A | -$0.24 A | $0.57 A | $0.41 A |
| 2010 | -$0.05 A | -$0.10 A | -$0.13 A | -$0.12 E | -$0.43 E |
| 2011 | | | | | -$0.37 E |
| 2012 | | | | | -$0.26 E |

Zacks Projected EPS Growth Rate - Next 5 Years % N/A

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## WHAT'S NEW

**Third Quarter Financials**

On November 10, 2010, Zalicus reported financial results for the third quarter ended September 30, 2010. The company reported total revenues in the quarter of $1.2 million, $1.1 million of which was government grants and collaborations, and $0.1 million of which was royalties on sales of Exalgo at Covidien. Total revenues of $1.2 million were generally in-line with our expectations of $1.3 million, although royalties on Exalgo disappointed. We remind investors that Exalgo launched in the second quarter 2010 and the initial royalty payment of $1.1 million included significant inventory stocking. Zalicus' royalty payment for the third quarter was down as a result of inventory work down from the initial stock.

Net loss of the third quarter totaled $11.4 million, or $0.13 per share. This was slightly wider than our expectations for a loss of $0.11 per share, and resulted from lower Exalgo royalties and higher R&D expense in relation to our model. Zalicus exited the third quarter with $48.6 million in cash and investments. We find this to be sufficient to fund operations into 2013 or beyond.

**Synavive Update**

Following consultation with the U.S. FDA, Zalicus has mapped out the next step in development for Synavive. Management plans to initiate a phase IIb program in rheumatoid arthritis (RA) in early 2011.

We note that prior to selecting RA, Zalicus conducted a series of interviews with key opinion leaders, practicing rheumatologists, primary care doctors and managed care personnel to fully explore the potential benefits of moving into RA as an initial indication for Synavive. Based on their feedback, management believes that RA is the most attractive choice on a number of fronts including current medical practice in which there is already a high prevalence of glucocorticoid use in RA to combat inflammation and restore function, as well as the unmet need for less expensive, easier to access options to biologic therapy. Beyond RA, we believe Synavive has potential in other steroid-responsive diseases such as polymyalgia rheumatica (PMR), lupus (SLE) and ulcerative colitis (Crohn's) as well as a replacement to NSAIDs and Cox-II inhibitors in osteoarthritis (OA).

**Pipeline Update**

Following the release of positive phase IIa data earlier this year, Fovea Pharma, now part of Sanofi-Aventis, initiated a phase IIb program with Prednisporin in June 2010 in subjects with persistent allergic conjunctivitis. Zalicus received a $500,000 milestone payment from Fovea relating to this initiation. The trial should complete before the end of the year 2010. We expect to see data from Sanofi late this year or early next year. As noted above, Zalicus is eligible to receive further development and regulatory based milestones on this candidate. The next milestone to Zalicus would be $3 million for the initiation of a phase III trial.

## INVESTMENT THESIS

***Exalgo Contributing***

In September 2010, we initiated coverage of Zalicus, Inc. with an 'Outperform' rating and $3 price target. We believe the company is well positioned from an existing and new product development, financial, and management standpoint. Zalicus has one commercialized product in Exalgo, an extended-release hydromorphone indicated for the treatment of moderate-to-severe pain in opioid tolerant patients requiring continuous (around the clock) analgesia. We believe Exalgo is poised to capture meaningful prescription and dollar share in the $6 billion long-acting opioid (LAO) market thanks to improved dosing and convenience, as well as improved safety and tolerability. Zalicus has licensed the U.S. commercial rights to Exalgo to Covidien, plc. Covidien is responsible for all commercialization activities for Exalgo in the U.S., including marketing and sales, and for all post-approval regulatory activities. Zalicus received a $40 million milestone payment following FDA approval of Exalgo in early March 2010. Covidien launched the product in late April 2010 with 250+ sales representatives and a dozen region directors. Zalicus is eligible to receive tiered royalties on net sales of Exalgo by Covidien. Cumulative royalties since that time have totaled $1.238 million.

***Synavive Progressing***

Zalicus' leading pipeline candidate is Synavive, a combination of the cardiovascular drug dipyridamole and an unconventionally low dose of the glucocorticoid steroid prednisolone, currently under mid-stage clinical development for the treatment of rheumatoid arthritis (RA) and osteoarthritis (OA). Previous phase II data studying Synavive in patients with moderate to severe arthritis demonstrated a statistically significant improvement in joint pain, stiffness, physical function, and patient assessment when compared to placebo. A larger-scale program in patients with knee osteoarthritis offered up encouraging results with the highest dose of Synavive tested, including demonstrating reductions in pain, stiffness, and physical function after 14 weeks of treatment. Management has been working to optimize and manufacturing a new modified-release formulation of Synavive. The new formulation supports once-daily dosing with improved tolerability and therapeutic index. We anticipate management will progress Synavive into a phase IIb program in rheumatoid arthritis (RA) 2011. If successfully commercialized, Synavive should be a meaningful revenue driver for Zalicus. Rheumatoid Arthritis (RA) and osteoarthritis (OA) are among the most common degenerative diseases and a frequent cause of physical disability among older adults. In the U.S. more than 100 million people suffer from RA and OA combined. A safe and effective treatment such as Synavive could present a meaningful alternative to the non-steroidal anti-inflammatory drugs (NSAIDs) or Cox-II inhibitor market, disease modifying anti-rheumatic drugs (DMARDs), or oral steroids.

***Pipeline Maturing***

Besides Synavive, Zalicus has several collaborations with some of the world's leading research organizations, including the National Institutes of Allergy and Infectious Disease (NIAID), the U.S. Army Medical Research Institute for Infectious Disease, Novartis, Amgen, and Sanofi-Aventis. These collaborations helped Zalicus generate $17.3 million in revenues in 2009. One candidate under collaborative development is Prednisporin, a topical ocular drug for the treatment of allergic conjunctivitis which Zalicus licensed to Sanofi-Aventis. Proof-of-concept data generated so far on prednisporin demonstrates efficacy on par with high-dose steroids with improved safety and tolerability.

Finally, Zalicus possesses one of the market's leading research and discovery programs in ion channel therapeutics. Management is focusing the company's efforts into the development of a new class of analgesics for the treatment of both acute and chronic pain using advanced understanding of medicinal chemistry and combination high throughput screening platforms. The company's goal is to find or create new chemical entity (NCE) oral compounds with anti-inflammatory and anti-proliferative characteristics that truly advance the treatment paradigm for acute and chronic pain.

**Equals = Undervalued Stock**

Zalicus is currently trading with a market capitalization of only $105 million. We believe this undervalues the firm by almost a factor of three. Our sum of parts valuation analysis yields a price target of $3 per share based on royalties from Exalgo, the potential market opportunity for Synavive and Prednisporin, early-stage development and collaborative programs, and the current solid financial position. We recommend investors establish a position in Zalicus at this level given the potential future upside to the stock over the next several quarters.

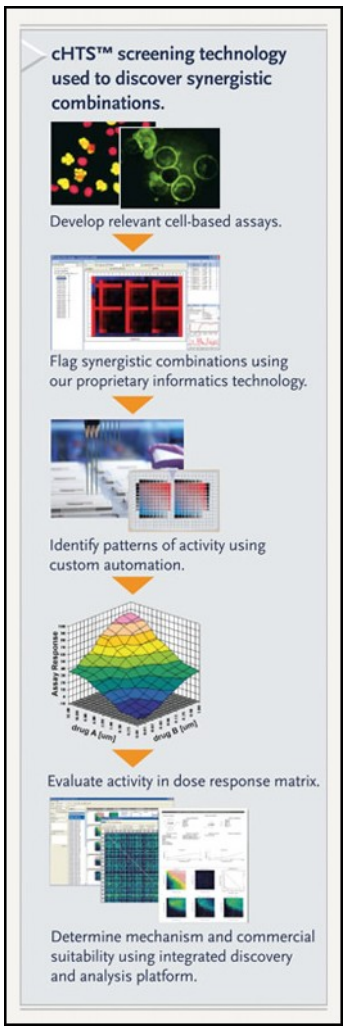
## OVERVIEW

Zalicus specializes in the development of combination drugs that are capable of targeting multiple pathways in a disease network. Many diseases affect the body through multiple biological pathways. As a result, the activity of a therapeutic compound against one pathway can be insufficiently effective because biological systems often compensate by using a secondary pathway. By targeting multiple pathways, the company's combination drug candidates aim to create synergistic therapeutic effects that could result in improved treatments for many diseases. The company harnesses the power of networked biological systems to reveal how alternations of critical targets can be combined to potentially produce profound medical effects. This affords management the opportunity to discover new targets via multiple cellular pathways at a level of sophistication and insight above current single target approaches. The added selectivity achieved through targeting multiple pathways may lead to improved safety as well as better efficacy in therapeutic applications.

Zalicus uses its proprietary combination high throughput screening (cHTS) technology for the identification of novel drug candidates. The cHTS technology screens the effects of millions of possible dose-specific combinations of approved drugs and small molecules in each of the selected disease models. Using existing active pharmaceutical ingredients allows management to move the candidates swiftly into human clinical studies without extensive preclinical toxicology and pharmacology studies. This greatly helps in cutting down costs and the time required for the development process.

***It's All About Synergy***

Zalicus has demonstrated that the combination of synergistic compounds can improve therapeutically relevant selectivity and circumvent drug resistance. Preclinical studies highlight the power of the company's cHTS technology to interrogate combination activity across multiple mechanisms for therapeutic application.




Despite their best efforts and hefty R&D spending, therapeutic selectivity is a large obstacle in drug discovery for major pharmaceutical companies. For example, drugs for infectious diseases often achieve selectivity by targeting proteins on the pathogen with no human counterparts. However, this strategy is unavailable for the treatment of cancer, metabolic or inflammation disorders. As such, drugs must rely on targets that are present in both healthy and diseased tissues. This shotgun approach often employs high drug doses that can induce unwanted side effects.

Synergistic combinations of two or more agents can overcome toxicity and other side effects associated with high doses of single drugs by countering biological compensation, allowing reduced dosage of each compound or accessing context-specific multi-target mechanisms (*Synergistic drug combinations tend to improve therapeutically relevant selectivity.* Nature Biotechnology, Vol.27, No.7, July 2009)

This is the value-driving opportunity for Zalicus. Therapeutically promising effects can be identified using experimental and theoretical techniques. These combinations make use of biological complexity, and are among the most promising avenues toward treating multifactorial diseases. However, synergistic compounds only make sense if the combination demonstrates improved therapeutic benefit without amplification of side-effects. Management at Zalicus uses its high-throughput screening platform to systematically test combinations of approved drugs, while analyzing the therapeutic characteristics necessary for an effective pharmaceutical product. The context specificity of synergistic combinations creates many opportunities for therapeutically relevant selectivity and enables improved control of complex biological systems.

The company's main drug development programs are in the areas of immuno-inflammatory disease and pain. Zalicus has one product commercialized with Exalgo, an extended release opioid for the management of moderate-to-severe pain. However, management also focuses on oncology, ophthalmic, and neurodegenerative diseases as well. This has allowed management to form research collaborations with some of the world's largest pharmaceutical companies in Covidien, Novartis and Sanofi-Aventis.

**Exalgo**

Through the merger with privately-held Neuromed in December 2009, Zalicus acquired its first commercial product in Exalgo. Exalgo is an extended release hydromorphone indicated for the treatment of moderate-to-severe pain in opioid tolerant patients requiring continuous (around the clock) analgesia. Exalgo was approved by the U.S. FDA in March 2010. Prior to the merger, Neuromed licensed the U.S. commercial rights to Exalgo to Covidien, plc. Covidien is responsible for all commercialization activities for Exalgo in the U.S., including marketing and sales, and for all post-approval regulatory activities. Zalicus received a $40 million milestone payment following FDA approval of Exalgo in early March 2010 (fully recognized in the first quarter). Covidien launched the product in late April 2010 with 250+ sales representatives and a dozen region directors. Zalicus is eligible to receive tiered royalties on net sales of Exalgo by Covidien. Cumulative royalties since the launch has totaled $1.238 million.

***Meaningful Market Potential***

Hydromorphone, a widely prescribed opioid, is intermediate in potency between oxycodone and fentanyl. Market research shows that many physicians prefer to use hydromorphone as their orally administered drug of choice given the products intermediate potency (more potent than oxycodone / less potent than oxymorphone and fentanyl) and significant prescribing history. Exalgo (hydromorphone HCl) is the only extended-release hydromorphone treatment available in the U.S. The product provides opioid-tolerant patients suffering from moderate-to-severe chronic pain, relief for 24 hours per dose. Hydromorphone, sold as branded Dilaudid, is an opioid analgesic that has been used in an immediate release formulation to treat pain for many years. However, these immediate release formulations require dosing 3 to 4 times per day. This frequent dosing creates the opportunity for misuse. Patients find the dosing regimen inconvenient, especially at night, and as such are often non-compliant.

Exalgo was developed J&J's OROS Push-Pull delivery technology to overcome the frequent dosing requirement of immediately release formulations. The technology employs an oral osmotic platform that J&J has been using for more than two decades, and is the extended release technology used in several of its successful products, including Procardia XL, Ditropan XL, and Concerta. The tablet core is made up of two layers: a "drug" layer containing hydromorphone and non-medicinal ingredients and a "push" layer containing osmotic agents. These layers are surrounded by a hard, non-dissoluble outer shell that has a precision laser drilled hole through it. Water from the gastrointestinal tract enters the tablet through this semi-permeable outer shell, causing the push layer to expand, which expels the drug into the gastrointestinal tract at a controlled rate. The outer shell itself does not dissolve and the residual tablet is excreted.



**Exalgo**

The concept of controlled-release opioids has been well defined in the market. The long-acting opioid (LAO) market in 2009 tallied nearly 25 million prescriptions and $6 billion in sales. Potent oral opioids such as morphine, fentanyl, oxymorphone, and oxycodone are available in both immediate release and extended release formulations, and are supported by significant sales force efforts. There are, however, no extended release hydromorphone products available in the U.S. Hydromorphone is widely available in generic form and is not supported by significant sales force coverage or promotion. Despite these factors, in the five year period from 2004 to 2008, on a percentage basis, the volume of prescriptions of hydromorphone grew more rapidly than other strong opioid products, including the extended release forms. For example, during this five year period, immediate release hydromorphone prescription volume, on a percentage basis, outgrew fentanyl (all forms combined), which is available in a long acting transdermal patch, Duragesic, and fast-acting buccal formulations, Actiq and Fentora. Exalgo has the potential to combine the benefits of oral therapies, such as ease of titration and intake, with the benefits of transdermal therapies, such as stable blood drug levels and an extended duration of action.

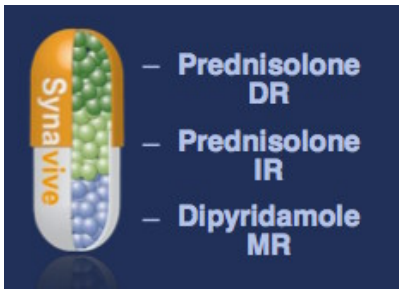
Exalgo is currently on the market in Europe as Jurnista, sold by J&J subsidiary, Janssen-Cilag. Since 2006, Jurnista has captured roughly 4% prescription share and 6% dollar share of the long-acting opioid market in Germany. In the U.S., short-acting hydromorphone products accounted for 3 million prescriptions in 2009. Capturing share of the immediate-release hydromorphone market could equate to a $250 to $300 million opportunity for Exalgo. For example, Endo Pharma's Opana ER, an extended release oxymorphone HCl, has an estimated 3% prescription share (5% dollar share) of the LAO market, and posted global sales of $231 million in 2009. Covidien has identified 11,500 high volume hydromorphone prescribers to target for the first-wave of the commercial launch. These 5% of total prescribing physicians account for roughly 50% of the total LAO market.

**Synavive**

Prior to the merger with Neuromed, Zalicus' lead product candidate was CRx-102, which they refer to as Synavive. CRx-102 is a combination of the cardiovascular drug dipyridamole and an unconventionally low dose of the glucocorticoid steroid prednisolone. The candidate is being developed for the treatment of immuno-inflammatory diseases. Synavive works through a novel mechanism of action in which dipyridamole selectively amplifies prednisolone's anti-inflammatory and immunomodulatory activities without replicating its side effects. Zalicus has recently developed a new modified-release, once-daily, formulation with an initial market focus of rheumatoid arthritis (RA).

***Proof-of-Concept***

Prednisolone is a well-known synthetic adrenal corticosteroid with significant anti-inflammatory properties and proven utility in multiple diseases such as arthritis, asthma, colitis, bronchitis, lupus, and allergic reactions. The product has been on the market for over 50 years, and its mechanism of action is well understood. On a molecular level, prednisolone enters the cell and reacts with the glucocorticoid receptor. This binding affects transcription of inflammatory mediators that gives the molecule its well-characterized efficacy. Unfortunately, at high doses necessary to achieve significant efficacy in chronic disease such as RA and OA, side effects such as insomnia, dry skin, headaches, dizziness, nausea, stomach pains, and bloating become common. More severe side effects such as rapid weight gain, high blood pressure, hyperglycemia, vision loss, and pancreatitis may also develop.

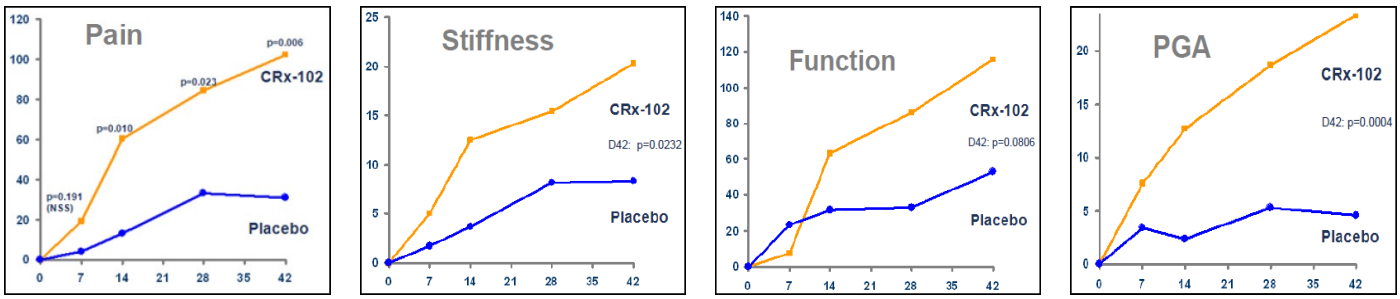



Dipyridamole interacts with a number of cellular targets that increase cyclic AMP (cAMP). Together, the increased levels of cAMP and the activation of the glucocorticoid receptor from prednisolone work in conjunction to suppression the release of mediators such as cytokines and proteases that could result in pain and stiffness associated with a disease such as OA and RA. The benefit of the synergistic combination in CRx-102 is that there does not seem to be an increase in the steroid-associated side effects listed above. CRx-102 also seems to present no increased risk of osteoporosis based on the clinical experience so far.

***Hand Osteoarthritis***

The first proof-of-concept program was a phase IIa program in 83 subjects with moderate to severe hand osteoarthritis. The study met its primary endpoint of improvement in joint pain using the AUSCAN index. The AUSCAN Osteoarthritis Index is a composite patient-reported outcome tool developed specifically for hand osteoarthritis, similar to the WOMAC index which is used for knee and hip osteoarthritis. Analysis of the primary endpoint shows mean change from baseline in the Synavive group of a 31% improvement in pain, compared to mean change from baseline in the placebo group of a 7% improvement in pain (p=0.007). Synavive demonstrated improvements in clinical secondary endpoints including stiffness, the AUSCAN physical function subscale, joint pain and patient global assessment scores.

***Mean Improvement Over Time***




Zalicus also conducted a phase IIa study in patients with rheumatoid arthritis (RA) that demonstrated statistically significant improvement over a 42 day period in American College of Rheumatology (ACR) scores. Approximately 63% of the patients on CRx-102 achieved an ACR-20 score vs. 28% for the placebo (p=0.025). The trial showed strong trends toward significance on the ACR-50 and ACR-70 scores.

***Rheumatoid Arthritis***

In November 2006, management presented positive data from a second phase IIa program studying Synavive in patients with rheumatoid arthritis (RA). The trial compared Synavive plus a disease-modifying antirheumatic drug (DMARD) to placebo DMARD (control) in subjects with RA over a 6-week treatment period. The primary endpoint was reduction in C-reactive protein (CRP) levels comparing CRx-102 plus DMARD to placebo plus DMARD from baseline at day 42. Secondary endpoints of the trial included ACR-20 responses and DAS-28 scores.

| | Synavive | Placebo | p-value |
|---|---|---|---|
| Primary Endpoint – CRP Level | -50% | -19% | p=0.024 |
| Secondary Endpoint – ACR-20 Response | 63% | 30% | p=0.025 |
| Secondary Endpoint – DAS-28 Level | -1.6 | -0.7 | p=0.016 |

Similar to the OA program, Synavive was generally well-tolerated with no serious adverse events (SAE). The most common side effect was headache, with gastro-intestinal symptoms and dizziness also reported. These are all common side effects of the dipyridamole.

***Knee Osteoarthritis***

Following the encouraging results in the above RA and hand OA program, Zalicus moved into a larger, multi-center, randomized, double-blind, placebo controlled phase II clinical trial of 279 subjects with knee osteoarthritis (OA) called COMET-1. Management also initiated a concurrent RA program called MARS-1, but later discontinued this program to focus on COMET-1. The trial design of COMET-1 was a standard flare design where subjects with active disease needed to demonstrate an increase in knee pain as determined by the WOMAC question #1 (related to pain while walking on a flat surface) upon withdrawal of their NSAID/COXIB therapy to be eligible. In the study, subjects were randomized to three different doses of Synavive (2.7mg prednisolone and 360mg, 180mg or 90mg of dipyridamole), vs. 2.7mg of prednisolone alone, or placebo, for a total of five arms.

Subjects were dosed for a total of 14 weeks (98 days) including an initial two-week dipyridamole titration phase. The primary endpoint of this study, to assess the efficacy of Synavive compared to placebo, was the change in WOMAC question #1 calculated from baseline to day 98. Results were released in early October 2008. The data presented below is based on the entire intent-to-treat (ITT) population:

| WOMAC Q1 | placebo | prednisolone (2.7mg) | Synavive (2.7/90mg) | Synavive (2.7/180mg) | Synavive (2.7/360mg) |
|---|---|---|---|---|---|
| Baseline (mm) | 79.0 | 78.0 | 80.0 | 74.5 | 78.0 |
| Day 98 Change | -24.5 | -41.0 | -30.0 | -35.5 | -43.0 |
| p-value | n/s | n/s | n/s | n/s | n/s |

The data clearly shows a dose-related improvement in baseline change. However, the results were not significant for any cohort tested. A key secondary endpoint, WOMAC stiffness, was significant for only the highest dose (2.7/360mg) tested. Another secondary endpoint, WOMAC physical function, was not significant for any dose tested. Discontinuation rates were higher than expected, at 32%, and mainly the result of adverse events and subject requests. The most common adverse event was headache.

Surprised by the results, management conducted an in-depth analysis of the data and discovered a number of patients were resorting back to their NSAID/COX-II inhibitor or other pain medications during the program. In fact, 26 patients violated study design by taking prohibited medications during the final weeks of the program. Over half (14 of 26) of the protocol violators were in the placebo or prednisolone alone cohort:

| | NSAID/Cox-II | Steroids | Aspirin | Total |
|---|---|---|---|---|
| Placebo | 6 | 1 | - | 7 |
| Prednisolone | 4 | 1 | 2 | 7 |
| Synavive (low) | 2 | 4 | - | 6 |
| Synavive (mid) | 1 | 1 | 1 | 3 |
| Synavive (high) | 1 | 1 | 1 | 3 |

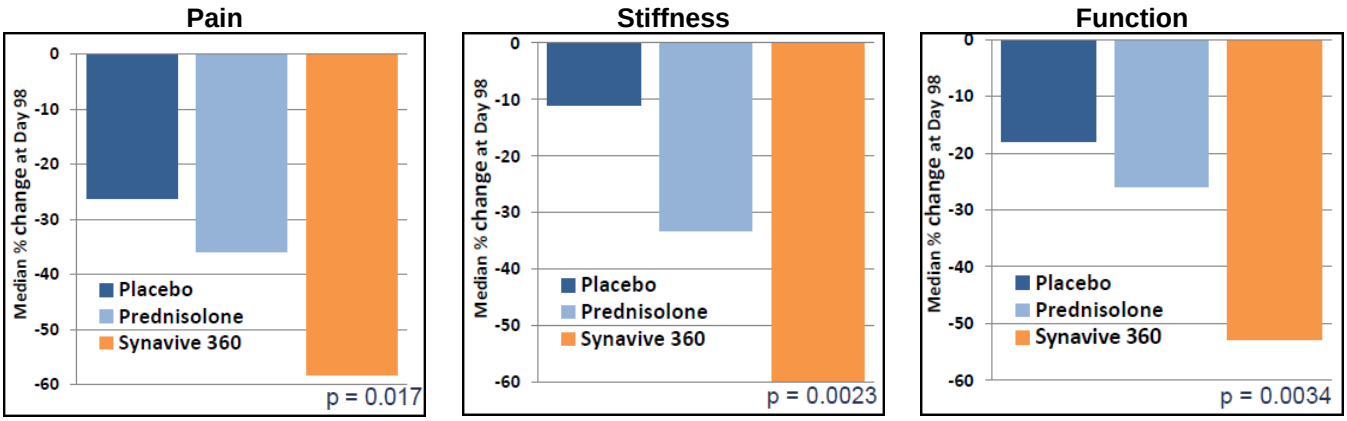
Therefore, management conducted a modified ITT analysis using the last observation carried forward for these non-compliant patients. Under the mITT analysis, the highest dose of Synavive (2.7/360mg) did demonstrate clinically meaningful benefits in WOMAC Pain, Stiffness, Physical Function, and Hand Pain VAS. The data also showed an improved dose response curve for the low and middle-dose Synavive cohorts.

| Change in Baseline… | placebo | prednisolone (2.7mg) | Synavive (2.7/360mg) |
|---|---|---|---|
| …WOMAC Pain | -19.1mm | -31.0mm | -37.2mm |
| …WOMAC Stiffness | -15.5mm | -29.5mm | -35.0mm |
| …Physical Function | -13.2mm | -21.8mm | -30.4mm |
| …Hand Pain VAS | -18.0mm | -17.5mm | -34.0mm |

The high dose of Synavive (2.7/360mg) demonstrated an 18.1mm improvement over placebo and a 6.2mm improvement over prednisolone alone on the primary WOMAN Pain endpoint.

| | | | |
|---|---|---|---|
| …WOMAC Pain (%) | ~ 28% | ~ 50% | **~ 57%** |
| | | | *p=0.030* |

Subjects who completed the 14-week core study were eligible to participate in a 12-month, open-label extension study designed to investigate the long-term safety and durability of response for Synavive. This data was presented in October 2009 at the American College of Rheumatology (ACR) 2009 annual meeting. The data demonstrated that Synavive subjects maintained efficacy levels throughout the 12 month extension trial. These findings further support the mITT data that demonstrated efficacy for the highest dose of Synavive. In addition, subjects on placebo were able to cross-over to Synavive for the 12 month extension study. These patients also experienced statistically significant improvements in all WOMAC measurement subscales upon crossing over.




Importantly, no treatment-related increase in glucocorticoid associated adverse events was observed in any Synavive treated subjects. This includes no worsening of vision, adrenal glucose, infection rate, hypotension, hyperglycemia, or osteoporosis (as measured by bone mineral density).

| Key Safety Analysis | |
|---|---|
| Blood Glucose | *No statistically significant change in baseline for any of the five arms testing in COMET-1.* |
| Serum Triglycerides | *Statistically significant rise noted in the Prednisolone arm only. All other arms showed a decrease in levels from baseline.* |

These results compare very favorably to pain, stiffness, and physical function scores on long-term NSAID or Cox-II treatment. In fact, based on systemic reviews and the mITT analysis from COMET-1, Synavive looks superior to daily NSAID/Cox-II treatment as a treatment for OA. While we are encouraged by the results of the mITT analysis and the 12 month follow-up, it is clear that more work needs to be done. The discontinuation rate in the trial was high at 32%. A significant number of patients on Synavive reported headaches. This is most likely the result of the dipyridamole component, which has been known to cause significant headache due to its vasodilating properties. Management has re-formulated the dipyridamole in Synavive from an immediate release to a modified release.

This new formulation of Synavive provides time-release co-exposure to both prednisolone and dipyridamole. It also offers a significantly improved tolerability and side-effect profile, as demonstrated in a small (n=24) patient study in which 0% of the subjects experienced headache vs. 41% for conventional dipyridamole. The modified release formulation also allows for a once daily dosing format.

***Next Step – Phase IIb In RA***

Over the summer 2010, Zalicus met with and discussed the development strategy for Synavive with the U.S. FDA. The company is also talking to regulatory bodies outside the U.S. on Synavive in an effort to conduct one global trial prior to the registration program. Therefore, we expect that a phase IIb trial in RA will begin during the first quarter 2011. The trial design has yet to be finalized, but we suspect it will include 200 to 400 patients, on a global basis, with a similar design and endpoints used in COMET-1, testing various doses of Synavive compared to 2.7mg of prednisolone alone and placebo.

The trial will probably take 12 to 18 months to complete, meaning we will see efficacy data from the trial mid-2012. We will also see initial safety data from the trial in 2012. Paramount to the future development of Synavive, specifically from a partnering standpoint, will be the long-term (1-year +) safety data amassed from this phase IIb trial. Therefore, management will continue to follow the patients from the program beyond the efficacy portion of the program.

***A Big Opportunity***

Over the past several months, management has been conducting a series of interviews with key opinion leaders, practicing rheumatologists, primary care doctors and managed care personnel to fully explore the potential benefits of moving into RA as an initial indication for Synavive. Based on their feedback, management believes that RA is the most attractive choice on a number of fronts including current medical practice in which there is already a high prevalence of glucocorticoid use in RA to combat inflammation and restore function, as well as the unmet need for less expensive, easier to access options to biologic therapy.

As such, if commercialized, Synavive could present a meaningful revenue driver for Zalicus. Rheumatoid Arthritis (RA) is among the most common degenerative joint diseases and a frequent cause of physical disability among older adults. In the U.S. more than 100 million people suffer from RA and OA, combined. The disease affects the hands, lower back, neck, and weight-bearing joints such as the knees, hips, and feet. Symptoms range from stiffness and intermittent mild pain to severe joint pain and impaired biomechanical function.

The current treatment paradigm is for patients to manage symptoms by using non-steroidal anti-inflammatory drugs (NSAIDS) and Cox-II inhibitors, local analgesics, opioids, oral steroids, disease modifying antirheumatic drugs, intra-articular corticosteroid injection and surgery. The withdrawal of two high-profile Cox-II drugs, Merck's Vioxx and Pfizer's Bextra, has created a significant void the prescription NSAID market. These two drugs were annualizing at sales over $6 billion worldwide before they were pulled from the market for cardiovascular safety concerns. As such, the market has dramatically shifted toward over-the-counter (OTC) NSAIDs such as naproxen and ibuprofen to management pain. Rheumatologists typically start patients with RA out on steroids or DARMSs such as cyclosporine and methotrexate (MTX). Failure of these pain and steroid medications leads to the use of stronger disease modifying anti-rheumatic drugs (DMARD) such as TNF-alpha molecules and biologics.

These drugs carry potential serious metabolic, gastrointestinal, renal, and liver risks. The biologics are also injectables, offering less convenience than a once-daily oral medication. Accordingly, a safer alternative such as Synavive could be a blockbuster product in the hands of a major pharmaceutical company.

Beyond RA, we believe Synavive has potential in other steroid-responsive diseases such as polymyalgia rheumatica (PMR), lupus (SLE) and ulcerative colitis (Crohn's) as well as a replacement to NSAIDs and Cox-II inhibitors in osteoarthritis (OA).

**Prednisporin**

Prednisporin (FOV1101) is a topical ocular drug candidate that Zalicus has exclusively licensed to Fovea Pharmaceuticals SA containing low doses of the glucocorticoid, prednisolone acetate, and the immunosuppressant cyclosporine A. Fovea has developed a proprietary co-formulation of Prednisporin and is seeking to develop Prednisporin to treat inflammatory ocular diseases such as allergic conjunctivitis.

Allergic conjunctivitis is inflammation of the conjunctiva (the membrane covering the white part of the eye) due to allergy. Although allergens differ between patients, the most common cause is hay fever. Symptoms consist of redness of the eye mainly due to vasodilation of the peripheral small blood vessels, oedema (swelling) of the conjunctiva, itching and increased lacrimation (production of tears). Symptoms are due to release of histamine and other active substances by mast cells, which stimulate dilation of blood vessels, irritate nerve endings and increase secretion of tears. Thus, treatment of allergic conjunctivitis is primarily with antihistamines, either topical (eye drops) or systemic (tablets). If this first-line therapy fails, ophthalmologists will frequently resort to more powerful steroids to reduce inflammation and control the disease. Prednisporin could represent an attractive second-line therapy behind antihistamines for patients with severe allergic conjunctivitis.

In May 2009, Fovea Pharmaceuticals, Zalicus' partner for the development of ophthalmic products, announced positive results from a proof-of-concept study that was conducted to evaluate the therapeutic effect of Prednisporin in patients suffering from persistent allergic conjunctivitis. In October 2009, Fovea agreed to be acquired by large-cap pharmaceutical company, Sanofi-Aventis. Sanofi has publically stated they are seeking to enhance their presence in the ophthalmology market; Fovea and prednisporin are at the forefront of those plans.

Zalicus has significant economic interest in Prednisporin and the other product candidates licensed to Fovea for further ophthalmic development. Zalicus is eligible to receive milestone payments of up to approximately $65 million and tiered royalty payments of up to 12% on the development and commercialization of certain Fovea products generated from the Zalicus platform.

The milestone $65 million schedule includes: $25 million in development and regulatory milestones, $25 million in sales-related milestones, and $15 million in additional indication approval milestones. We note prednisporin may have potential for the treatment of dry eyes as well.

***Proof-of-Concept***

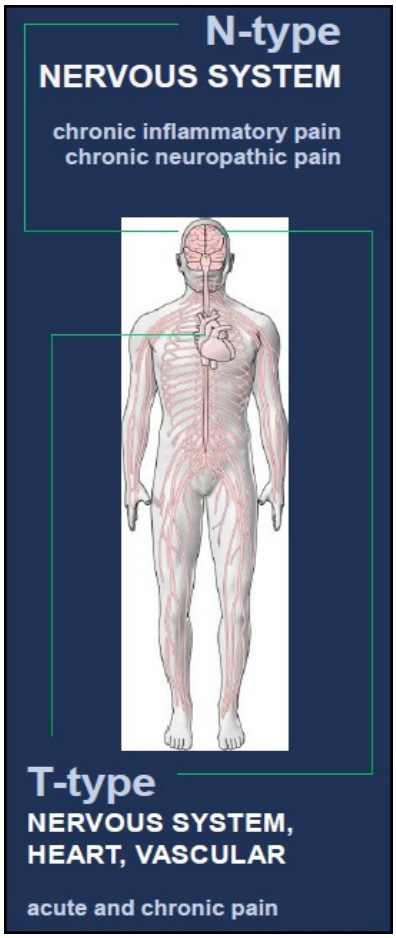
In May 2009, Fovea investigated Prednisporin in a phase IIa proof-of-concept clinical trial in the U.S. in approximately 150 subjects with persistent allergic conjunctivitis. The clinical trial was an inflammatory conjunctival antigen challenge trial, where subjects were first administered a topical ocular antihistamine for seven days to simulate an inflammatory allergic response, followed by 14 days of treatment with either a higher dose of prednisolone acetate, the combination of a lower dose of prednisolone acetate with two different doses of cyclosporine A or placebo. Fovea has reported that on the primary endpoint of evening ocular itching, the Prednisporin combination with the higher dose of cyclosporine A was superior to placebo ($p=0.048$) and non-inferior to the higher dose of prednisolone acetate alone. The Prednisporin combinations were generally well tolerated and there were no serious adverse events reported.

These were encouraging results. The trial demonstrated that Prednisporin has an efficacy profile similar to high doses of a potent steroid like prednisolone acetate, but with improved safety and tolerability. Based on these data, Fovea has announced its intentions to prepare further advanced clinical trials for Prednisporin both in the U.S. and in Europe.

***Phase IIb Underway***

Accordingly, in June 2010, Fovea initiated a phase IIb clinical program testing Prednisporin in subjects with persistent allergic conjunctivitis. Zalicus received a $500,000 milestone payment from Fovea relating to this initiation. The trial should complete before the end of the year 2010. We expect to see data from Sanofi late this year or early next year. As noted above, Zalicus is eligible to receive further development and regulatory based milestones on this candidate. The next milestone to Zalicus would be $3 million for the initiation of a phase III trial.

**Ion Channel Programs**




Through its merger with Neuromed, Zalicus has one of the market's leading research and discovery programs in calcium channel programs. Management is focusing the company's efforts into the development of a new class of analgesics for the treatment of both acute and chronic pain. The goal of the program is to develop highly effective oral molecules with improved safety and tolerability advantages over existing treatment options.

Calcium ions play critical roles in the biochemistry, physiology and anatomy of cells and organisms. The rapid entry of calcium ions into cells is mediated by a class of proteins called voltage-gated calcium channels. These channels respond to electrical signals by the opening of a calcium-selective pore in the cell membrane. Calcium channels are involved in a large number of normal physiological processes including muscle contraction, hormone secretion, gene expression, and electrical signaling in the nervous system.

We are particularly excited about the ion channel discovery at Zalicus given the significant research efforts and knowledge base of medicinal chemistry at Neuromed and the screening capabilities and synergistic combination platform at Zalicus. The combined company's goal is to find or create new chemical entity (NCE) oral compounds with anti-inflammatory and anti-proliferative characteristics that truly advance the treatment paradigm for acute and chronic pain.

We believe the market is missing this synergistic potential for the new Zalicus, either to develop its own in-house candidates, or form partnerships and research collaborations with larger pharmaceutical organizations.

***N-Type Programs***

Zalicus' N-type calcium program is focused on developing oral and intravenous drug candidates to treat chronic pain. N-type calcium channels are expressed exclusively in the nervous system and are highly concentrated in the dorsal horn of the spinal cord where incoming sensory pain information is processed and then relayed to the brain. Zalicus' research efforts has focused on controlling the flow of calcium into spinal nerve cells through the N-type calcium channel, and thus on reducing pain signaling as it relates to chronic inflammatory, neuropathic, and other complex pain conditions.

Preclinical research shows that deletion of the N-type channel gene in animals, which has the effect of eliminating N-type calcium channel activity, results in the animals retaining normal acute sensation yet with limited pain response in reaction to inflammatory or nerve damage. Management believes that by uniquely combining rational drug design with innovative biological assays, it can produce orally available N-type calcium channel blockers with properties suitable to test in human clinical trials.

One candidate, NMED-160, has shown efficacy in multiple animal models of pain, and safety and tolerability in approximately 200 patients during phase I and phase IIa clinical trials. Neuromed was previously developing NMED-160 in collaboration with Merck, but the company reacquired development rights to the compound in September 2009. The data show NMED-160 to be well tolerated and to exhibit a good safety profile with no serious drug-related adverse effects. The opportunity for NMED-160, or another ion channel blocker, is meaningful in our view. An oral candidate that exhibits efficacy on par with opioids, but with far less risk for abuse and withdrawal could capture sizable share in the $20+ billion chronic pain market.

We point to Azur Pharmaceutical's Prialt as an example for commercialized N-type calcium channel blockers. Prialt delivered sales of only $20 million in 2009 due to drugs lower therapeutic window and the fact that it is spinally administered using an implanted pump in the patients back. Prialt is also an irreversible blocker of the N-type

calcium channel, creating the potential for significant neuropsychiatric side-effects. An oral, reversible, N-type molecule like, NMED-160, could have broad use for various pain states such as cancer pain, lower back pain, osteoarthritis, herpes zoster neuropathy, and AIDS neuropathy far above this level. It's a billion-dollar opportunity, and one in which we expect Zalicus to funnel significant research efforts toward in the next few years.

***T-Type Programs***

Similar to the N-type program, Zalicus' T-type calcium channel program is focused on developing drug candidates to treat a variety of chronic pain conditions. However, because the T-type calcium channels are found in the brain, heart, endocrine cells, and other tissues, the mechanism provides for potential broadening of the indication to include additional indications such as epilepsy, cardiovascular disease, and hypertension.

Animal models show an attractive profile in treating both acute and chronic pain, as well as in both partial and generalized animal seizure models, and in hypertension models and cancer cell migration. All of the partial-seizure epilepsy data was generated in collaboration with the National Institute of Health, or NIH.

***IND Soon, Phase I Early 2011***

Zalicus remains on schedule to file an IND with its first Ion Channel candidate before the end of the year. We expect a phase I program to start in early 2011.

**Synergistic Discovery**

In April 2010, Zalicus announced the publication of new preclinical data in BLOOD, The Journal of the American Society of Hematology, entitled, "Adenosine A2A receptor agonists and PDE inhibitors: a synergistic multi-target mechanism discovered through systematic combination screening in B-cell malignancies," (Rickles, et.al., 2010; DOI 10.1182/blood-2009-11-252668). Zalicus researchers, in collaboration with the Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Harvard Medical School, demonstrate the powerful and unexpected synergistic interactions of A2A agonist and PDE Inhibitors as potential adjunctive therapy to glucocorticoid (GC) containing regimens in the treatment of multiple myeloma (MM) and other B-cell malignancies.

Glucocorticoids are a key component of combination therapy regimens in multiple myeloma and other hematological cancers. However, glucocorticoid use comes with substantial dose limiting toxicities. The ability to enhance glucocorticoid dependent effects while sparing associated toxicities may have important implications for the treatment of multiple myeloma and other B-cell malignancies. Zalicus is using it s cHTS technology to identify compounds that synergize with GCs to inhibit the proliferation of the MM cells. Therapeutic synergies were observed broadly across a large panel of MM and diffuse large B-cell lymphoma (DLBCL) cell lines when exposed to A2A agonists and specific PDE inhibitors.

These findings were also presented as a poster at the American Association for Cancer Research 2010 annual meeting in April 2010 (Abstract #5509: Wednesday, April 21, 2010, 8:00 AM - 11:00 AM, "Identification of synergistic drugs using combination high-throughput screening," Rickles, et.al., Exhibit Hall A-C, Poster Section 25, Poster Board 29).

These preclinical studies demonstrate that both agonists synergize with standard of care, even after chronic exposure, and highlight the company's ability to rapidly screen large numbers of drug combinations in many cell lines to identify novel synergistic pairings and potential drug candidates.

This is what is particularly interesting from a multi-target discovery engine standpoint given the extensive ion channel capabilities at Neuromed. Zalicus now has core competencies in small-molecule medicinal chemistry and advanced screening technology. The universe includes:

- Empirical combinations: >4000 agents → >1000 targets & mechanisms
- Comprehensive Automation: >250 cell lines → >20 disease-relevant controls

***Novartis***

In May 2009, Zalicus entered into a strategic alliance and research collaboration with Novartis for the discovery of novel anti-cancer combinations. Under the agreement, each party will contribute compounds and evaluate the anti-cancer effects by utilizing Zalicus' proprietary cHTS platform and Chalice analyzer software to screen a unique library of molecules, including Novartis compounds in multiple cell lines representing a broad spectrum of cancers. Zalicus received an upfront payment of $4 million, plus $3 million per year for two years in research support funding. The company is also eligible to receive up to $58 million in clinical, regulatory and commercial milestones for each combination that is commercialized under the collaboration.

The research program has an initial two-year term that may be extended by Novartis for three additional one year periods. Besides this, Zalicus has retained the right to conduct oncology research on its own as well as with partners, and will retain certain intellectual property rights which may arise from the collaboration research. Novartis also has a right of first negotiation to exclusively license the intellectual property owned by us that was discovered as a part of the collaboration, under terms to be negotiated by the parties at such time.

***Amgen***

Zalicus continues to leverage the power of its proprietary cHTS combination drug discovery platform by entering into a pilot discovery research collaboration with Amgen in December 2009. Amgen licensed non-exclusive access to the cHTS drug discovery platform focused on identifying synergistic combinations for two oncology targets, for a limited period of nine months (September 2010), with the option of extending the term and scope of the collaboration. Zalicus has received a $750k license fee for this trial period. We fully expect the deal to extend beyond September 2010, which should allow Zalicus to earn additional revenues from milestones and reimbursement.

***U.S. Army***

In May 2010, the U.S. Army Medical Research Institute of Infectious Diseases awarded Zalicus a $1.056 million contract to utilize its proprietary cHTS technology to discover drug combinations to treat infections by Alphaviruses, which are mosquito borne viruses whose infection can cause severe and fatal encephalitis in humans.

Both deals, with Amgen and the U.S. Army, represents small steps forward towards the company's stated goal of continuing to seek additional revenue-generating research and technology collaborations for the cHTS combination drug discovery platform.

**Out-Licensing Opportunities**

Given the company's primary focus on pain and inflammatory diseases following the merger with Neuromed, management has the opportunity to out-license non-core pipeline candidates at Zalicus for upfront cash and potential backend development and commercialization milestones – similar to the prednisporin deal with Fovea (now part of Sanofi-Aventis).

***CRx-191 for Psoriasis***

Approximately 15 million people in the United States are affected by atopic dermatitis. Although topical corticosteroids are usually used for treating atopic dermatitis, their use is limited by steroid-associated side effects. Topical calcineurin inhibitors are often used as an alternative to topical corticosteroids. However, sales of topical calcineurin inhibitors have gone down significantly following the introduction of a black box warning on the approved products. This market should therefore present significant commercial opportunity for topical immunomodulatory agents with novel mechanisms of action

CRx-191 is a topical synergistic combination drug candidate which is being studied for the treatment of psoriasis and other steroid-responsive dermatoses. CRx-191 is combination of mometasone, a mid-potency glucocorticoid steroid, and nortriptyline, a tricyclic anti-depressant. CRx-191 has a novel multi-target mechanism that inhibits TNF-α and interferon-gamma, both key cell mediators of inflammation. Management believes that nortriptyline amplifies mometasone's anti-inflammatory activities without enhancing steroid side effects such as skin atrophy. CRx-191 has demonstrated efficacy in multiple experimental and preclinical models of inflammation, including psoriasis. CRx-197 has been co-formulated into a topical cream for delivery.

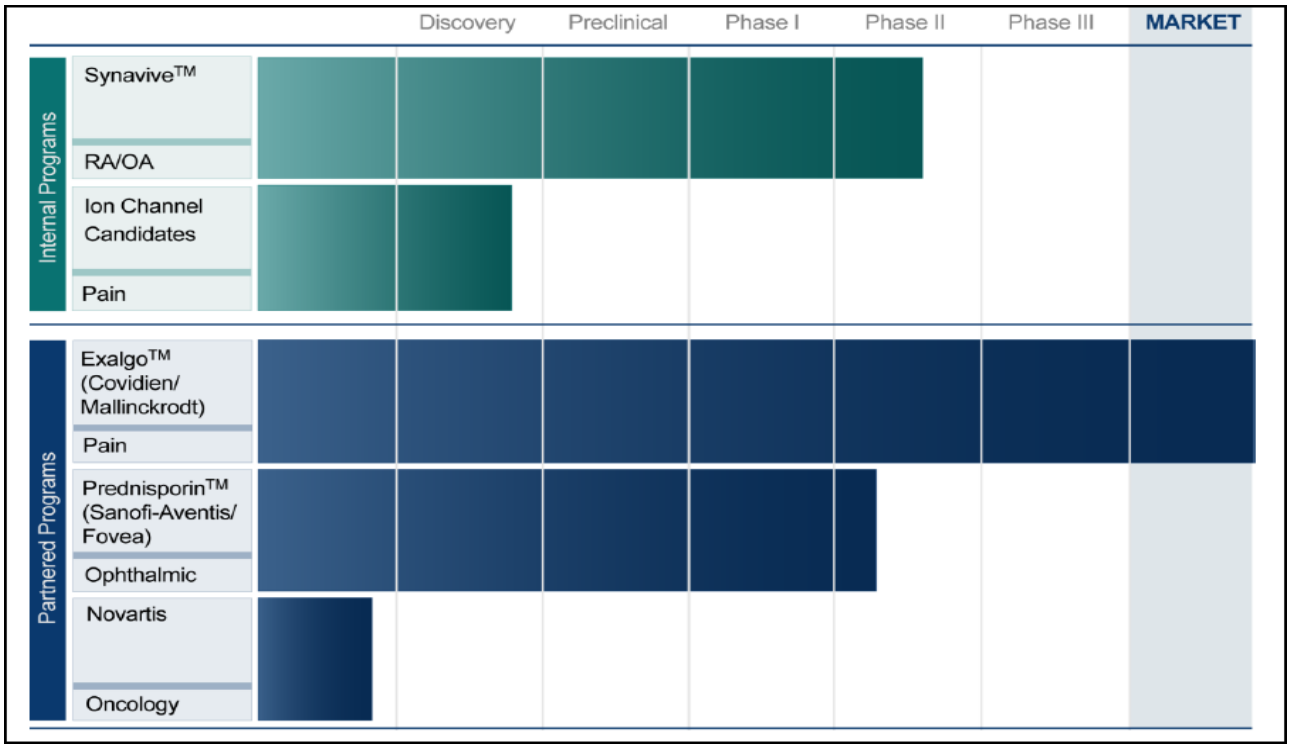
In March 2008, Zalicus released phase IIa "proof-of-concept" data on CRx-191. The trial enrolled a total of 21 patients with plaque psoriasis, and tested both a high and low-dose combination of CRx-191 over a 12-day treatment window vs. the individual components of CRx-191 and placebo. In the trial, the high dose of CRx-191 demonstrated an 81% reduction in psoriatic infiltrate from baseline to day 12, compared to 11% for placebo ($p<0.0001$). Similarly, CRx-191 demonstrated a 58% reduction in erythema (redness) from baseline to day 12, as compared to 6% with placebo ($p<0.0001$). In clinical assessments of skin condition, CRx-191 demonstrated clinically significant improvements from baseline to day 12 in 100% of all test fields, as compared to 0% for placebo. CRx-191 was also found to be well tolerated with no adverse events reported. We find the data to be encouraging.

***CRx-401 for Diabetes***

CRx-401 is a synergistic combination drug candidate containing sustained-release bezafibrate, an anti-dyslipidemia agent approved outside the U.S. to lower LDL and triglycerides and increase HDL, and a low dose of diflunisal, a widely available analgesic.

In May 2009, results from a phase IIa proof-of-concept study (n=117) showed that CRX-401 performed significantly better than bezafibrate on the primary efficacy endpoint of reduction in fasting plasma glucose (FPG) at day 90 with a difference of 12 mg/dL ($p=0.049$). The study was designed to demonstrate the synergistic anti-diabetic activity of CRx-401 compared to bezafibrate as an add-on to metformin therapy in subjects with poorly controlled diabetes. Consistent trends were observed in favor of CRx-401 on other supportive efficacy endpoints including glucose control, with reductions in HbA1c and homeostasis model assessment of insulin resistance (HOMA-IR), and inflammatory control, with a reduction in C-reactive protein (CRP), providing a favorable overall impact on the treatment of subjects with type II diabetes. Moreover, treatment with CRx-401 was associated with an expected reduction in serum triglyceride levels, consistent with the benefit of bezafibrate therapy.

## PIPELINE



**Pipeline & Business Goals**

| Goal | Status |
|---|---|
| See Covidien launch Exalgo for the management of moderate-to-severe pain in opioid tolerant patients requiring continuous analgesia. Begin collecting royalties! | **Done!** |
| Advance Synavive into phase IIb program for RA | *Early 2011* |
| File IND and advance lead N-Type program into clinical development | *Early 2011* |
| Advance discovery collaborations with Novartis and Amgen | *2011* |
| Continue to apply cHTS technology for discovery of new pain and inflammation product candidates for the internal pipeline | *Ongoing* |
| Seek additional revenue-generating research and technology collaborations using the cHTS platform technology | *Ongoing* |
| Maintain financial strength with sufficient resources to fund operations into 2014 | *Ongoing* |

## VALUATION

***Sum Of Parts Show Zalicus Is Under-Valued***

Zalicus is in an enviable position within the biotechnology industry. The company has an approved product on the market in Exalgo, and is collecting royalties from a strong partner in Covidien. The company's pipeline contains Synavive, a mid-stage candidate with proof-of-concept data in a significant market opportunity with rheumatoid arthritis (RA) and osteoarthritis (OA). Zalicus also possess one of the market's leading research and discovery programs in calcium channel programs. Management is focusing the company's early-stage discovery efforts into the development of a new class of analgesics for the treatment of both acute and chronic pain. Finally, the cash position is strong, with nearly $50 million on hand at the end of September 2010, with the potential to raise additional funds in 2011 through the sale or out-license of non-core candidates for psoriasis (CRx-191) and diabetes (CRx-401). Accordingly, we believe the best valuation methodology for Zalicus is a sum-of-parts analysis that takes into account the strong cash flows from Exalgo and the upside in future development from Synavive, the ion channel programs, and potential out-licensing opportunities.

Based on our forecast for Exalgo sales, guided broadly by Covidien's estimation that Exalgo is a $250 to $300 million product, we have conducted a net present value (NPV) analysis on the cash flow royalties. Our analysis shows that the royalties from Exalgo alone are worth more than the entire market value of Zalicus at $105 million. Our NPV calculations show that Exalgo alone is worth $135 million, or $1.50 per share. This is based on an estimate low double-digit royalty rate on Exalgo sales peaking at $250 million in 2018.

Over the past several months, management at Zalicus has been working on optimizing and manufacturing the new modified release formulation of Synavive. The new formulation allows for once-daily dosing with improved tolerability and therapeutic index. The company plans to progress Synavive into a phase IIb clinical development program for the treatment of rheumatoid arthritis (RA) in early 2011. Based on previous proof-of-concept data with the old formulation of Synavive in osteoarthritis (OA), we believe this asset is worth $35 million in value. Once additional proof-of-concept and safety has been established with the planned new phase IIb program, we believe that management can work to secure a development and commercialization alliance with a larger pharmaceutical company with an NPV far above this level.

Zalicus is in a unique position with respect to discovery and collaborations. The company is one of the few small biotech companies in the world with a dual platform to fuel its product pipeline expansion and potential revenue generating alliances. Zalicus, created between the merger of CombinatoRx and Neuromed, is a market leader in both selective ion channel modulation discovery and high throughput screening. The selective ion channel modulation platform from Neuromed allows management to identify product candidates that harness the potential of the electrophysiology of calcium channel blockers for acute and chronic pain. CombinatoRx' proprietary cell-based combination High Throughput Screening (cHTS) technology evaluates the therapeutic potential of various drug combinations while elucidating new mechanisms to treat diseases. Together these two platforms should allow management at Zalicus to discover and monetize candidates at a significantly improved rate when compared to traditional industry standards. Zalicus currently has existing collaborations with the National Institutes of Allergy and Infectious Disease (NIAID), the U.S. Army Medical Research Institute for Infectious Disease, Novartis, Amgen, and Sanofi-Aventis. Our sum-of-parts analysis includes $40 million for the company's dual discovery platform and existing collaborations.

| ***Sum of Parts Analysis*** | **NPV** |
|---:|:---:|
| …Royalties from Exalgo | $135 million |
| …Synavive Development Plan | $35 million |
| …Dual Discovery Platform + Collaborations | $40 million |
| **Total Firm Value** | **$210 million** |

Adding in the existing cash on hand totaling $48.6 million as of September 30, 2010, and our sum of parts / NPV analysis for Zalicus yields a total firm value of roughly $260 million, or $3 per share. At the current value of only $105 million we believe the company is far under-valued.

## MANAGEMENT

In January 2010, Zalicus, Inc. announced changes to its senior management team, following the closing of the merger with privately-held Neuromed in December 2009. Mark Corrigan, MD, former EVP of Research & Development at Sepracor and a member of the Zalicus board of directors, assumed the role of President and Chief Executive Officer (CEO) and Christopher Gallen, MD, Ph.D., former CEO of Neuromed, assumed the role as Executive Vice President (EVP) of Research and Development.

**Mark H.N. Corrigan, M.D. -** President and Chief Executive Officer

Dr. Corrigan has served as President and Chief Executive Officer Since January 2010. Dr. Corrigan joined U.S.-based specialty pharmaceutical company Sepracor Inc. in 2003 and served as their Executive Vice President, Research & Development until December 2009. Prior to joining Sepracor Inc., Dr. Corrigan spent 10 years with Pharmacia & Upjohn, most recently as Group Vice President of Global Clinical Research and Experimental Medicine. Dr. Corrigan has been a member of the board of directors and the audit committee of Cubist Pharmaceuticals, Inc. since 2008. Prior to joining the pharmaceutical industry, Dr. Corrigan spent five years in academic research at the University of North Carolina Medical School, focusing on psychoneuro-endocrinology. Dr. Corrigan holds a B.A. and an M.D. from the University of Virginia and subsequently received specialty training in Psychiatry at Cornell and Maine Medical Center.

**Christopher C. Gallen, MD, Ph.D. -** Executive Vice President of Research and Development

Dr. Gallen has served as Executive Vice President of Research and Development since January 2010. Dr. Gallen served as the President and Chief Executive Officer of Neuromed from July 2004 to December 2009. Prior to joining Neuromed, Dr. Gallen worked for Wyeth Research beginning in April 2002 and most recently served as its Vice President and Chief of Operations, Clinical Research and Development. Prior to Wyeth, Dr. Gallen was VP of Clinical Research at Pharmacia Corporation for three years. From January 1996 to December 1998, Dr. Gallen was the President of the Clinical Research Organization division at Premier Research Worldwide. Dr. Gallen holds a B.A. from the University of Florida, and an M.D. and Ph.D. from Emory University School of Medicine in Atlanta, Georgia and trained in Psychiatry at Stanford and Neurology at the University of California, San Diego.

**Justin Renz** - Senior Vice President and Chief Financial Officer

Justin Renz joined Zalicus in September 2006 as Vice President, Finance and Treasurer and has served as its Senior Vice President and Chief Financial Officer (CFO) since July 2009. From August 2005 to September 2006, Mr. Renz was Director, Accounting and Financial Operations at EMD Serono. From 2002 to 2005, he was Senior Director, Global Accounting and Finance at Coley Pharmaceutical Group and has also held financial and accounting positions at ArQule, Inc., Millipore Corporation and Arthur Andersen LLP. Mr. Renz is a certified public accountant and holds a B.A. in Economics/Accounting from the College of the Holy Cross, a Masters in the Science of Taxation from Northeastern University and an MBA from Suffolk University.

**C. Eugene Wright, Pharm.D., Ph.D.** - Senior Vice President and Chief Development Officer

Dr. Wright has served as Senior Vice President and Chief Development Officer since December 2009. Dr. Wright served as Neuromed's Vice President, Project Leadership from October 2007 to December 2009. Dr. Wright worked for Schering-Plough Corporation from April 2005 to October 2007 where he most recently served as Executive Director and Senior Project Leader of the Antiviral/Antifungal groups. From October 2003 to April 2005, Dr. Wright was Vice-President of CNS/Pain Development, Project Management and Pharmacokinetics at Biovail Technologies Ltd. From April 2003 to October 2003, Dr. Wright served as Sr. Director, Project Leader at Pfizer Inc. Dr. Wright holds a Doctor of Pharmacy from the University of the Pacific, an M.B.A. from National University in San Diego and a Ph.D. in Pharmaceutical Sciences from the University of Kentucky.

**Jason F. Cole, Esq.** - Senior Vice President, General Counsel and Secretary

Jason F. Cole, Esq. has served as Senior Vice President, General Counsel and Secretary of Zalicus since January 2006. From 1999 to 2006, Mr. Cole was a corporate and securities attorney at Ropes & Gray LLP. Mr. Cole holds an A.B. in Government from Dartmouth College and a J.D. from Columbia University School of Law.

## PROJECTED INCOME STATEMENT

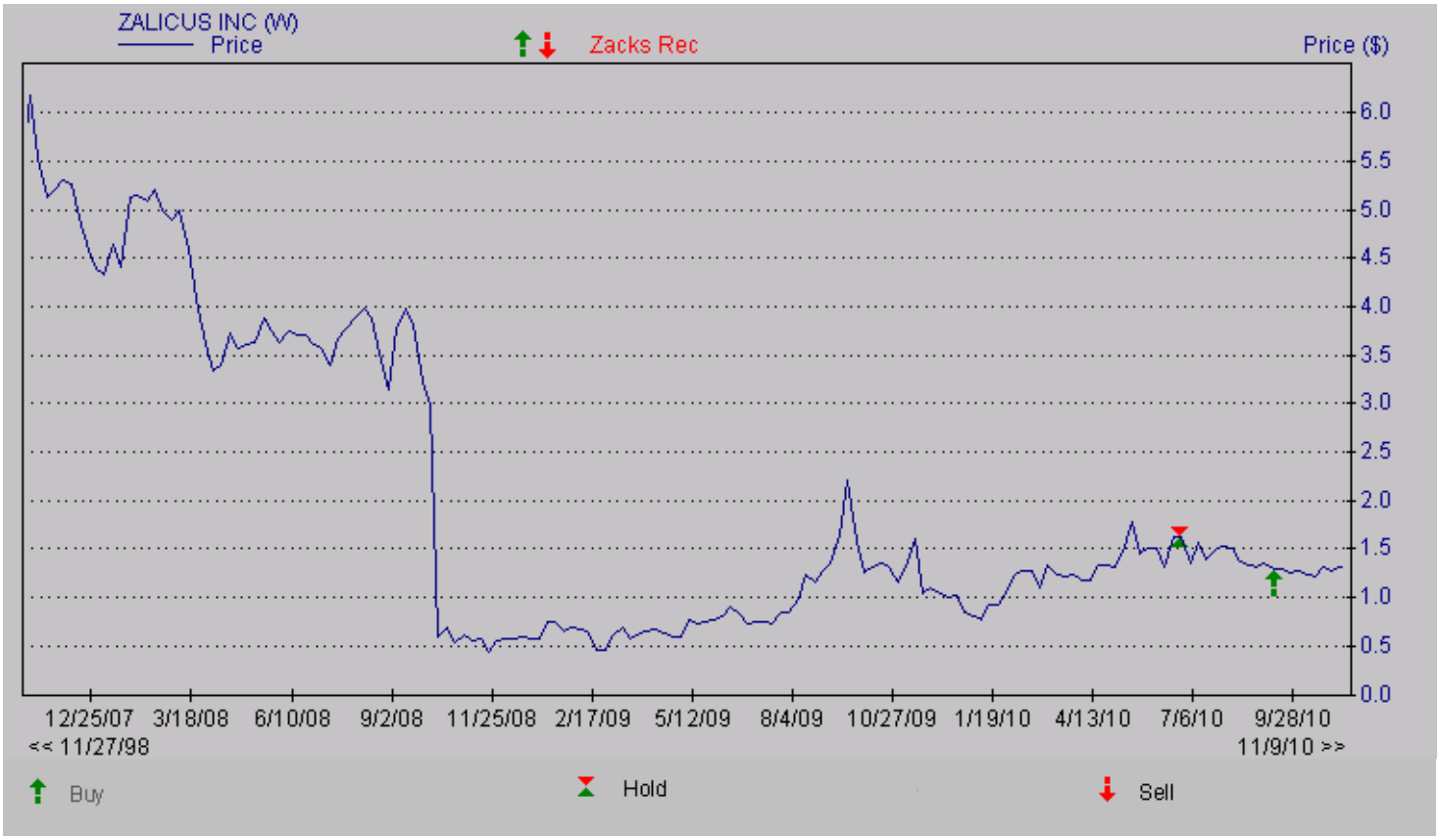
**Zalicus, Inc.**
Income Statement

| | 2009 A | Q1 A | Q2 A | Q3 A | Q4 E | 2010 E | 2011 E | 2012 E | 2013 E |
|---|---|---|---|---|---|---|---|---|---|
| **Collaborations & Grants** | **$17.3** | **$41.3** | **$1.8** | **$1.1** | **$1.5** | **$45.7** | **$10.0** | **$15.0** | **$15.0** |
| *YOY Growth* | *22.3%* | *1260.9%* | *-44.6%* | *-61.1%* | *-82.5%* | *164.8%* | *-78.1%* | *50.0%* | *0.0%* |
| **Exalgo Royalty** | **$0** | **$0** | **$1.1** | **$0.1** | **$0.5** | **$1.7** | **$9.8** | **$16.1** | **$22.5** |
| *YOY Growth* | - | - | - | - | - | - | - | - | - |
| **Synavive (CRx-102)** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** | **$0** |
| *YOY Growth* | - | - | - | - | - | - | - | - | - |
| **Total Revenues** | **$17.3** | **$41.3** | **$2.9** | **$1.2** | **$2.0** | **$47.4** | **$19.8** | **$31.1** | **$37.5** |
| *YOY Growth* | *22.3%* | *1260.9%* | *-11.8%* | *-57.5%* | *-76.7%* | *174.6%* | *-58.4%* | *57.5%* | *20.6%* |
| Cost of Goods Sold | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 |
| Gross Income | $17.3 | $41.3 | $2.9 | $1.2 | $2.0 | $47.4 | $19.8 | $31.1 | $37.5 |
| *Product Gross Margin* | *100.0%* | *100.0%* | *100.0%* | *100.0%* | *100.0%* | *100.0%* | *100.0%* | *100.0%* | *100.0%* |
| General & Administrative | $17.1 | $3.9 | $2.6 | $2.8 | $2.8 | $12.1 | $12.5 | $13.0 | $14.0 |
| *% SG&A* | *98.9%* | *9.3%* | *87.7%* | *242.5%* | *140.0%* | *25.4%* | *63.3%* | *41.8%* | *37.3%* |
| Research & Development | $21.2 | $7.4 | $4.6 | $5.1 | $5.5 | $22.6 | $26.0 | $30.0 | $30.0 |
| *% R&D* | *123.0%* | *17.9%* | *157.7%* | *434.1%* | *275.0%* | *47.6%* | *131.6%* | *96.5%* | *80.0%* |
| Amort & Restruct | ($0.4) | $4.7 | $4.7 | $4.7 | $4.7 | $18.8 | $15.0 | $12.5 | $10.0 |
| *% Other* | *-2.6%* | *11.3%* | *160.0%* | *401.6%* | *235.0%* | *39.5%* | *75.9%* | *40.2%* | *26.7%* |
| Operating Income | ($20.6) | $25.4 | ($8.9) | ($11.4) | ($11.0) | ($5.9) | ($33.8) | ($24.4) | ($16.5) |
| *Operating Margin* | - | *61.5%* | - | - | - | - | - | - | - |
| Interest & Other Net | $21.8 | ($29.4) | $0.0 | $0.0 | $0.0 | ($29.3) | $0.1 | $0.1 | $0.1 |
| Pre-Tax Income | $1.2 | ($4.0) | ($8.9) | ($11.4) | ($11.0) | ($35.2) | ($33.7) | ($24.3) | ($16.4) |
| Taxes | ($0.1) | (0.9) | (0.3) | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| *Tax Rate* | *-6%* | *23%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* |
| Discontinued Operations | $14.1 | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 |
| Net Income | $15.4 | ($3.1) | ($8.6) | ($11.4) | ($11.0) | ($35.2) | ($33.7) | ($24.3) | ($16.4) |
| *YOY Growth* | - | - | - | - | - | - | - | - | - |
| *Net Margin* | - | - | - | - | - | - | - | - | - |
| **Reported EPS** | **$0.41** | **($0.05)** | **($0.10)** | **($0.13)** | **($0.12)** | **($0.43)** | **($0.37)** | **($0.26)** | **($0.17)** |
| *YOY Growth* | - | - | - | - | - | - | - | - | - |
| Weighted Ave. Shares | 37.3 | 63.3 | 88.9 | 89.0 | 89.1 | 82.6 | 91.0 | 93.0 | 95.0 |

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

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## HISTORICAL ZACKS RECOMMENDATIONS




## DISCLOSURES

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