Bellus Health, Inc. (T.BLU-TSX)

**INITIATION**

On August 13, 2014, Bellus Health, Inc. announced financial results for the second quarter of 2014. The company recorded $0.42 million in revenue and had a net loss of $0.77 million, or $0.02 per share. The company exited the quarter with approximately $13.1 million, which we estimate will be enough to finance operations past the conclusion of the Kiacta Phase 3 clinical trial.

During the second quarter the Phase 3 confirmatory trial of Kiacta™ reached the targeted enrollment of 230 patients. The study continues to be on track to conclude in 2016.

We continue to be bullish on the Kiacta™ Phase 3 trial and are maintaining our Buy rating, even with shares up almost 50% since we initiated coverage.

| 52-Week High | $1.18 |
| 52-Week Low  | $0.32 |
| One-Year Return (%) | 217.16 |
| Beta         | 2.66 |
| Average Daily Volume (sh) | 4,524 |
| Shares Outstanding (mil) | 47 |
| Market Capitalization ($mil) | $47 |
| Short Interest Ratio (days) | 10.25 |
| Institutional Ownership (%) | 0 |
| Insider Ownership (%) | 24 |
| Annual Cash Dividend | $0.00 |
| Dividend Yield (%) | 0.00 |

**ZACKS ESTIMATES**

**Revenue (In millions of C$)**

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**Earnings per Share**

(EP is operating earnings before non-recurring items)

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WHAT’S NEW

Financial Update (in Canadian dollars)

On August 13, 2014, Bellus Health, Inc. announced financial results for the second quarter of 2014. Revenues for the quarter totaled $0.42 million, compared to $0.38 million in the corresponding period of 2013, and consisted mostly of revenue recognized for accounting purposes from the asset sale and licensing agreement and the service agreement entered into with Auven Therapeutics in 2010 in relation to Kiacta™. Operating expenses consisted of $0.85 million in G&A and $0.37 million in R&D. In addition, there was a net finance gain of $0.03 million, which was mainly attributable to the depreciation of the Canadian dollar versus the U.S. dollar during the current quarter. The company reported a net loss of $0.77 million, or $0.02 per share.

As of June 30, 2014 the company had cash, cash equivalents, and short-term investments of approximately $13.1 million, compared to $15.3 million on Dec. 31, 2013. We estimate that this will be enough to finance the company’s operations beyond the end of the Kiacta™ Phase 3 confirmatory study.

Kiacta™ Phase 3 Study Fully Enrolled

On May 27, 2014, Bellus announced that the Kiacta™ Phase 3 confirmatory study in AA Amyloidosis had completed its target enrollment of 230 patients. Eligible patients that were currently in the screening process at the time of this announcement were also given the opportunity to enroll in the study, thus the final patient population may number slightly more than 230. Patients that completed the Kiacta™ Phase 3 confirmatory study are being offered the opportunity to continue in an extended program, for which the first patients were enrolled during the second quarter of 2014.

For an overview of AA Amyloidosis, prior Kiacta™ clinical data, and the current Phase 3 study we invite investors to review our Investment Thesis, which follows in this report.

Valuation and Recommendation

Not much has changed in the past 3 months to alter our opinion on Bellus or the Kiacta™ Phase 3 trial, thus we are maintaining our Buy rating on the stock as we believe an investment at this juncture still represents an attractive risk/reward opportunity for investors, even with the stock up almost 50% since we initiated coverage.

The main driver for the stock in the near future will continue to be the success or failure of Kiacta™ in the confirmatory Phase 3 trial and the ability of Bellus to monetize that asset in the form of a licensing deal or sale. We believe that the trial has a 75% chance of success, and base this on the results seen from the first trial, as well as the changes in primary outcomes and design that we think facilitate a successful trial outcome. Bellus has obtained the services of investment banking firm, Lazard Capital, as a financial advisor to explore the sale of Kiacta™ with the idea that a potential sale prior to the completion of the Phase 3 trial would provide the acquirer with the opportunity to offer input into the regulatory process for approval of Kiacta™.
INVESTMENT THESIS

Kiacta™

Bellus’ lead development product is Kiacta™ (eprodisate), an orally available small molecule intended for the treatment of Amyloid A Amyloidosis. Kiacta™ has already been evaluated in 183 patients in Phase 2/3 clinical trial and is currently being studied in a confirmatory Phase 3 trial under a U.S. FDA Special Protocol Assessment (SPA), with results expected mid to late 2016.

Amyloid A Amyloidosis

Amyloidosis is the generic term for a number of diseases related by the extracellular deposition of insoluble fibrillar proteins (amyloid) in specific organs, which eventually leads to the failure of the involved organs. Amyloid A (AA) Amyloidosis, also referred to as secondary amyloidosis, is a systemic amyloidosis that is associated with chronic inflammatory diseases (i.e. rheumatoid arthritis, Familial Mediterranean fever, Crohn’s disease) or chronic infections (e.g. tuberculosis, chronic bronchiectasis). In this disease, the extracellular fibrillar depositions are composed of proteolytically derived fragments of serum amyloid A (SAA) protein. SAA is a major acute phase protein and serum marker for inflammatory diseases that is secreted during the inflammatory response. The most common organ affected by AA amyloidosis is the kidney, which typically leads to nephrotic syndrome and end-stage renal disease.

...Serum Amyloid A Protein...

The SAA family was once thought to comprise only a single circulating precursor of the amyloid A protein; however, it is now known that the SAA family contains a number of differentially expressed apolipoproteins that are primarily synthesized by the liver and can be divided into two main classes based upon their responsiveness to inflammatory stimuli. Acute phase SAA (A-SAA) are secreted into the blood stream in response to inflammation. The proteins serve a number of different roles, including the transport of cholesterol to the liver for secretion into the bile as a component of high-density lipoprotein (HDL), the recruitment of immune cells to inflammatory sites, and the induction of enzymes that degrade the extracellular matrix. The concentration of A-SAA can increase by more than 1,000-fold to levels that exceed 1 mg/mL during inflammation (Kushner, 1982). During the course of inflammation, A-SAA displaces apolipoprotein-A1 from HDL particles and facilitates HDL-cholesterol uptake by macrophages. Constitutive SAAs (C-SAAs) are a second class of SAAs that are expressed most minimally during the acute-phase response and are associated with both normal and acute-phase HDL (Whitehead et al., 1992).

There are four SAA genes in the human genome, denoted SAA1-4, with SAA1 and SAA2 encoding A-SAAs and having multiple alleles. The nomenclature for SAA families changed in 1999 when new guidelines were developed by the SAA Subcommittee of the Amyloidosis Nomenclature Committee with alleles of SAA1 formerly labeled α, β, γ changed to 1.1, 1.2, 1.3, respectively (Sipe et al., 1999).

The crystal structure of the SAA protein is shown in Figure 1. The mature SAA proteins range in size from 104 to 112 amino acids and are derived from a primary translation product having an 18-amino acid leader peptide that is removed. Interestingly, unlike many other amyloid-prone proteins, A-SAA does not contain any β-strands, and is instead composed of an up-down-up-down four-helix bundle structure (Lu et al., 2014).

The major site of A-SAA synthesis is the liver, where A-SAA mRNA can be dramatically induced by inflammatory stimuli and may become one of the most abundant hepatic mRNAs (Lowell, 1986). As it is an acute phase protein, A-SAA is catabolized by the liver, has a short half-life of only 1 day, and is cleared from the plasma much more quickly than other HDL lipoproteins that have typical half-lives of 4-6 days. In addition to the rapid increase in transcription/translation of A-SAA during an acute phase response, there is also a subsequent decrease in the ability of the liver to degrade A-SAA by approximately 14% (Gollaher et al., 1990).
Amyloidosis Pathophysiology

Elevated levels of A-SAA are necessary but not sufficient for the development of AA Amyloidosis. There are many individuals who have long-standing inflammatory disease who do not develop amyloidosis, thus what determines a patient’s risk of developing the disease is currently not known. Different therapeutic regimens, genetic factors, and environmental factors have all been proposed as possible contributors to the development of the disease.

Normally, A-SAA is degraded without developing into amyloid fibrils. However, in patients with amyloidosis, the intermediate A-SAA products combine to form fibrils, which are then deposited into the extracellular space of tissues and organs. Glycosaminoglycans (GAGs) such as heparin or dextran sulfate, and serum amyloid P then bind to the fibrils and render them invulnerable to degradation (Figure 2).

Mononuclear phagocytes may play a role in degradation of A-SAA and initiation of development of AA Amyloidosis. Genetic differences in the mannose-binding lectin 2 gene have been associated with defective macrophage function, which suggests that genetic background may affect the ability of macrophages to properly process and degrade A-SAA proteins. In addition, extracellular proteases, such as matrix metalloproteinases (MMPs), are involved in the generation of SAA N-terminal fragments. This has been supported by in vitro studies showing that MMPs can generate different sized fragments of A-SAA, although the susceptibility of A-SAA to degradation by MMPs is also influenced by genotype.

The exact mechanism by which the deposits affect organ function is not well known. Large deposits of fibrous protein can distort the integrity and function of a tissue on a structural level. It may be the amyloidogenic precursor proteins and intermediate filaments that have a direct toxic effect on organs. This is supported by data showing a marked reduction in proteinuria (protein in the urine) in AA Amyloidosis patients after treatment of the underlying inflammatory condition, which results in a notable reduction in the production of the precursor amyloidogenic protein. The factors responsible for determining the exact site of fibril deposition have not been identified.

Since A-SAA fibrils have been generated in vitro by incubating A-SAA protein with macrophages, deposits are typically found in tissues with large numbers of phagocytic cells such as the liver and spleen. However, this is does not account for the large deposition in kidneys, which do not share the same cellular composition.

AA Amyloidosis patients typically present (90%) with renal complications, thus symptoms associated with the disease involve the appearance of proteinuria, renal insufficiency, and nephrotic syndrome. Other symptoms include weight loss and peripheral edema. Cardiac complications are not common with AA amyloidosis patients, only occurring in approximately 5% of patients.

Epidemiology of AA Amyloidosis

The absolute rate of AA Amyloidosis is difficult to ascertain; however, there are statistics available both for the prevalence of the underlying diseases associated with amyloidosis in different parts of the world as well as the prevalence of those with the underlying diseases that suffer from amyloidosis. Market research conducted by Navigant Consulting on behalf of Bellus estimates that there are over 15,000 AA amyloidosis patients in the United States and EU Big-5 (United Kingdom, France, Italy, Germany and Spain). The breakdown is approximately 9,100 patients in the U.S. and 6,200 patients in the EU Big-5.

Most of the data from literature used to estimate the prevalence of AA amyloidosis has come from autopsies, with a difficulty in ascertaining exact numbers of symptomatic patients affected due to the fact that most AA Amyloidosis patients die from causes other than amyloidosis. Therefore, mortality data based on death certificates is of limited value in AA amyloidosis. A 1994 study indicated that the overall autopsy incidence of AA amyloidosis in Western nations ranged from 0.50 – 0.86% (Simms et al., 1994).
Rheumatic diseases such as rheumatoid arthritis (RA), ankylosing spondylitis, psoriatic arthritis, and juvenile idiopathic arthritis are thought to be the most frequent causes (70%) of AA amyloidosis. A 1999 study using autopsy records of 1,666 RA patients showed a prevalence of amyloidosis of 5.8% (Myllykangas-Luosujärvi et al., 1999). A 2008 study from Finland examined amyloidosis as a cause of death in 369 RA and 370 non-RA patients and found that amyloidosis was a cause of death in 9.5% of the RA patients but in none of the non-RA patients (Koivuniemi et al., 2008).

Current Treatment Options for AA Amyloidosis

There is currently no cure for AA Amyloidosis. Treatment is focused on getting the underlying inflammatory disease under control to decrease the levels of circulating A-SAA. The typical concentration of A-SAA in the blood of healthy individuals is approximately 3 mg/L (Ledue et al., 1998), and intensive treatment to get the A-SAA levels in AA amyloidosis patients to less than 10 mg/L may halt disease progression and induce a slow progressive recovery of renal function. The relative risk of death amongst patients with plasma A-SAA concentrations greater than 155 mg/L is 18 times greater than those with a plasma A-SAA concentration of less than 4 mg/L (Lachmann et al., 2007).

With no specific therapeutic agents recommended for the treatment of AA amyloidosis, most of the documented AA amyloidosis treatment successes come from case reports in the literature and not from large-scale clinical trials.

Examples include:

- A report from Japan noted the success in treating a 55-year old female patient with AA amyloidosis with infliximab, a TNF-α inhibitor (sold in the U.S. as Remicade®). The patient presented with nephrotic syndrome and upon treatment with infliximab her SAA levels normalized, the nephrotic syndrome disappeared, and her creatinine clearance improved.

- Another case study from Japan described the treatment of a 35-year old female RA patient who developed AA amyloidosis. The patient was successfully treated with intravenous hyperalimentation, steroids, and methotrexate, with continuation of steroids and methotrexate resulting in long-term survival without recurrence of amyloidosis.

- A small, uncontrolled study from Spain described the treatment of 25 patients with AA amyloidosis using TNF-α inhibitors. The investigators explained that the rationale for using TNF-α inhibitors arose from the fact that they suppress TNF-α inflammatory response, which decreases the synthesis of acute-phase proteins, lowers inflammation, and SAA levels are lowered leading to a reduction in amyloid deposits. A majority of patients in this study were successfully treated with anti-TNF-α agents, with stabilization or improvement noted in renal function in 83% of the patients with renal amyloidosis.

While there have been documented cases of treating AA Amyloidosis, specifically with TNF-α inhibitors, there are no FDA approved medications. Thus, there is clearly still an unmet medical need for this condition.

Kiacta™ for the Treatment of AA Amyloidosis

As mentioned previously, sulfated GAGs, such as dextran and heparin sulfate, are associated with amyloid deposits and are necessary for the assembly of amyloid fibrils as well as the stability of tissue amyloid deposits (Stenstad et al., 1994). Pre-clinical studies using small-molecule anionic sulfonates or sulfates significantly reduced murine splenic AA amyloid progression by inhibiting the binding of the sulfated glycosaminoglycans to the amyloidogetic precursor protein, thus inhibiting fibril polymerization and amyloid deposition (Kisilevsky et al., 1995).

One of these tested compounds, 1,3-propanedisulfonic acid disodium salt (eprodisate, Kiacta™, Figure 3) is currently being evaluated by Bellus for the treatment of AA amyloidosis in a confirmatory Phase 3 clinical trial.

Figure 3: Structure of Kiacta™. Source: Rumjan et al., 2012.
Eprodisate is a small, negatively charged molecule that shares certain structural similarities with heparin sulfate and is known to bind to A-SAA (Revill et al., 2006). Eprodisate binds to the GAG binding site of A-SAA and competes with naturally occurring GAGs, thus inhibiting amyloid fibril polymerization and deposition in tissues (Ancsin et al., 1999). The anti-amyloid activity of eprodisate was shown in an inflammation-induced mouse model of AA amyloidosis. This model was a particularly aggressive form where the mice were injected intravenously with a nucleating agent, the amyloid enhancing factor, and subcutaneously with a strong inflammatory agent (AgNO₃) a day prior to initiation of treatment with eprodisate. The eprodisate was delivered in the drinking water at different concentrations (15, 30 and 50 mg/mL) for five consecutive days.

A total of 261 patients were screened and 183 were randomly assigned to either treatment with Kiacta™ or placebo (n = 94). Patients were stratified according to nephrotic status, with a classification of nephrotic requiring a 24-hour urinary excretion of more than 3 g of protein, a serum albumin concentration of less than 3.4 g/dL, and either the presence of peripheral edema or the use of diuretics to treat peripheral edema. Study drug was administered orally twice a day either 1 hour before or 2 hours after a meal. Dosage was based upon creatinine clearance since Kiacta™ is excreted by the kidney. Patients with creatinine clearance rates of less than 30 mL/min received a total of 800 mg of Kiacta™ per day, those with rates of 30 to 80 mL/min received a total of 1600 mg of Kiacta™ per day, and those with rates of more than 80 mL/min received a total of 2400 mg of Kiacta™ per day.

Figure 4 shows that there was a significant and dose-dependent reduction in amyloid deposition in the spleens of mice treated with eprodisate compared to mice not treated with eprodisate.

Pre-clinical pharmacokinetic analyses of eprodisate showed it to have good bioavailability when administered orally. The molecule is not metabolized, it does not bind to plasma proteins, and it is primarily excreted by the kidney (Gandhi et al., 2010). Pharmacokinetic analyses in healthy volunteers revealed a high inter-individual variability in eprodisate plasma concentrations. Following single and repeated dose administration, the maximum plasma concentrations were achieved between 15-60 minutes post-dose. An approximate half-life of 10-20 hours was derived from a multiple rising oral dose study (Gandhi et al., 2010). As expected for a drug eliminated primarily by renal excretion, eprodisate plasma concentrations increased as renal function decreased in subjects with renal impairment, resulting in a significant increase in drug systemic exposure. Consequently, a decrease in dose appears to be necessary to maintain a comparable systemic exposure in patients with impaired renal function.

**...Phase 3 Trial of Kiacta™...**

Kiacta™ is currently being evaluated in a confirmatory Phase 3 study for the treatment of AA Amyloidosis. This trial will be the major driver for the stock in the foreseeable future, thus its importance cannot be overstated. While it’s impossible to know for certain whether a clinical trial will succeed or fail, in this instance we have the opportunity to critically evaluate the first Phase 3 trial that tested Kiacta™ for the treatment of AA amyloidosis. Below we discuss this first Phase 3 trial, outline the results for investors, and provide the key differences between the current trial and the previous one. This information provides for investors a reasonably good estimate for the likelihood of success of the current trial.

Kiacta™ was first evaluated for the treatment of AA amyloidosis in patients with renal involvement in a Phase 2/3 trial that was conducted from 2001 to 2004 (Dember et al., 2007). This was a multicenter, randomized, double-blind, placebo-controlled trial. Renal involvement for patient inclusion was defined as proteinuria of greater than 1 g/day or a creatinine clearance of less than 60 mL/min. Patients were excluded if their creatinine clearance was less than 20 mL/min (which is indicative of irreversible renal failure) or they had renal disease attributable to something other than AA amyloidosis. Significant liver dysfunction, diabetes, elevated liver enzymes, or serum creatinine of greater than 3 mg/dL were additional exclusion criteria.

A total of 261 patients were screened and 183 were randomly assigned to either treatment with Kiacta™ (n = 89) or placebo (n = 94). Patients were stratified according to nephrotic status, with a classification of nephrotic requiring a 24-hour urinary excretion of more than 3 g of protein, a serum albumin concentration of less than 3.4 g/dL, and either the presence of peripheral edema or the use of diuretics to treat peripheral edema. Study drug was administered orally twice a day either 1 hour before or 2 hours after a meal. Dosage was based upon creatinine clearance since Kiacta™ is excreted by the kidney. Patients with creatinine clearance rates of less than 30 mL/min received a total of 800 mg of Kiacta™ per day, those with rates of 30 to 80 mL/min received a total of 1600 mg of Kiacta™ per day, and those with rates of more than 80 mL/min received a total of 2400 mg of Kiacta™ per day.

**Figure 4: The effect of eprodisate (1,3-PO) in drinking water on development of amyloid fibrils. Each point represents an individual mouse with dashed lines representing the production and confidence intervals. Source: Gervais et al., 2003.**
Figure 5 gives a breakdown of the enrollment and outcomes for the patients in the study. Of the 183 patients that entered the study, 63 in the Kiacta™ group (~71%) and 61 (~65%) in the placebo group completed two years of the study.

There were a similar number of adverse events in both the Kiacta™ and placebo groups. At the end of follow-up, disease was worsened in 24 of 89 patients taking Kiacta™ (27%) and 38 of 94 assigned to placebo (40%, P = 0.06).

There were five deaths in each group either during the study or within 15 days after the final administration of the study drug. Two patients in the Kiacta™ group died of ischemic stroke, one patient had nephrotic syndrome, one patient had gastrointestinal hemorrhage, and one patient died of pneumonia. No deaths in the study were considered to be related to Kiacta™.

Follow-up visits occurred at 1, 4, 8, 12, 16, 20, and 24 months after randomization, with creatinine clearance and urinary protein excretion measured by 24-hour urine collection. At baseline and at the 12- and 24-month visits, abdominal fat was collected by aspiration for Congo red staining (to test for the presence of amyloid fibrils), with quantification of amyloid ascertained through an enzyme-linked immunosorbent assay. The medication was continued for 24 months unless the patient had progression to end-stage renal disease, had an adverse event that precluded further use of study medication, withdrew from the study, or required a rescue medication, which included cytotoxic agents, colchicine, and anti-TNF-α agents.

The primary end point was a composite assessment of renal function or death. Disease was classified as worsened if the serum creatinine concentration was twice the baseline value, creatinine clearance decreased by 50% or more from baseline, progression to end-stage renal disease occurred, or the patient died. End-stage renal disease was defined as the need for initiation of maintenance dialysis.

Patient deaths in the placebo group were due to ischemic stroke, amyloid cardiomyopathy, bowel perforation, sepsis, and pancytopenia.
Treatment with Kiacta™ was associated with a 42% reduction in the risk of worsening renal disease or death (hazard ratio, 0.58; 95% confidence interval [CI], 0.37 to 0.93; *P* = 0.025). Even after adjusting for potentially important baseline variables (e.g., renal function, underlying disease, etc.) and for SAA concentration the risk reduction was still maintained (Figure 6). There was no effect on urinary protein excretion, with the benefit of Kiacta™ on the primary composite end point being due to its effect on progression of renal disease. In addition, there was no significant difference between the two groups in the risk of death (Figures 6 & 7).

A key secondary endpoint in the study was examination of the change in creatinine clearance between the beginning of the study and the end. The mean slope of creatinine clearance was -10.9±5.1 mL/min per 1.73 m² of body-surface area per year in the Kiacta™ group, as compared to -15.6±4.0 mL/min per 1.73 m² per year in the placebo group (*P* = 0.02). Using the slope of creatinine clearance decline, the company was able to calculate a delay to time of dialysis of approximately two years with Kiacta™ treatment compared to placebo.

While this study did show Kiacta™ reduced the progression of AA amyloidosis-associated renal disease, there were some limitations that are worth noting. Even though the study was randomized, the baseline serum creatinine concentrations were slightly higher in the placebo group than in the Kiacta™ group. While the difference in baseline renal function could explain the better outcomes in the Kiacta™ group, the risk reduction associated with Kiacta™ was shown to persist even when the analyses were adjusted for baseline creatinine concentration or creatinine clearance. Additionally, data shows an improvement in kidney function for the placebo patients that crossed-over to the Kiacta™ group during the open-label extension study (Figure 8).

Another potential confounding factor was that treatments for the underlying inflammatory condition were not standardized. However, this was most likely not an issue as treating physicians were unaware of which arm of the study their patients were assigned to, the inflammatory markers did not differ between groups throughout the study, and the effect of Kiacta™ on the primary outcome was not affected by adjustment for SAA levels. Furthermore, a sub-group analysis by underlying inflammatory diseases (e.g. arthritic diseases, Familial Mediterranean fever, other conditions) has shown that Kiacta™ had comparable beneficial effect in all groups of underlying conditions. Therefore, it is unlikely that the observed benefit of the drug was caused by the differences in the underlying inflammatory conditions.

Even with those limitations, there were a number of strengths in the trial. The sample size of 183 patients was quite substantial for a rare disease such as AA amyloidosis. The consistent treatment effects of Kiacta™ across renal endpoints, sub-group analyses, and sensitivity analyses promote confidence in the study findings and provide evidence that the study results are scientifically and clinically valid. There was a heterogeneous group of patients in the study, with a wide variety of underlying diseases, races, and durations of disease. This means that the results can most likely be applied to a generalized population of patients suffering from AA amyloidosis and not just to a specific subset.

...**Regulatory Timeline After the First Phase 3 Trial**...

Bellus (then Neurochem, Ltd.) filed an NDA for Kiacta™ (then known as Fibrillex) on April 18, 2006 and was granted priority review with a PDUFA date of August 13, 2006. The company received an “Approvable Letter” from the FDA, in which the agency requested additional efficacy information along with a safety update. The FDA stated that the efficacy information would probably need to be addressed by one or more additional clinical trials. Alternatively, the FDA stated that significant findings from a complete follow-up of patients from the Phase 2/3 study could be persuasive.

On October 16, 2006 the company submitted a complete response to the FDA that included data on safety and efficacy from a follow-up of all 183 patients who were enrolled in the Phase 2/3 clinical trial. Included in the complete response was the most recent health information (e.g., dialysis/end stage renal disease or death from all causes, regardless of when the clinical even occurred) for all 183 study subjects, including patients that were then currently enrolled in the open-label extension study and all patients who discontinued their participation in the study. The median time of follow-up was approximately 36 months.
The results of the follow-up analysis included the following:

- Fewer patients progressed to dialysis/ESRD in the Kiacta™ group (n = 18) compared to the placebo group (n = 32). The Kaplan-Meier plot and log-rank analysis showed that it took longer for the Kiacta™ group to progress to dialysis/ESRD than the placebo group ($P = 0.018$). This was similar to the results seen during the initial trial, where the Kaplan Meier plot for Time to First Worst Event was also in favor of the Kiacta™ group vs the placebo group ($P = 0.025$) (Figure 9).

![Kaplan Meier: Time to First Worst Event](image)

*Figure 9: Time to First Worst Event, Source: Bellus Health*

- Follow-up analysis on the composite endpoint of dialysis/ESRD or death was also in favor of the Kiacta™ group as fewer patients (n = 32) progressed to dialysis/ESRD or death versus the placebo group (n = 44). The Kaplan-Meier plot and log-rank analysis showed that it also took longer for the Kiacta™ group to progress to dialysis/ESRD or death than the placebo group ($P = 0.062$). The follow-up analysis also showed that 56 patients progressed to death from all causes: 25 patients were from the group originally randomized to Kiacta™ and 31 patients were from the group originally randomized to placebo.

On July 17, 2007 the company received a second approvable letter from the FDA. In this letter, the FDA indicated that the Phase 2/3 clinical trial provided some evidence of the effectiveness of Kiacta™ in the treatment of AA amyloidosis; however, the FDA also indicated that an additional efficacy trial with a target $P$-value of 0.05 would be necessary before Kiacta™ could be approved. The regulatory agencies in the European Union also agreed that a second clinical trial would be necessary to gain marketing approval. On March 13, 2008, the company announced that they were withdrawing the application for marketing authorization for Kiacta™ and would be initiating a second clinical trial to comply with the recommendation of the regulatory agencies.

**Second Phase 3 Trial of Kiacta™**

An agreement was reached under a Special Protocol Assessment (SPA) with the FDA in 2009 to conduct a Phase 3 Confirmatory Trial for Kiacta™. The first Phase 2/3 trial was accepted as the first of two pivotal trials with statistical significance of $P < 0.05$ required in the confirmatory study. This was clearly good news because a single pivotal trial application requires a more stringent statistical threshold of $P < 0.01$.

To finance the second confirmatory clinical trial, in April 2010, Bellus entered into a partnership with Auven Therapeutics (then Celtic Therapeutics) whereby Auven acquired the worldwide rights to Kiacta™ for an upfront payment of $10 million. In addition, Auven agreed to fund 100% of the development costs associated with the confirmatory Phase 3 study. The plan is to sell or license the rights to Kiacta™ to a commercial entity before or right after conclusion of the confirmatory Phase 3 study.

There were a number of changes made to the confirmatory Phase 3 study in comparison to the initial Phase 2/3 study. These changes are summarized in Table 1.
Table 1: Comparison Between KIACTA™ Clinical Trials

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<td>Number of Patients/Trial Locations</td>
<td>183 patients in 13 countries</td>
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<td>Creatinine clearance ≥ 25 mL/min/1.73 m²</td>
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<td>Creatinine clearance ≥ 20 mL/min/1.73 m²</td>
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<tr>
<td>Trial Timeline/Statistical Power</td>
<td>Fixed treatment time of 2 years ~80% power</td>
<td>Attainment of 120 events ~90% power</td>
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As of April 2014, there were 70 sites operating in greater than 25 countries with 227 patients currently enrolled in the study. We estimate that study recruitment will be completed in the second quarter of 2014. Thus far, there have been 55 first events recorded (out of 120 events that will conclude the trial), with the distribution of first events as follows: 57% had a 40% decrease in creatinine clearance; 9% had an 80% increase in serum creatinine; 34% had multiple first events. Of course, we do not know if these events are occurring in the placebo or Kiacta™ group. Thus far there have been no safety concerns with an independent safety committee recommending in April 2014 that the study continue as per protocol. The study is projected to finish in mid to late 2016, based on the rate events have taken place and an estimate of future rates (Figure 10).

![Figure 10: Patient-events over time and Projection of End of Kiacta™ Confirmatory Phase 3 Study. Source: Bellus Health.](image)

Based upon the data gathered from the initial Phase 2/3 study, along with the changes made in the confirmatory Phase 3 study, WE CONCLUDE that the confirmatory Phase 3 study is likely to be successful. We base this on the fact that the two composites of the primary endpoint in the initial trial that were statistically significant were the doubling in serum creatinine and the 50% decrease in creatinine clearance, and these endpoints have been altered such that a smaller change in each of them is required to qualify as an event. We believe this is likely to result in reaching a statistically significant difference between Kiacta™ treatment and placebo for each of these endpoints. In the initial study reaching ESRD/dialysis only trended toward significance, thus we are uncertain about how this endpoint will look at the end of the trial. The death endpoint was removed from the confirmatory study, which we believe will be helpful in showing significance in the composite primary endpoint as there was no differences in the number of deaths between Kiacta™ and placebo groups in the first Phase 2/3 study.

Another change that we believe will be positive for the confirmatory study is the alteration in inclusion criteria. The first Phase 2/3 study allowed patients into the study who had proteinuria ≥ 1 g/day or a creatinine clearance of ≤ 60 mL/min/1.73 m² as long as their creatinine clearance was ≥ 20 mL/min/1.73 m². For the confirmatory study, the patients will have to have proteinuria of ≥ 1 g/day and a creatinine clearance of ≥ 25 mL/min/1.73 m². In the initial Phase 2/3 trial, the effect of Kiacta™ was more apparent in the subgroup of patients with the nephrotic syndrome (characterized by proteinuria >3.0 g/day, hypoalbuminemia, and edema), thus while Bellus did not want to limit the study to only those patients suffering from nephrotic syndrome, by changing the inclusion criteria to only allow patients who had proteinuria of ≥ 1 g/day they are more likely to include a greater percentage of patients in the study with nephrotic syndrome, which should lead to a greater likelihood of showing statistical significance.
...Market Potential for Kiacta™ for Treating AA Amyloidosis...

Bellus and partner, Auven, have stated that their goal is to sell or license the rights to Kiacta™ either shortly before or just after the confirmatory Phase 3 trial has concluded. It is expected that the parties will share aggregate proceeds equally, assuming that total divestment transaction proceeds reach a pre-determined threshold. Proceeds will be shared between Auven and Bellus based on a formula that provides for Auven to have certain preference rights on exit proceeds related to their investment costs in Kiacta™. For the purposes of deriving a value for Kiacta™, we are producing a discounted cash flow model based upon what we forecast Kiacta™ could provide in future revenues and assume that the total realized consideration from a partnership transaction will reach, or exceed, the threshold necessary for Bellus and Auven to attain 50:50 revenue split. We anticipate the confirmatory Phase 3 trial to be completed in mid to late 2016, with an NDA filed at the end of 2016 and subsequent approval by the FDA in 2017.

Given the fact that AA Amyloidosis is a rare disease, it is difficult to determine a precise number of patients that are eligible for treatment with Kiacta™. Market research performed by Navigant Consulting on behalf of Bellus indicates that there are approximately 12,300 AA amyloidosis patients eligible to receive Kiacta™ in the world, with approximately 6,800 in the U.S., 3,500 in the E.U., and an additional 2,000 in the rest of the world. In order to model pricing for Kiacta™, we are assuming that it will be priced in-line with other ultra-orphan therapies and as such command a significant premium. Table 2 shows other ultra-orphan therapeutics, the U.S. patient population size and the price for treatment in both the U.S. and E.U.

Table 2: Kiacta™ Pricing Analogues. Source: Bellus Health

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<tbody>
<tr>
<td>1,500</td>
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<td>-</td>
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<tr>
<td>9,500</td>
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</table>

We are modeling for Kiacta™ to be priced at $200,000/year in the U.S. and $150,000/year in the E.U. For our model, we have evaluated peak market shares of between 25-45% seven years after approval. We have modeled discount rates of between 15-25% to future cash flows and give the probability of approval at 75%. Based on these numbers we believe that Kiacta™ is worth approximately $150 million for Bellus in a future licensing deal/sale, taking into account the 50:50 split that will occur with Auven Therapeutics.

Sarcoidosis

In May 2014, Bellus and Auven announced they had signed a license agreement with Mount Sinai Hospital under which Auven obtained rights to develop Kiacta™ as a treatment for chronic sarcoidosis. By obtaining the rights to utilize Kiacta™ in a second indication, Bellus and Auven could further expand the commercial potential of the drug while helping patients suffering from this sometimes debilitating chronic disease.

Sarcoidosis is an inflammatory disease of unknown origin that results in the collection of inflammatory cells in different parts of the body, but most commonly in the lungs and the skin. These groups of inflammatory cells are known as granulomas, and they appear to be triggered by an immune reaction to an infection or some other trigger that continues even after the initial infection is cleared (Baughman et al., 2011). A variety of cells make up the granulomas, which include T lymphocytes, fibroblasts, and B lymphocytes. In addition, a variety of chemokines and cytokines are involved in granuloma formation, including tumor necrosis factor alpha (TNF-α).

Diagnosis of sarcoidosis is often arbitrarily made based on clinical features that are typical of the disease; however, there are none that are specific for sarcoidosis. A tissue biopsy is usually warranted, or a less invasive diagnosis can be made based on a chest x-ray coupled with additional clinical features. The difficulty in diagnosing the disease is exemplified by the fact that patients generally need at least three or more encounters with a health care professional before a specific diagnosis is made (Judson et al., 2003).

Table 2: Kiacta™ Pricing Analogues. Source: Bellus Health
The lungs are affected in more than 90% of sarcoidosis patients. While pulmonary function studies are abnormal in a large number of patients with sarcoidosis, there doesn’t appear to be a diagnostic pattern (Peitunalho et al., 1996). There is only a modest correlation between the forced volume vital capacity (FVC), a test to measure lung function, and the level of dyspnea reported by the patient (Yeager et al., 2005). To aid in diagnosis, a staging system of the chest x-ray is utilized where patients are grouped from stage 0 through stage 4. This provides general information regarding the prognosis of the pulmonary disease over time, as it was shown that those with stage 1 findings had a greater than 90% chance of resolution of their disease within two years while those with stage 3 had resolution in less than 1/3rd of cases in two years (Scadding, 1961).

Sarcoidosis most frequently occurs between the ages of 20 and 40, with women being diagnosed more frequently than men (Rybicki et al., 1997). African Americans are approximately three times more likely to suffer from the disease than white Americans (Iannuzzi et al., 2007). In total, the disease affects approximately 120,000 individuals in the United States, with 30% going on to develop chronic disease, leading to clinically significant organ impairment. Fewer than 5% of patients die from sarcoidosis, with death usually the result of pulmonary fibrosis with respiratory failure or of cardiac or neurological involvement (Iannuzzi et al., 2007).

...Current treatment options for sarcoidosis...

Treatment options for sarcoidosis patients are limited, and thus treatment is typically reserved for those patients who are at the risk of losing organ function. An international panel has suggested starting treatment with oral prednisone at 20 to 40 mg per day, with an evaluation period after one to three months of treatment to determine response (“Statement on Sarcoidosis”, 1999). There have been a very limited number of studies on the use of immunosuppressive and cytotoxic drugs in sarcoidosis patients. The only randomized, controlled trial compared methotrexate with placebo in patients receiving corticosteroids (Baughman et al., 2000). Results of that study showed that those receiving methotrexate required significantly smaller doses of corticosteroids than the control group, however there was no differences seen in terms of lung function, symptoms, or side effects.

Since TNF-α is known to be involved in granuloma formation, inhibiting TNF-α would appear to be a potentially useful treatment. There have been a number of case reports, and one randomized, controlled trial that involved the use of the TNF-α inhibitors infliximab and etanercept to treat sarcoidosis (Baughman et al., 2006). The results of the six month controlled trial indicated only modest improvements in FVC and chest x-ray findings with no differences seen in dyspnea scores or 6-minute walking distance.

...Development plan for Kiacta™ in sarcoidosis...

The current plan for the development of Kiacta™ as a treatment for sarcoidosis is for Auven to conduct a Phase 2 proof-of-concept clinical trial to evaluate the safety and effectiveness of Kiacta™ as a treatment for certain medical manifestations of sarcoidosis. A study protocol should be finalized by the middle of 2014 with the first dosing of patients likely to commence in the fourth quarter of 2014. The Phase 2 trial should take approximately 18 months to complete. Just as with the confirmatory trial in AA amyloidosis, all costs related to the development of Kiacta™ in sarcoidosis will be borne by Auven. Any proceeds from potential future revenue of Kiacta™, including the rights to Kiacta™ for sarcoidosis, are subject to the proceeds sharing agreement between Bellus and Auven.
Shigamab™

Bellus has an additional clinical stage compound in Shigamab™ that was acquired through the purchase of Thallion Pharmaceuticals in 2013. Shigamab™ is a monoclonal antibody treatment designed to bind to and eliminate Shiga toxin 2, which is secreted by certain strains of *Escherichia coli* during an infection and can lead to the development of hemolytic uremic syndrome (HUS). The compound has been tested in multiple Phase 1 safety trials and a Phase 2 safety/efficacy trial and Bellus is currently performing additional pre-clinical studies with the drug before beginning additional Phase 2 studies.

STEC-HUS

Hemolytic uremic syndrome (HUS) was first described in 1955, and at that time it was typically a fatal condition (Gasser *et al*., 1955). The disease is characterized by hemolytic anemia (a decrease in red blood cell count due to destruction of the cells), acute kidney failure (uremia), and a low platelet count (thrombocytopenia). The more common form of the disease, Shiga-like toxin-producing *E. coli* HUS (STEC-HUS), is caused by infection with *E. coli* O157:H7 or another Shiga toxin producing microbe. The association between STEC and HUS was first made in the 1980’s when it was found that infections with various serotypes of STEC were strongly associated with the subsequent development of HUS (Karmali *et al*., 1985).

STEC are enterohemorrhagic serotypes of the bacterium *Escherichia coli*. Transmission typically occurs via consumption of undercooked, contaminated ground beef or pork. Susceptibility to the toxin requires the presence of highly specific cell-surface receptors, which humans have but other species such as cattle do not. Thus cattle may harbor STEC bacteria and contamination of beef by fecal material can result in the spread of the bacteria to humans. Ingestion can lead to hemorrhagic diarrhea and kidney failure.

The STEC serotypes express Shiga toxin (Stx), which is a multi-subunit protein composed of one molecule of the A subunit (responsible for the toxic action of the protein), and five molecules of the B subunit, which is responsible for binding to a specific cell type (Figure 11).

The two main types of Stx are Stx1 and Stx2, with only 56% amino acid homology between the A subunits of each toxin. Stx2 is approximately 100 times more toxic than Stx1 and most frequently involved in the development of HUS.

Within each Stx type there are a number of subtypes that vary in amino acid sequence, specificity, and toxicity. There are three characterized subtypes of Stx1 and seven subtypes of Stx2 (Schwarz *et al*., 2012).

Shiga toxin binds to the cell surface component glycolipid globotriaosylceramide (Gb3) leading to eventual uptake of the toxin into the cell (Melton-Celsa *et al*., 1998). Once inside the cell, the A subunit then binds to the ribosome and halts protein production. This leads to the death of the cell, breakdown of the lining of the vascular endothelium, and to hemorrhage, which manifests itself as bloody diarrhea. As more Stx is produced by the bacteria in the colon, the toxin travels via the bloodstream to the kidney, where it damages renal endothelial cells and occludes the microvasculature through a combination of direct toxicity and induction of local cytokine and chemokine production, resulting in renal inflammation (Andreoli *et al*., 2002).

Specifically, the toxin targets the vascular endothelium of the glomerulus, which is the filtering structure of the kidney. Destruction of these structures leads to kidney failure and development of HUS. The series of events leading up to the development of HUS is depicted in Figure 12.
STEC-HUS primarily affects young children. The annual incidence of the disease in North America and Western Europe is approximately 2 to 3 per 100,000 children less than five years of age (Tarr et al., 2005). The highest incidence of the disease occurs during the summer months (Gerber et al., 2002) and it is more common in rural than in urban areas (van de Kar et al., 1996). While sporadic cases make up most of those seen, it is not uncommon to have outbreaks due to contaminated food or water. This was shown by a mass outbreak of STEC caused by the E. coli O104:H4 strain in Germany in 2011, which affected 3,816 people resulting in 845 cases of HUS and 54 deaths (Mellmann et al., 2011). A 2009 outbreak of E. coli O157:H7 in the U.S. was linked to contaminated Nestle Toll House cookie dough and sickened 70 people in 30 states. While ingestion of contaminated food is the most common cause of infection, secondary human-to-human transmission is also a major risk factor for HUS (Vaillant et al., 2009).

STEC cause at least 70% of cases of post-diarrheal HUS in the U.S., with 80% of those caused by E. coli O157:H7, however non-O157 strains are also involved (Boyer et al., 2011). Approximately 10-15% of children with E. coli O157:H7 infection go on to develop HUS, which means that there are additional host factors that contribute to its development in addition to pathogen factors (Scheiring et al., 2008).

A patient infected with STEC can suffer from a wide range of symptoms including asymptomatic carriage, diarrhea that may be uncomplicated or bloody, and HUS. The diarrhea and associated gastrointestinal complaints may mimic those of ulcerative colitis, other enteric infections, and appendicitis. HUS is defined by the sudden onset of microangiopathic hemolytic anemia with fragmented erythrocytes and negative Coombs' tests, thrombocytopenia, and acute kidney injury (Gerber et al., 2002).

Renal symptoms include anything from hematuria (blood in the urine) and proteinuria, to severe renal failure (oliguria and anuria) that occurs in one-half of cases. In addition, hypertension is quite common. Patients with severe renal failure are typically put on dialysis to correct any metabolic abnormalities with the short-term renal prognosis being generally favorable. However, the risk of long-term sequelae such as hypertension or chronic renal failure 20 years after recovering from STEC-HUS is not negligible, and renal histology showing a glomerular microangiopathy affecting >50% of glomeruli, arterial micro-angiopathy, and/or cortical necrosis is the best indicator of long-term prognosis (Gagnadoux et al., 1996).

The kidney is not the only organ affected by STEC-HUS. Central nervous system involvement occurs in 20-50% of children with STEC-HUS and is the most threatening complication associated with increased morbidity and mortality (Nathanson et al., 2010). Patients may exhibit seizures, coma, stroke, hemiparesis, facial palsy, dysphagia and cortical blindness. The more severe manifestations include severe hemorrhagic colitis, bowel necrosis and perforation, rectal prolapse, peritonitis, intussusception, cardiac ischemia, and transient diabetes mellitus (de Buys Roessingh et al., 2007). The mortality rate for STEC-HUS is approximately 5%, with most of those deaths caused by neurological or cardiac involvement (Oakes et al., 2006). Risk factors for death include persistent oliguria, dehydration, elevated white blood cells > 20,000 per mm$^3$, and hematocrit > 23%.
...Current Therapeutic Options for STEC-HUS...

Approximately 15% of patients infected with E. coli O157:H7 progress to HUS, however that figure can reach as high as 50% if antibiotics are used (Serna et al., 2008). Current treatment guidelines call for the avoidance of unnecessary use of antibiotics or antimotility agents during the diarrheal course of the disease. Quinolones (e.g., ciprofloxacin) can exacerbate the effects of Stx toxicity, as they induce the bacterial SOS response, which has the effect of increasing expression of Stx as well as lysing the bacterial cell and allowing for the release of the toxin (Zhang et al., 2000). For this reason, antibiotics are typically only used for cases of sepsis.

Most of the treatment of HUS is supportive, with dialysis used as necessary. Maintaining proper fluid levels and treating hypertension with standard antihypertensive agents are standard treatments and in most children with post-diarrheal HUS there is a very good chance of spontaneous resolution (~85%). For more severe cases, plasmapheresis is the treatment of choice and is performed daily until remission is obtained.

While not approved for the treatment of STEC-HUS, there are reports of experimental treatments with eculizumab (sold in the U.S. as Soliris®), a monoclonal antibody directed against complement protein C5, utilized for severe cases of STEC-HUS (Lapeyraque et al., 2011). In one report, three 3-year-old patients with STEC-HUS that required hemodialysis and involved severe central nervous system involvement were treated with eculizumab, with rapid clinical improvement noted within 24 hours of the first dose.

...Shigamab™ for the treatment of STEC-HUS...

Bellus is developing Shigamab™, a chimeric monoclonal antibody (cαStx2) designed to bind specifically and exclusively to Stx2. The antibody approach enables the use of Shigamab™ to treat infections caused by any E. coli strain that secretes Stx2. Shigamab™ was well tolerated in four Phase 1 clinical trials in healthy adults, where 50 individuals were treated with no significant drug-related adverse events reported in any of the trials.

Shigamab™ was further evaluated in a randomized, double-blind, placebo-controlled Phase 2 study involving 45 STEC patients in Argentina, Chile, and Peru. The study (SHIGATEC Trial) began in November 2011 and consisted of two arms: A) standard of care plus Shigamab™ or B) standard of care plus placebo. The main objective of this study was the assessment of safety and pharmacokinetic profiles of Shigamab™. The secondary endpoint was to evaluate the efficacy of Shigamab™ in stopping the progression of STEC to HUS (prophylaxis). Top line results were reported in May 2012 with Shigamab™ being safe and well-tolerated. There was no statistically significant trend of efficacy with no reliable conclusion drawn due to the low number of patients progressing to HUS (1/30 on drug and 1/15 on placebo). The challenge for development of Shigamab™ has always been a well-validated clinical endpoint in the STEC infection population.

While progression to HUS after STEC infection would be an efficient way to examine clinical efficacy, given the very low numbers of those infected with even fewer progressing to HUS, it would likely require thousands of patients in a prevention clinical trial to show statistically significant efficacy. Limiting treatment to those who have already progressed to STEC-HUS would be a way to lower the number of patients in a clinical trial; however, this runs the risk of not being able to detect significant efficacy, as it may be too late in the progression of the disease for the drug to have a meaningful effect. Thus the challenge for Bellus in the development of Shigamab™ will be deciding how to properly design the clinical trials to limit the number of patients while still being able to show statistically significant efficacy.

Shigamab™ has already received Orphan Drug designation in the U.S. and in Europe. Over the next 12 months, Bellus plans to initiate additional pre-clinical proof-of-concept studies in animal models to optimize the amount and timing of administration of the drug. They then plan to initiate discussions with regulators in regards to proper clinical trial design and to determine reasonable clinical endpoints for future clinical trials. In addition the company plans to seek a development partner for the drug.
Financial Position and 2013 Company Highlights
(in Canadian dollars)

Bellus exited the first quarter 2014 with approximately $14 million in cash, cash equivalents, and short-term investments. The company is currently burning approximately $300,000 per month, and we forecast that the current cash position will be enough to last through 2017, which currently looks like it will be enough until all data from the confirmatory Phase 3 data has been reported, and even provides roughly 12-15 months to sign any potential licensing deals for Kiacta™ commercialization. For the year 2013, Bellus recorded revenues of $2.256 million, which consisted mainly of revenue recognized for accounting purposes from asset sales and license agreements as well as the service agreement entered into with Auven Therapeutics in 2010 for Kiacta™. The company spent just $1.27 million on R&D and $4.275 million on G&A expenses in 2013.

In August 2013, Bellus acquired all the issued and outstanding common shares of Thallion Pharmaceuticals Inc. for a purchase price of $6.266 million in cash or $0.1889 per common share and the issuance of one contingent value right (CVR) per common share. The transaction added a clinical stage product to Bellus' pipeline in a rare disease indication and increased the company's cash and short-term investment position by more than $1.1 million as Thallion had cash and short-term investments of approximately $7.4 million on closing of the transaction.

The CVRs issued to Thallion’s shareholders entitle the holder to: A) any additional purchase price consideration to be received by Premium Brands Holding Corp in 2016 (estimated by management to be up to approximately $1.5 million, or $0.0404 per CVR), B) 5% of the Shigamab™ revenue generated or received by Bellus, capped at $6.5 million (or $0.1812 per CVR), and C) net proceeds generated from the licensing, selling or otherwise commercializing of (i) diagnostic products or services using certain Caprion Proteomics Inc. products and (ii) all issued patents or pending patents pertaining to such Caprion Proteomics Inc. products, in respect of which Thallion has an ownership interest or monetary entitlement. Bellus had applied to list the CVRs on the Toronto Stock Exchange, but that request was rejected. Therefore, the CVRs will not be listed on a stock exchange.

During 2013, Bellus divested two non-core assets, Vivimind™, a natural health product for memory protection, and BLU8499, a drug candidate for the treatment of central nervous system diseases including Alzheimer's disease. Bellus licensed the Vivimind™ worldwide rights to FB Health S.p.A. for more than $2 million to be received over the next four years. FB Health is an Italy-based distributor of specialty natural health and pharmaceutical products targeting neurologists and geriatricians.

Bellus also entered into a worldwide license agreement with FB Health for BLU8499 and a family of analogs, along with an associated platform of chemotypes and clinical datasets, in exchange for an equity stake in FB Health. FB Health then sublicensed all its rights to Alzheon Inc., with Bellus set to receive a portion of all future payments received by Alzheon related to BLU8499 and royalties on net sales of BLU8499. Alzheon is a clinical-stage biotechnology company focused on developing the next generation of medicines for Alzheimer's and other neurodegenerative diseases.
MANAGEMENT PROFILES

**Roberto Bellini – President and Chief Executive Officer**
Mr. Bellini has served as President and CEO of BELLUS Health since January 1, 2010. Mr. Bellini previously oversaw the licensing and partnering activities of BELLUS Health Inc. Mr. Bellini’s experience includes responsibility for the investment and operational activities of Picchio Pharma Inc., a joint venture healthcare investment firm owned by FMRC Family Trust and Power Technology Investment Corporation. He is a sitting member of the Board of Directors of BELLUS Health. Mr. Bellini has been a member of The Neuro External Affairs Steering Committee since 2009 and he also sits on the McGill University Vice Principal (Research and International Relations) External Advisory Committee. Mr. Bellini holds a Bachelor of Science in Biochemistry from McGill University.

**Dr. Denis Garceau – Senior Vice President, Drug Development**
Dr. Garceau directs BELLUS Health’s drug development program, from toxicology to clinical evaluation through to approval of new products, and has been with the company since March 1997. He is also currently the Auven Therapeutics Global Project Leader for the Kiiacta™ development program. From 1986 to 1997, as a clinical scientist and product team leader for Hoechst Marion Roussel (now Sanofi-Aventis), Dr. Garceau successfully oversaw North American clinical programs and participated in global clinical development steering committees. He was responsible for developing clinical operating plans, designing clinical protocols, and supervising clinical trials. In 1985-86, Dr. Garceau completed a post-doctorate Research fellowship in Pharmacology at Merck Frosst Canada. Dr. Garceau holds a Ph.D. in Pharmacology from the Université de Montréal, and is currently a guest lecturer for the faculty of pharmacy of the Université de Montréal and Université Laval. He serves on the Board of Directors of CEPMED.

**François Desjardins – Vice President, Finance**
Mr. Desjardins is responsible for BELLUS Health’s finance and administration functions. He joined the company in 2003 as Director, Finance and Control and has held the position of Vice President, Finance since 2009. Mr. Desjardins has more than 15 years of experience in the biopharmaceutical industry, having held the position of Corporate Controller at BioChem Pharma for a period of six years. Mr. Desjardins is a member of the Canadian Institute of Chartered Accountants and holds a Bachelor’s Degree in Commerce from Sherbrooke University.

**Tony Matzouranis – Vice President, Business Development**
Mr. Matzouranis joined BELLUS Health in 2010 and currently oversees the company’s licensing and business development activities. He has over 15 years of experience in structuring and building successful partnerships via in / out-licensing, mergers and acquisitions and alliance management. Prior to joining BELLUS Health, Mr. Matzouranis was Director of Licensing at Thalian Pharmaceuticals (TSX: TLN). From 1999 to 2007, he held Business Development positions of increasing responsibility at Caprion Pharmaceuticals Inc. Mr. Matzouranis holds a Master’s degree in Molecular Biology from the Université du Québec à Montréal.
VALUATION AND RECOMMENDATION

We are initiating coverage of Bellus Health, Inc. (TSX: BLU) with a Buy rating and a price target of $2.50. Bellus is developing Kiacta™ for the treatment of AA amyloidosis. The compound is currently in a confirmatory Phase 3 trial after showing signs of efficacy in an earlier Phase 2/3 trial. The trial should finish patient enrollment in the second quarter of 2014 with results expected to be available in the middle of 2016. We have derived a fair value for Bellus based solely upon the value of Kiacta™, and believe a sale or licensing agreement will be the main value driver for the stock in the near term.

Bellus is partnered with Auven Therapeutics for the development of Kiacta™. Under terms of the agreement, Auven is funding 100% of the costs associated with the development of Kiacta™, including all costs associated with the confirmatory Phase 3 trial. Any revenue derived from Kiacta™, including a licensing deal or sale, will be split evenly between Auven and Bellus, assuming that the total divestiture transaction proceeds reach a pre-determined threshold. The two companies have employed the services of Lazard Capital as a financial advisor to explore the possible sale of Kiacta™. While the original intention was to complete the confirmatory Phase 3 study before offering Kiacta™ for sale, the companies have decided that a sale in the near term would allow the acquiring company sufficient lead time to prepare for a global launch of the compound and to have input into the regulatory approval pathway.

DCF Model

We have constructed a model to derive a fair value for Bellus Health based upon a discounted cash flow analysis where we estimate the future revenues that Kiacta™ would likely bring in after approval if Bellus were to market the drug on their own. We use this as a guide for what an acquiring company would reasonably be expected pay for Kiacta™. We are modeling for Kiacta™ to be priced at $200,000/year in the U.S., $150,000/year in the E.U., and have conservatively modeled peak market share of between 25-45%. We model that Bellus would receive 50% of revenues per their agreement with Auven and estimate a 50% net income rate. We apply a discount rate of between 15-25% and believe that the Phase 3 confirmatory study has a 75% chance of success.

The following tables give the net present value (NPV) of Bellus’ future cash flows from sales of Kiacta™ based on the aforementioned assumptions as well as the price per share based on 65.659 million shares fully diluted.

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<th>Market Share</th>
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NPV of Bellus’ Future Kiacta Revenues

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Bellus’ fair value per share

Based upon our model, we value Bellus at $2.50/share. This is based on a conservative 35% peak market share for Kiacta™ using a 20% discount rate. Given the current stock price, we believe that Bellus is significantly undervalued and offers investors tremendous upside at the current valuation.
We constructed the tables above to give investors a sense of the various scenarios we considered while deriving a fair value for Bellus. As this is a very fluid model, there are a number of caveats to our valuation that are worth discussing. The first is that for our model we assume Bellus will be selling Kiacta™ outright. We have forecasted what we believe are reasonable estimates for future sales of the drug and derived a net present value for those revenues to ascertain what an acquiring company might pay for Kiacta™. However, we note that a larger pharmaceutical company, with a greater sales and marketing force, could justify a much higher peak market share than what we have assumed, which could significantly increase the amount of money they would be willing to pay for the drug. This would in turn move our valuation in the above table to the lower left and would offer investors an even greater return than what we are forecasting. We reiterate the fact that Bellus and Auven have hired Lazard to facilitate the sale of Kiacta™, which we believe increases the likelihood that a larger pharmaceutical company will end up acquiring the drug.

Another caveat to our valuation is that our model does not account for Bellus signing a licensing deal instead of selling Kiacta™. We forecast Kiacta™ to have peak revenues of between $500 million and $1 billion, which would justify an upfront payment of $50 to $100 million coupled with mid-teens royalties. The upfront cash would certainly cause the market to re-price the stock appropriately, and depending upon the royalty rate could supply Bellus with a steady stream of income to deploy for development of additional products.

Lastly, even if our model is overly optimistic, and no company believes that Kiacta™ could achieve greater than a 25% market share and their cost of capital is greater than what we have forecast, the lowest fair value derived from our model still represents close to a 100% gain from the current share price (the upper right portion of the above table). Thus, we are confident that an investor in Bellus at today’s price can still expect a substantial rate of return on their investment.

Potential Risks to our thesis

- **The confirmatory Phase 3 study for Kiacta™ fails:** While we do not believe that this is likely to occur, and have assigned a probability of success for the confirmatory Phase 3 trial at 75%, we cannot entirely rule out the possibility that the Phase 3 study does not reach statistical significance. If this were to occur before Bellus was able to sell or license Kiacta™ it would have a severely negative impact on the stock and would require us to significantly reduce our fair value.

- **Bellus cannot sell/license rights to Kiacta™ for a reasonable price:** Bellus and Auven have recently indicated that they will look to sell or license rights to Kiacta™ in the near term before the end of the Phase 3 confirmatory trial. However, there is no guarantee that this will occur or that it will result in a significant financial gain for Bellus. While we forecast that Kiacta™ could potentially bring in hundreds of millions of dollars of revenue, we cannot forecast with any degree of certainty what a potential acquiring company would be willing to pay for the rights to Kiacta™ and the eventual sale price or licensing deal could be significantly lower than what we have forecast.

- **Bellus in-licenses another drug that costs money, increases burn, and means they have to raise cash again before the Kiacta™ Phase 3 data around mid 2016:** Bellus has stated that they are actively looking for additional products to in-license to bolster the pipeline. This could result in the company having to significantly increase their cash burn to develop these products and could result in the need to raise additional capital before a sale/licensing deal is reached for Kiacta™, resulting in dilution of current shareholders.
Bellus Health, Inc.
Income Statement (in Canadian dollars)

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<tr>
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Source: Zacks Investment Research, Inc.
Jason Napodano, CFA
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