CytoSorbents™

Working to Save Lives Through Blood Purification

CytoSorbents Corporation (NASDAQ: CTSO)
Q1 2016 Earnings and Operating Results Conference Call
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This official company transcript has been edited for clarity and does not differ materially in content from the actual conference call except where noted. Slide numbers have been inserted to allow readers to follow along with the associated presentation.

Operator

Good day everyone, and welcome to the CytoSorbents First Quarter 2016 Financial and Operating Results Conference Call. If you have a question during today's call, please press the star key followed by the digit one on your touchtone phone and be sure your mute button is turned off to allow your signal to reach our equipment. Today's call is being recorded and at this time, I would like to turn the call over to our moderator, Lee Roth. Please go ahead.

Lee Roth - Moderator

Thanks Leanne, and good afternoon. Welcome to the CytoSorbents First Quarter 2016 Operating and Financial Results conference call. Joining me today from the company are:

- Dr. Phillip Chan, Chief Executive Officer and President
- Vincent Capponi, Chief Operating Officer
- Kathleen Bloch, Chief Financial Officer
- Dr. Christian Steiner, VP of Sales and Marketing from Germany, and
- Chris Cramer, VP of Business Development

Before I turn the call over to Dr. Chan, I'd like to remind listeners that during this call, management's prepared remarks may contain forward-looking statements, which are subject to risks and uncertainties; and that management may make additional forward-looking statements in response to your questions today. Therefore, the company claims protection under the Safe Harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. Our actual results may differ from the results discussed today. And therefore, we would like to refer you to a more detailed discussion of these risks and uncertainties in the company's filings with the SEC.

Any projections as to the company's future performance represented by management include estimates that are current as of today, May, 9, 2016, and we assume no obligation to update these projections in the future as market conditions change. During today's call, we will have an overview presentation covering the financial and operating highlights for first quarter 2015 by Dr. Chan and Ms. Bloch.

Following that presentation, we'll open the line to your questions during the live Q&A session with the rest of the management team.

At this time, it's my pleasure to turn the call over to Dr. Phillip Chan. Dr. Chan, go ahead, please.

Phillip Chan

Thank you very much, Lee, and welcome everyone to the call this afternoon. We encourage all new investors to review our earnings release this afternoon and the investor presentation on our website, which provides detailed background information about the company. After a relatively short presentation, we will open up to a live Q&A session and an official transcript of today's call will be available within the next week on our website at www.cytosorbents.com.

Slides 4-5:

CytoSorbents is a leader in critical care immune therapy. We are leading the prevention or treatment of life-threatening inflammation in the ICU and cardiac surgery using our CytoSorb® blood purification. CytoSorbents targets a $20 billion opportunity in critical care and in cardiac surgery. It is the only specifically approved extra-corporeal cytokine filter in the European Union and is clinically proven to remove key cytokines in the blood of critically-ill patients. It has a very broad indication for use and is approved for any situation where cytokines are elevated.

CytoSorb® works with standard hemodialysis machines, continuous renal replacement therapy, or CRRT, machines, and heart-lung machines found in most hospitals today. CytoSorbents is a plug and play cartridge. CytoSorbents also removes many other inflammation mediators such as free hemoglobin, bacterial toxins, bilirubin, myoglobin, activated complement and others that are driving an uncontrolled inflammatory response. CytoSorb® has been safe and well-tolerated in more than 12,000 human treatments.

The goal of CytoSorb® is to control the deadly inflammatory response in an effort to try to prevent or treat organ failure, which is the leading cause of death in the intensive care unit today. In doing so, we hope to be able to improve patient outcomes and survival, while decreasing the cost of ICU and patient care.

We believe CytoSorb® is a very unique product that has the potential to revolutionize the treatment of many life-threatening illnesses such as those commonly seen in the intensive care unit today such as sepsis, acute respiratory distress syndrome, burn injury, trauma, pancreatitis, influenza, cytokine release syndrome and cancer therapy, and complications of cardiac surgery.

With that, let me turn it over to Kathy to go over our operating and financial highlights. Kathy?

Kathleen Bloch

Thank you Phil and good afternoon everyone. For today's call, I will be providing an update regarding CytoSorbents' First Quarter 2016 financial results including product sales as well as our working capital and cash runway.

Slide 7:

Turning to our reported financial results, CytoSorb® product sales for the quarter ended March 31, 2016 were approximately $1.6 million, which is a 127% increase over product sales of $704,000 for the quarter ended March 31, 2015. Our annualized product sale run rate, based on Q1 2016 sales, rose to $6.4 million; as compared to an annualized run rate of approximately $2.8 million one year ago. Total revenues, which includes product sales and grant revenue, was approximately $1.8 million for the quarter ended March 31, 2016 as compared to $723,000 for the same quarter in 2015, which is an increase of approximately 150%. In the first quarter of 2016, our gross margin rose to approximately $1 million, which is more than double our gross margin of $419,000 for the first quarter of 2015.

We continue to experience strong gross profit margins on product sales. Gross profit margins were approximately 62% for the quarter ended March 31, 2016 as compared to gross profit margins of approximately 59% for the first quarter of 2015.

Slide 8:

Now let's take a look at our quarter-over-quarter product sales. Our first quarter 2016 product sales of $1.6 million represent our best quarterly product sales ever. This is our fourth consecutive period for which we have reported quarter over quarter product sales growth. It is also our third consecutive quarter of achieving record sales. In the past, we have reported on the impact of the Euro. The Euro was relatively stable when comparing the first quarter of 2016 to the first quarter of 2015. Because of this, we have omitted adjustments for changes in the Euro. We do note that if the Euro to dollar exchange rate was unchanged from 2015, first quarter to 2016 sales would have been approximately $33,000 higher than the reported sales.

Slide 9:

Next, we will take a look at our trailing 12 month product sales chart. On this chart, the increasing trajectory of sales can be seen, which is especially evident in the most recent two quarters, Q4 2015 and Q1 2016. We are very pleased to be experiencing increases in both direct and distributor sales, both as a result of new customers and territories but primarily as a result of repeat orders from our existing customers. We expect that revenues will continue to climb as direct sales continue to grow, as existing distributors complete product registrations and generate repeat sales, and as additional distributors and strategic partners come on-board in new regions. Furthermore, as we continue to develop clinical data from our registry, investigator-initiated studies, and FDA trial, we believe we will be able to further accelerate acceptance and adoption of CytoSorb® in the marketplace.

Slide 10:

Finally some notes on our working capital position and our cash runway. As of March 31, 2016, we had approximately $6 million in cash and short term investments. Our burn rate, which includes expenditures related to our REFRESH I clinical trial, was approximately $1.8 million for the first quarter of 2016; which is lower than the average burn rate per quarter experienced in 2015 of approximately $2.6 million per quarter. The reduction in the quarterly burn was primarily a result of product sales growth. We believe our current cash will allow us to fund our operations into the fourth quarter of 2016. As we build sales and drive our operations towards break-even, we are exploring all potential funding sources with the goal of doing what makes the best sense for the company and our shareholders.

We have a variety of potential sources of capital available to us including the equity markets, debt-financing, and potentially strategic partners. Given the current state of the equity markets right now, we think debt-financing may be the best way to provide working capital to fund our operations into 2017 and serve as a useful bridge to more traditional fundraising. We currently have several competitive debt proposals that we are evaluating and we will have more to report on this in the future.

Turning to our capital structure as of March 31, 2016, on a fully diluted basis, we have approximately 29 million fully-diluted shares.

Now I would like to turn the call back to Phil. Phil?

Phillip Chan

Thanks very much, Kathy. Since we just gave a fairly comprehensive update a couple of months ago, I would like to focus more on the interest from clinical users as well as the clinical data that are being generated and published.

Slide 12:

Specifically, I wanted to focus on some recent events since our last update to shareholders. This is a picture from the 3rd International CytoSorb Users Meeting held in Brussels, Belgium in March 2016. This meeting brought together 107 people from 23 countries around the world to share their experiences, and to learn from each other, on how best to use CytoSorb® on their patients. This community of CytoSorb® users is very broad and continues to get larger every year, with many new people attending the meetings each time.

Slide 13:

This slide shows our activities at the ISICEM, or the International Symposium on Intensive Care and Emergency Medicine, conference that was held in Brussels immediately after our 3rd International CytoSorb® Users Meeting. On the left hand side, you can see the publication, ISICEM News, with Professor Jean-Louis Vincent, who is the organizer this event. As one of the largest critical care conferences in the world, this is one of our largest events. You can see that we are prominently featured on the front page of this daily update. Here is a picture of our booth, not in the same area with most of the others vendors, but in one of the major foyers through which most of the attendees pass by to get to their various lectures. You can see some of the activity in our booth that we are able to draw from the interest in our CytoSorb® technology.

Slide 14:

This next slide, I think, captures the sense of interest in CytoSorb®. This is a picture of our sponsored research symposium. During this time, we compete with all of the other major sponsors, and their programs, for attendees. Last year, we were in a room called the Arc room, where we were standing room only. This year, because of the interest in our therapy, we decided to upgrade our room to the Copper room, one of the largest auditoriums in this congress facility. From this picture, you can see that we had a great turnout, with more than 300 people attending our session on CytoSorb®.

In addition to the formal lectures we also had five posters selected for presentation. In the lower left and upper right hand corners, you can see a couple of pictures of the speakers during their CytoSorb® poster sessions. We will touch upon some of these presentations in just a moment.

Slide 15:

Fresenius Medical Care, the largest dialysis company in the world and our partner in the countries of France, Poland, Denmark, Norway, Finland, and Sweden, was also at ISICEM. At the conference, Fresenius initiated the marketing push behind CytoSorb®. You can see, on the right hand side, the Fresenius multiFiltrate dialysis machine in Fresenius' booth, and in the magnified picture on the left hand side, you can see CytoSorb®, which is hooked into the machine. Their sales people were there, in the booth, to answer questions for potential customers that were interested in the CytoSorb® therapy.

Fresenius also sent approximately 18 people from their dedicated countries to our 3rd International CytoSorb® Users Meeting from their dedicated countries and Fresenius has also been marketing CytoSorb® in country specific conferences such as the one in Poland last month. On the right hand side is an example of some of the marketing literature that they have used.

Most importantly, Fresenius has now confirmed to us that it plans to begin selling CytoSorb® in France, Poland, Denmark, Finland, Norway, and Sweden later this month. We will have an update later this month as that happens.

Slide 16:

There have now been more than 12,000 human treatments where CytoSorb® has been used, most of which have been in critically-ill patients, but there have also been more than 1,500 cases where CytoSorb® has been used during open-heart surgery. The vast majority of these treatments have been performed in day-to-day clinical practice. This is a graph of just a fraction of the patients that have been treated overall, but represents patients treated and reported in peer-reviewed journals.

What is interesting to note is that since the market launch of this product in late-2012, we have been gradually increasing the number of studies that have been published. In addition, during the first several years, most of the published studies were case reports, involving one to a handful of patients each. What you can see now, in the first four months of 2016 alone, we are easily within grasp of outpacing the number of studies that were published last year but on a significantly larger number of patients. This reflects our migration, in terms of studies, from predominantly case report studies to now more case series and small, randomized control studies. In addition to studies that we are sponsoring, there are now more than 55 investigator-initiated studies that are in various stages, 12 of which are now in the advanced stage and are enrolling patients actively, 13 already to enroll, and four studies that have been completed. Again, as those studies move towards publication, we will inform you of those as well.

Slides 17-18:

I wanted to give a quick update on our REFRESH I trial. REFRESH stands for the REduction in FREe Hemoglobin trial. We are currently running a 40-patient, eight center study, evaluating the safety and efficacy of intra-operative use of CytoSorb® in a heart-lung machine during elective, non-emergent complex cardiac surgery that is expected to last longer than three hours. These include cases such as aortic reconstruction, coronary artery bypass graft surgery (CABG) redo operations, multiple valve replacements, heart-lung transplant, and other procedures. The goal is to safely reduce plasma free hemoglobin and other inflammatory mediators generated during the surgery that can cause post-operative complications.

We are working with major cardiac surgery centers including Baylor College of Medicine and Texas Heart Institute, Baystate Medical Center, Columbia University, Cooper University Hospital, University of Kentucky, University of Maryland, University of Pennsylvania, and the University of Pittsburgh Medical Center. I am pleased to say that all sites are currently active in the trial and the trial is now nearly two thirds enrolled at 63%. We fully expect to be complete, in terms of enrollment, by mid-2016 with database lock and top-line results available in the third quarter of 2016. If everything goes well, we will have discussions with the FDA to decide upon a pivotal registration trial called REFRESH II, which we hope to start in early 2017.

Slide 19:

In addition to REFRESH I, there has been a lot of other activity on the cardiac surgery side, particular in Europe. This first study is being conducted at the University of Cologne and an interim analysis was reported at the 3rd International CytoSorb® Users Meeting. 165 patients out of a total of 300 patients have been enrolled into this three-arm randomized study, evaluating the intra-operative use of CytoSorb® during low risk open heart surgery. In the interim analysis, they reported a statistically significant reduction in sternal wound infections, which is a very complex and expensive complication following cardiac surgery, so it's very exciting.

The second study that was reported at our 3rd International CytoSorb® Users Meeting was the 10 patient cardiac surgery evaluation study led by Professor Christophe Baufreton, M.D., PhD, who is an accomplished cardiothoracic surgeon and Vice Dean of Research at the University Hospital at Angers, France. In a complex cardiac surgery patient population similar to those in the REFRESH I study, they demonstrated improved hemodynamic stability in most of the patients, particularly in two patients undergoing valve replacement surgery due to endocarditis. Endocarditis is caused by a bacterial infection, often Staphylococcal or Streptococcal, of the heart valve which can destroy the valve and cause valvular incompetency. Patients often exhibit a septic phenotype and are often unstable post-operatively. In the patients of this study, the investigators observed a reduction in the need for vasopressors, and a decreased need for expensive extracorporeal life support.

Just recently, a study was published from the Medical University of Vienna, which represented the first published randomized controlled study of CytoSorb® used during cardiac surgery. The study followed 37 patients randomized to either have CytoSorb® or not have CytoSorb® intra-operatively during low to medium risk cardiac surgery. The study demonstrated safety and technical feasibility using CytoSorb® with no complications noted.

Interestingly, within this low to medium risk patient population, and unlike REFRESH I and other patients undergoing complex cardiac surgery, these patients did not have severe inflammation with IL-6 levels peaking post-operatively at only approximately 125 pg/mL, which is what a patient might experience with a community acquired pneumonia that is treated successfully with outpatient antibiotics. Many of these patients underwent relatively less invasive cardiac surgery procedures like CABG or bypass graft surgery where there is not a lot of cutting into the heart and therefore not a lot of bleeding or hemolysis. These procedures also have relatively short cardiopulmonary bypass times, and not much hemolysis. This is in contrast to the much more complex procedures being performed in REFRESH I and in other studies, where patients can be on the operating table on cardiopulmonary bypass for four to ten hours at a time.

Slide 20:

Another study that was recently published was a study on post-operative SIRS, or the Systemic Inflammatory Response Syndrome following cardiac surgery, by Prof. Dr. med. Karl Traeger at the University of Ulm, Germany, one of the original pioneers in the use of CytoSorb® in this indication. This was yet another key series on 16 consecutive cardiac surgery patients who developed post-ops SIRS following prolonged cardiopulmonary bypass with shock, requiring vasopressors, and acute kidney injury requiring hemofiltration - a form of blood purification similar to dialysis. These graphs depict the data from individual patients, where they either received one CytoSorb® treatment, two CytoSorb® treatments, or three CytoSorb® treatments.

On the left-hand side you can see that their levels of cytokines are very high. For example, IL-6 in many of these patients was on order 500 to 8,000 pg/mL. This, again, is in contrast to those in the previous study where those patients had peak IL-6 cytokine levels of 125 pg/mL, and in contrast to all of us on the phone who have an IL-6 of less than 10 pg/mL. Therefore, these patients were highly inflamed after their surgery, with shock requiring vasopressors and kidney failure requiring hemodialysis.

What these charts also show, however, is that in addition to reducing these key cytokines, treatment with CytoSorb® also correlates with improvement in hemodynamic stability. You will recognize hemodynamic stability as a common theme through these various slides and this is what doctors are seeing as well. They are able to regain control of their "out-of-control" patients and get their blood pressure up to a stable level that is sufficient to push oxygenated blood to their vital organs. What you can see on the right-hand side is the mean arterial blood pressure increasing - a good thing in these patients. While simultaneously in the lower two graphs, we see the reduction in the need for vasopressors broadly, from baseline compared to right after treatment and then 24 hours after CytoSorb® treatment is done. Overall, the key findings of the study was that the therapy was safe and well-tolerated, with a marked decrease in cytokines during the course of CytoSorb® treatment and the achievement of hemodynamic stability and reduction in vasopressors and lactate. Interestingly, although the mortality here was approximately 37% mortality in these patients, most of those deaths couldn't have been helped by CytoSorb®. The first patient who died, expired from complications to a GI bleed related to a coagulopathy, four died based on a withdrawal of care, due to an advanced directive. This is similar to a "do not resuscitate or intubate" advanced directive order, where a patient can limit the extent of medical care in case of a life-threatening illness. These patients did not want to be hooked up to machines and were taken off of life support. The last patient died from refractory multi-organ failure. Generally, the therapy has been very helpful in resolving this post-op SIRS, which is a major problem following cardiac surgery all over the world.

Slide 21:

Switching gears a little is our next slide on the removal of bilirubin. The liver is a major detoxification organ and patients with either chronic liver failure - due to alcoholic cirrhosis, NASH, or non-alcoholic steatohepatitis, or viral hepatitis - as well as those with acute liver failure due to fulminant infection, poisoning from mushrooms or from drugs like Tylenol, shock, or other causes, will have high levels of unconjugated bilirubin which can be neurotoxic. This clinically manifests itself as jaundice. On the lower left hand side you can see a person who has jaundice by the yellowish coloration of her normally white sclera in her eyes and the yellow pigmentation of her skin. CytoSorb® is very effective in reducing bilirubin, as you can see on the right hand side in this poster, which was presented at ISICEM. The CytoSorb cartridge normally has white beads. After having treated this liver failure patient and flushing the blood out of the cartridge with saline, what is left are beads that are no longer white but are heavily pigmented yellow with bilirubin, as the bilirubin has been absorbed into the beads. CytoSorb® is very

effective at removing bilirubin, cytokines and other potential toxins that a compromised liver cannot remove.

In some hospitals, CytoSorb® is being used as an adjunct therapy to other types of liver dialysis therapies, such as MARS (Molecular Adsorbent Recirculating System) and others. Some have used it even as a standalone therapy for liver failure because it can remove many toxins that the liver normally detoxifies and it has also been capable of removing many cytokines, which other liver dialysis therapies cannot. These cytokines and other inflammatory mediators are often a major problem in patients with liver failure. This has the potential to be a large market for us, as liver failure is estimated to be the 12th leading cause of death in the U.S. and the fourth leading cause of death in China and in many other countries around the world where hepatitis is a major heath concern.

Slide 22:

Switching gears again, I wanted to go over a few of the posters that were presented at the ISICEM conference. This poster was a case series of eight patients; two with severe sepsis and six with septic shock where CytoSorb® was used with continuous renal replacement therapy, which is typically used for patients with kidney failure for 24 hours at a time; with a median treatment time of two days. Those that benefited from CytoSorb® showed a very rapid and very quick improvement in hemodynamics with a rapid reduction of vasopressors, a reduction in procalcitonin (a sepsis biomarker), and an improvement in renal function.

Typically, what we see in clinical practice today, is that when CytoSorb® works, we can see it work relatively quickly. These are typically patients that are treated early. In this patient population, the mortality was 25%. The two patients who died showed no positive response to therapy and what we have heard is that these patients were treated on the later side. The authors suggest that the timely use of CytoSorb® is very important and recommend additional studies to confirm their findings.

Slide 23:

This is another case series on septic shock and SIRS (the systemic inflammatory response syndrome) where researchers looked at 14 patients with both infectious and non-infectious causes of massive inflammation, respectively. 29% had abdominal sepsis, 50% had pneumonia, 14% had pancreatitis and 7% had other causes. All of these patients were very, very ill with a mean APACHE II score of 37, predicting a risk of death greater than 85% in patients with sepsis. CytoSorb® use led to a pronounced tenfold decrease in vasopressor requirements, which are strong medicines, like epinephrine, that are required to help boost the blood pressure in cases of shock. Simultaneously, they saw a reduction in blood lactate levels. Lactate is a product of anaerobic metabolism that occurs when there is not enough oxygen or blood delivery to tissues. Lactate levels can go very high particularly when organs are not well-perfused.

In this particular case series, CytoSorb® lead to a reduction in lactate levels by approximately 50% on average with an overall survival of 36%. But when CytoSorb® therapy was started early, within 24 hours of admission to the ICU, survival was 67%. This was a quite dramatic increase in survival compared to what was expected. Investigators recommended early usage of CytoSorb®, less than 24 hours after admission, similar to how CytoSorb® is being used clinically today.

Slide 24:

Last but not least, we would encourage you to visit www.cytosorb.com for the Case of the Week. We have had excellent feedback from both physicians and investors on the many exciting cases reports discussed in the CytoSorb® Case of the Week at our cytosorb.com website. These cases highlight the ongoing successes that clinicians continue to have as they treat earlier and more aggressively. And our goal using these reports, as well as our Proceedings of the International CytoSorb® Users Meeting publication that you can see above here on the right, as well as our Case study summary booklet, is to broadly teach users how and when the CytoSorb therapy is being used most effectively so that we can improve survival rates around the world. Today, CytoSorb® is being used to help regain control patients and to help save the lives of those who either have SIRS or sepsis around the globe.

That now concludes my formal remarks. Lee, let me turn the call back to you for questions.

Lee Roth

Thanks Dr. Chan, Leanne we are ready to begin polling for questions.

Question-and-Answer Session

Operator

Thank you. [Operator Instructions] we will go ahead and take our first question from Jonathan Aschoff with Brean Capital.

Jonathan Aschoff

Thanks. Phil, I was wondering with Fresenius, it seems to be taking more time to launch than I would have originally expected? What has been going on there in the last few months? And Kathy can you just give me a little more detail on the different types of debt financing you're looking at?

Phillip Chan

I think in terms of Fresenius, they did not become the largest dialysis company in the world because they were careless about what they were doing. I think they have been extremely methodical and very careful in terms of making sure all the pieces were in place before launching the product in these territories. It is their reputation on the line, it is their sales people out there pitching CytoSorb® and so I think as a large corporation they have been working to make sure that everything is in place before they go out there.

We call these "last mile" issues, of which there are so many, particularly when looking to launch in the multi-country territory as Fresenius is doing. So during the prior months, I would say in the last six months, Fresenius has been out there actively talking to their key opinion leaders, prepping the market for this market launch and availability of CytoSorb® in six countries. I certainly don't think that it has been wasted time. In fact, I think they have been generating a lot of pent up demand for the product and that will hopefully translate into more rapid adoption when the product is finally launched as they have told us later this month.

Jonathan Aschoff

How would you contrast your sales force's pitch versus what Fresenius' is planning and how they are planning on pitching it?

Phillip Chan

We have worked very closely with Fresenius to make sure they have learned from our extensive direct sales experience with CytoSorb® in the German, Austrian and Swiss market. Much of their marketing materials, for example, reflect a lot of the content provided by our team. Their people have undergone extensive training through multiple sessions with our sales force and trainers. I think they are very well prepared for this market launch. The approach and the pitch will be very similar to how we sell in Germany which is, of course, the home base for Fresenius. We look forward to see what their sales people and distribution can do.

Jonathan Aschoff

Okay and Kathy?

Kathleen Bloch

Hi Jonathan, we ran a process that involved about 12 different lenders, some of whom we have known from the past. I don't want to be too specific at this time but I will tell you that it was a very competitive process. The net was cast wide in terms of what we looked at because we would like this to be an uncomplicated financing. That is what we are working towards.

Jonathan Aschoff

Okay. Thanks guys.

Phillip Chan

Thanks very much Jonathan.

Operator

We will take our next question from Sean Lee with H.C. Wainwright.

Sean Lee

Good afternoon Kathy and Phil. Congratulations on a great quarter and thank you for taking my questions.

Phillip Chan

Thanks Sean.

Sean Lee

In addition to Fresenius, do you have any update on the other geographies such as Russia and the Middle East?

Phillip Chan

We have been making substantial progress in those areas and although we are not prepared to talk about it today, we expect to be able to talk about that in the near future.

Sean Lee

Okay. Also on the international registry data, how is that being compiled and when can we expect some interim results from that analysis?

Phillip Chan

The International CytoSorb® Registry collects treatment data from countries all over the world. We have more than a 100 institutions now registered to submit data, with many of them actively submitting data. The registry is being independently managed by the University of Jena and the Center of Clinical Studies in Germany, led by Professor Frank Brunkhorst. University of Jena is well-known as the epicenter of sepsis research in Germany, and perhaps in all of Europe. They founded and are the home of the German Sepsis Society, they started the Global Sepsis Alliance, and have the only government-funded sepsis institute in the country. So they are very well-positioned to manage this registry.

The actual data analysis of the registry is being managed by a scientific steering committee that is independent of CytoSorbents. Because of this, they may evaluate the data in the best way they see fit. We do have access to the data, so we can use it for our own purposes. They have told us that the first analysis is completed. That has been on a small number of initial patients, and a report will be issued soon. The next analysis will be coming up shortly as the numbers of patients have increased.

The goal of this International CytoSorb® Registry, again, is not just a sepsis registry, but is much broader, collecting data in cardiac surgery, liver failure, acute respiratory distress syndrome, pancreatitis, trauma, burn injury, and many other indications.

Sean Lee

Thank you for the color on that. Final question for me, last week I saw that you guys established a subsidiary for Switzerland, what are your plans for the country?

Phillip Chan

Switzerland has always been considered one of our direct markets and establishment of a Swiss subsidiary is more of a virtual entity and is not resulting in any significant cost to the company. It allows us, however, to better serve key opinion leaders and to better respond to expected demand with our sales force in Switzerland falling under that umbrella. There are also advantages in terms of the value-added tax (VAT) and other benefits. So as we grow our business in Switzerland, it just made sense to form that subsidiary at this time.

Sean Lee

I see, thank you for taking my questions.

Phillip Chan

Sure Sean. Thank you.

Operator

We will take our next question from Jason Kolbert with Maxim GRP.

Gabrielle Zhou

Hi, it's Gabrielle Zhou for Jason. My question is can you walk me through the direct sales process in the EU and how does each adoption translate into product revenue? Thank you.

Phillip Chan

Welcome, Gabrielle. The sales process is relatively straight-forward. On the ICU side, we typically market to the head of the department in either the medical ICU (MICU), the surgical ICU (SICU), the cardio thoracic ICU (CTICU), or the trauma ICU. The sales pitch is fairly simple because physicians today already know about the massive inflammatory response that occurs in many life-threatening illnesses such as sepsis and infection, trauma, and many of the other diseases that we have talked about.

The role that cytokines play in this massive inflammatory response that can lead to organ failure and death is well-understood, and the physicians we talk to all understand that there have not been any effective therapies that can remove cytokines and other inflammatory mediators. Not that others haven't tried, and we can certainly talk about the competitive landscape if you would like. The important part is that CytoSorb® is currently viewed as a leader in the field. When we approach new key opinion leaders in Germany, most have already heard about CytoSorb®. We find that many are very interested in talking to us and potentially starting CytoSorb® at their institutions because they've heard positive word of mouth from their colleagues at other institutions, often in the major hospitals in the major cities throughout Germany. In other countries, it is similar. We continuously work with our distributors to make sure they also have the tools and the messaging to best drive adoption in their countries.

It only takes about 10-15 minutes to explain the technology to a physician. And the good part is that it is a very easy therapy for them to wrap their arms around. They already do a lot of extracorporeal (out of the body) blood purification therapy in the ICU today. For example, a third to a half of all patients in the ICU will develop kidney failure and require hemodialysis or hemofiltration, the two leading forms of extracorporeal blood purification. So adding CytoSorb® to a hemodialysis circuit or using it by itself is relatively simple.

Once they agree to use it, they typically start off with a small order that they push through their purchasing department. Depending on where the account is, we either fill the order from the U.S. or from our European GmbH subsidiary in Berlin, Germany. Whenever they want to use the therapy again they just place another order through purchasing and that order then comes directly to us. So it's a fairly simple process. The other element in the process is reimbursement. Hospitals typically purchase directly from CytoSorbents and then the hospital seeks reimbursement as a separate measure. We, of course, help to drive reimbursement in our direct territories, and have recently hired a reimbursement specialist who will be helping us establish reimbursement in many of the other major territories around the world. And so that's a little bit about this sale process. Did that help to answer your question?

Gabrielle Zhou

Yes, thank you for the detail. Do you have any post sales strategies for each patient treated with CytoSorb®? In the EU, will you be able to monitor them and use the data from these studies for a potential US trial?

Phillip Chan

Yes, we established the International CytoSorb® Registry to collect treatment data from all over the world, in a variety of indications. The registry is also a repository of clinical trial data from investigator initiated studies. The CytoSorb® registry is a GCP or good clinical practice registry and the data collected can be used to support our U.S. regulatory applications, but would not be used in lieu of a U.S. based trial. But certainly any kind of papers that are published in peer review journals as well as reports from our registry could be used in support of our discussions with the FDA.

Gabrielle Zhou

Okay, great. Thank you.

Phillip Chan

Thank you very much.

Operator

We will take our next question from Andrew D'Silva with Merriman Capital.

Andrew D'Silva

Good afternoon everyone. Thanks for taking my questions. I just have a couple of quick questions here. First off, during the quarter, were there any initial large stocking orders that took place from any large first time customers that you can discuss, or was it a fairly stable order process as we have seen in previous quarters?

Phillip Chan

Kathy would you like to take that?

Kathleen Bloch

Yes, I will take that one. No, there were no initial stocking orders that were material to our sales. So I would characterize the growth as due to strong repeat sales.

Andrew D'Silva

All right. And did the fourth quarter, by chance, have any large stocking order or is that the same situation as with the first quarter of this year?

Kathleen Bloch

That will be the same Andy, no large initial stocking orders for the fourth quarter of 2015 either.

Andrew D'Silva

Okay great. And then with Biocon, anything going on there? A little while ago, they were working on gathering data and increasing marketing. Has there been any progress with them that you can discuss and then staying on that topic, maybe discuss some of the differences between the strategic partnerships with Biocon and Fresenius. Do you expect the ramp up with Fresenius to be quicker than with Biocon?

Phillip Chan

The relationship with Biocon has been going very strong. We met recently with their leadership and they reiterated their commitment to CytoSorb® and are actually looking to establish a separate division within Biocon to help ensure that they have dedicated resources to push CytoSorb® further into the market. Today, Biocon is pursuing the market in India as well as Sri Lanka, but we have been in discussions with them about expanding that relationship given the great job they have been doing to date. Biocon is an example of a large multinational corporation that has a very strong sales and marketing arm similar to Fresenius. Biocon has been selling critical care antibiotics, particularly the carbepenem class of antibiotics, into the ICU for a long time and have established a lot of key opinion leader relationships in critical care. Because of this, it has been a very smooth process to add CytoSorb® to the selling process. Together, we believe we are providing the most comprehensive approach to the treatment of sepsis with Biocon's antibiotics treating the infection and CytoSorb® treating the runway immune response.

We anticipate that Fresenius, because they manufacture and sell the dialysis machines and dialysis disposables, such as hemodialysis and hemofiltration filters, and own this channel in these hospitals, may ultimately roll out much faster than Biocon, because they can put the CytoSorb therapy directly into their sales channel. Fresenius is a leader in extracorporeal therapy, but unlike standard hemodialysis or hemofiltration which cannot remove cytokines, CytoSorb® is adding a new capability to the Fresenius acute care arsenal to reduce cytokines in patients with a massive inflammatory response and to potentially reduce the risk of organ failure and death. For these reasons, we are very excited about the Fresenius pending launch and look forward to see what they can do.

Andrew D'Silva

All right, just a couple more quick questions here. As far as interest goes, have you seen any increased interest with existing hospitals or key opinion leaders since you released your most recent data from the 3rd International CytoSorb® Users Meeting or other conferences where you have had data come out? That could be sales-related inquiries, or just inquiries about the data. Has there been increased traction that's new and attributable to that data?

Phillip Chan

Yes, Christian would you like to comment on the response of key opinion leaders following our recent conferences and other activities?

Christian Steiner

Certainly. As you have said, there were a number of presentations on new clinical data at the different conferences. In particular, the presentation on the refractory septic shock study at the University of Greifswald was a nice milestone for CytoSorb® and has led to a situation where many key opinion leaders can see that we are at a new quality level of data. Currently we are waiting for the publication of this study, confirmation of these data from others, and publication of other studies. Based on the sales cycle, it often takes weeks to months for these new publications to begin to affect usage and to impact sales, but the good news is that we have been supporting clinical studies for many years, with the goal of generating clinical data, and getting these data published. We are already seeing the impact of these efforts in our current sales growth.

Andrew D'Silva

Okay. Good. Last question is: Kathy, I noticed that your R&D spend dropped sequentially and year-over-year. I was expecting maybe a slight increase going forward primarily due to the REFRESH study. Is there a reason for the decline or is that just an anomaly with respect to the increase going forward?

Kathleen Bloch

Our grant activity, which absorbs many of our fixed R&D expenses is up over last year so that's the reason that the R&D spend that you see is smaller. The portion of spend in R&D that relates to revenue is included in cost of goods sold and that results in a reduction in the amount shown on the R&D expense line.

Andrew D'Silva

Got it. Great. All right, thank you very much for answering my questions and good luck going forward for the rest of the year.

Phillip Chan

Thank you very much Andy.

Operator

We will take our next question from Jan Wald with Benchmark.

Jan Wald

Thank you. Good afternoon everybody and congratulations on the quarter. You had a good one. I have two questions. My first question is: As you move more towards a distributor model in Europe, what percentage of your sales do you think you are going to be distributor based and what's the effect on margins do you think?

Phillip Chan

Currently our blended gross margin is 62% and that is a blend of higher margin direct sales versus lower margin distributor as well as partner sales. As we move forward, we expect that our gross margin will continue to rise, as we expect to see a good balance between direct sales as well as distributor and partner sales. We also expect to benefit from economies of scale as our volumes increase and as we expand the market worldwide, while continuing to reduce costs and achieving manufacturing efficiencies. At the end of the day, we should have a nice mix between dollar and euro based revenues. We have not broken out the exact ratio of direct to distributor sales because of the high degree of variability from one quarter to the next. However, we have a product and business model that is expected to drive excellent profitability while increasing gross margins over time.

Jan Wald

Okay. My last question is just trying to understand the U.S. regulatory strategy little bit more. It sounds like you believe you will begin a US pivotal trial in early 2017 in cardiac surgery. When do you think you will be able to submit to the FDA? Would you do something else in parallel or wait for approval in cardiac surgery?

Phillip Chan

As we discussed last time, we believe the cardiac surgery trial represents a lower risk way to get approved in the United States compared to a critical care trial. In open heart surgery, the patients are more homogenous, the length of the injury caused by the surgery and cardiopulmonary bypass is known, the injury can be quantitated by the production of inflammatory mediators such as free hemoglobin and cytokines, and importantly, there is an opportunity to intervene immediately with CytoSorb® and potentially reduce the injury to the body from these inflammatory mediators as they are being generated. Numerous studies correlate the levels of inflammatory mediators with adverse clinical outcomes post-operatively, including kidney and lung failure and circulatory collapse. Because of this, cardiac surgery remains the focus of our U.S. regulatory strategy. In our discussions with the FDA in the past, they have left the door open for a potential *de novo* 510(k) application to get CytoSorb® approved as a tool during open-heart surgery, but that is not the default. That would be just upside for the company.

However, the default regulatory pathway for CytoSorb® in cardiac surgery is the PMA (pre-market approval) path. We estimate that REFRESH 2 will be a 300 to 400 patient randomized controlled registration trial in a patient population similar to what we are using in REFRESH 1. REFRESH 2 will likely be focused on demonstrating improvement in clinical outcomes, such as a reduction in organ dysfunction following surgery. The regulatory path that we take will be determined by the FDA. Although a *de novo* 510(k) looking at biomarker reduction would be smaller and faster to complete than a PMA trial, we would still likely extend the study, taking advantage of an adaptive trial design, to demonstrate clinical benefit in the post-market period. Enrollment in either study is expected to go relatively quickly, as CytoSorb® would only be used during surgery, with only blood samples taken and clinical outcomes recorded, in the post-operative period. Patients are followed through their ICU stay and are then called or visited at 30 days to see how they are doing.

So, we think that this study can be done very rapidly as one center can do more than one patient a month. We expect to complete a future REFRESH 2 PMA trial in 1.5 to 2 years, followed by an accelerated review by the FDA, and then if everything went well, we would be on the market in 2019.

Jan Wald

And would you be looking for other labels during that time or will you focus the effort in the U.S. and wait until that trial is completed and you are able to launch the product for cardiac surgery?

Phillip Chan

We are absolutely looking at a parallel path to add to the label for CytoSorb® in the United States and are actively designing smaller clinical studies, in the area of sepsis for example, to be conducted here as well as other studies aboard. These studies are designed to help define a pivotal trial in the U.S. for that particular indication. As we have discussed in the past, there are many, many other applications that CytoSorb®, as a broad spectrum filter, can be used for, so we are actively evaluating other strategies to get CytoSorb® approved in United States and add to that label in parallel.

Jan Wald

Okay thank you very much.

Phillip Chan

Sure Jan, thank you.

Operator

And we will take our next question from **Keay Nakae** with Chardan Capital Markets.

Keay Nakae

Thanks. Phil, can you remind us about some of the details associated with the Fresenius contract, and for the launch here shortly, are you providing them with some amount of initial inventory and at what point do you recognize that as revenue? Thanks.

Phillip Chan

Sure. We have not made the details of the agreement with the Fresenius publicly available but what we have said in the past is that this is an exclusive strategic distribution arrangement with Fresenius where they are bound to minimum annual purchases to maintain exclusivity in the six countries. I think that those numbers, should they be able to meet their annual minimums, would be material over time and I think on the last call we mentioned that they would be potentially 7 digits or more. Recall that Fresenius is a $17 billion year in revenue company and this is a product that addresses a $20 billion total addressable market in critical care medicine worldwide and a $1.0 to 1.5 billion market in Germany alone. The numbers we are talking about are very doable, particularly in these major markets. If Fresenius meets our expectations, they could be a very significant partner for us.

Keay Nakae

Okay. That's all I have thanks.

Phillip Chan

Thank you very much Keay.

Operator

And we will take our next question from Brian Marckx with Zacks Investment Research.

Brian Marckx

Hi guys congratulations on the quarter. Was any of the Mycotoxin grant in the Q1 revenue?

Kathleen Bloch

There was a very minor piece of that Q1 grant revenue related to Mycotoxin.

Brian Marckx

Okay. So you talked about the Cologne cardiac study. Can you talk a little bit more in detail about that and when you think that may read out in terms of the full results? Is there any sort of overlap in terms of end points or efficacy measures that you are looking at in that study as it compares to the REFRESH study?

Phillip Chan

The University of Cologne study is a three arm study looking at three groups. One is patients undergoing cardiopulmonary bypass without CytoSorb®. The second is patients undergoing cardiopulmonary bypass with CytoSorb®. And the third is patients undergoing off pump surgery, which is typically for less complex procedures. In our discussions with the investigators, because this was one of the first randomized controlled studies of CytoSorb® during cardiac surgery in the world, their ethics committee wanted them to start off with a low risk population similar to the population that was presented in the Medical University of Vienna paper where they were low to moderate risk patients. In these patients, we do not expect to see major changes in cytokines, although they may have presented some data already where they have seen some changes in cytokine levels. The therapy has been safe and well-tolerated with no complications so far in the study. Safety, ease of use, and tolerability are common themes running through these CytoSorb® studies in cardiac surgery patients. At the most recent 3rd International CytoSorb Users meeting, the investigators did report on a statistically significant reduction in sternal wound infections. This is an important finding because of the potential complications that sternal wound infection and mediastinitis may cause in these patients, including a high mortality rate if it gets that far.

Brian Marckx

Okay, great, and relative to liver failure which sounds like it's kind of a new application, if you will, that you have been looking at, is that something you think you may pursue more directly in future case studies or maybe even a formal clinical study in Europe or potentially in the U.S.?

Phillip Chan

Yes, there are some ongoing studies being planned for liver failure. Christian if you want to talk a little bit about some of that you can. I think that liver failure is a very interesting market for us and that we have seen a lot of physicians who are using the product in this indication and seeing a lot of very exciting results using the therapy. These are anecdotal but physicians are reporting the ability to bring some patients out of hepatic encephalopathy, which is one of the major complications in patients with end stage liver disease. The reduction of bilirubin and other inflammatory mediators is also another common observation. It is becoming an area of increasing focus for us, and certainly if the market wants this and if the data continues to come back very positive, it will of course be an area that we would look to get more randomized controlled data on, in a company sponsored study.

Brian Marckx

Great. Thank you.

Phillip Chan

Sure.

Operator

And at this time I would like to turn it back to management for any additional or closing remarks.

Phillip Chan

Thank you everyone for taking the time today for this call. We really appreciate your participation. If you do have any other questions, please feel free to reach out to Amy Vogel at avogel@cytosorbents.com and we will try to answer your questions where possible. In the meantime, we hope to meet many of you at our annual meeting on June 7, 2016 in New York City and look forward to the next update on the next quarterly call. Thank you very much everyone. Good night.

Operator

Thank you. That concludes our conference for today. I would like to thank everyone for their participation and have a great day.