CytoSorbents™

Working to Save Lives Through Blood Purification

CytoSorbents Corporation (NASDAQ: CTSO)
2015 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 2015 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. At this time, I'd like to turn the conference over to our moderator, Lee Roth. Please go ahead.

Lee Roth – Moderator:

Thank you and good afternoon. Welcome to CytoSorbents 2015 Operating and Financial Results Conference Call. Joining me today from the company are:

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

Before I turn the call over to Dr. Chan, I'd like to remind listeners that during the call, management's prepared remarks may contain forward-looking statements which are subject to risks and uncertainties. Management may make additional forward-looking statements in response to your questions today. Therefore, the Company claims protection under Safe Harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. Actual results may differ from results discussed today and therefore, we 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 today as of March 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 2015 by Dr. Chan and Ms. Bloch. Following that presentation, we will open the line to your questions during the live Q&A session with the rest of the management team.

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

Phillip Chan - CEO:

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. An official transcript of today's call will be available in the next week on our website at www.cytosorbents.com.

Slides 3-5:

CytoSorbents is a leader in critical care immunotherapy. We are leading the prevention or treatment of life-threatening inflammation in the ICU and cardiac surgery using CytoSorb® blood purification. CytoSorb® removes the fuel to the fire of inflammation and targets the more than $20 billion opportunity in critical care and in cardiac surgery. It is the only specifically approved extracorporeal 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 use in any situation where cytokines are elevated. It works with standard dialysis and continuous renal replacement therapy (CRRT) machines as well as heart lung machines that are found in hospitals today and is a plug-and-play cartridge. CytoSorb® also removes many other inflammatory mediators such as free hemoglobin, bacterial toxins, bilirubin, myoglobin, complement and other factors that are driving an uncontrolled inflammatory response.

CytoSorb® has been safe and well-tolerated in more than 10,000 human treatments. And 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 seen in the intensive care unit today, such as sepsis, ARDS, burn injury, trauma, pancreatitis, influenza, cytokine release syndrome in cancer immunotherapy, and complications of cardiac surgery.

With that, let me turn it over to Kathy Bloch to go over some of 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 2015 financial results including product sales and also an update around our working capital and cash runway. But before I go into these details, I would just like to say

that we had a really solid year from a financial standpoint, which concluded with ringing the NASDAQ opening bell to celebrate our one year anniversary of being on the NASDAQ exchange.

We are also now classified as an accelerated filer by the SEC. Today, we filed our annual report on Form 10-K. for the year ended December 31, 2015 in advance of the filing deadline required for accelerated filers, which is March 15th.

Also, as required by the Sarbanes-Oxley Act, and our annual financial audit for 2015, we have had our system of internal controls audited. I'm pleased to report that our auditors have given their opinion that we have maintained, in all material respects, effective internal controls over financial reporting. This should give our shareholders assurance regarding the reliability of our financial information and reports.

So with that, let us look at our year-over-year sales.

CytoSorb® product sales for the year ended December 31, 2015 were approximately $4 million, which is a 29% increase over our product sales for the year ended December 31, 2014 of approximately $3.1 million. 2015 product sales were negatively impacted by approximately $637,000 as a result of the declining exchange rate for the euro. In other words, if the Euro would have remained unchanged from 2014, 2015 product sales would have been approximately $4.7 million, which is an increase of 49% over 2014 product sales.

Our grant revenue for 2015 was approximately $748,000 as compared to approximately $987,000 in 2014.

We continue to experience strong gross profit margins on product sales. Gross profit margins were approximately 64% for the fourth quarter of 2015 and approximately 62% for the year ended December 31, 2015.

Slide 8:

I want to turn to our fourth quarter 2015 product sales chart. Our product sales were $1.5 million, our best quarterly revenue ever. This is an increase of approximately $624,000, or 72% over the fourth quarter 2014 product revenue, which was approximately $871,000.

This chart shows the Euro adjusted quarterly sales of the company since we began commercialization of our product. The dark blue portion added to the top of the 2015 quarterly bars adjust the sales for the four quarters of 2015, as if the Euro to dollar exchange rate was unchanged from the same period in 2014. Our Euro-adjusted sales for the fourth quarter of 2015 were approximately $1.7 million or an annual run rate of approximately $7 million. And we are seeing steady quarter-over-quarter improvements in direct sales both as a result of new customers, but also from repeat orders from existing customers.

As we have said, we believe we are just scratching the surface of our revenue potential and anticipate that revenues should continue to climb as direct sales continue to grow, as existing distributors complete product registrations and generate repeat sales, and as additional distributors and/or strategic partners come onboard in new regions. Furthermore, as we continue

to develop clinical data from our registry, our investigator initiated studies, and our FDA trial; we believe we will be able to accelerate acceptance and adoption of CytoSorb® in the marketplace.

Slide 9:

Finally, I would just like to provide some notes on our working capital position and cash runway. As of December 31, 2015, we had approximately $7.5 million in cash and short-term investments. In addition, in January 2016, we received another $325,000 in funding from the sale of our NOLs through the New Jersey Technology Business Tax Certificate Transfer Program. We believe that we have sufficient cash to fund our operations through 2016.

Now as we build sales and drive our operations towards breakeven, helped by a highly profitable product with blended gross margins of 62% or better, we are exploring a number of different funding sources in order to fund clinical activity that is intended to help drive CytoSorb® as standard of care and achieve United States regulatory approval. Consistent with our past history and overall philosophy, we look to do so in a financially responsible way with the goal of limiting shareholder dilution.

As we have previously announced, our existing $100 million shelf-registration gives us tremendous flexibility to raise capital under a wide range of financing options. We believe that amount is in vast excess of what we will require. Of this, we have a $25 million controlled equity offering sales agreement in place with Cantor Fitzgerald. During the fourth quarter of 2015, we raised approximately $225,000 in net proceeds at an average selling price of $8.02 per share under this facility.

We also believe that strategic partners can provide potential future sources of capital and in light of the current state of the equity markets, we are additionally investigating non-dilutive debt financing as a bridge to more traditional fundraising. Turning to our capital structure, as of December 31, 2015 on a fully diluted basis, we have approximately 29 million common shares outstanding.

And with that, I'd like to turn the call back over to Phil.

Phillip Chan

Thanks very much, Kathy. So rather than go over our accomplishments for 2015, which you can read about in our press release today, what I thought I would do is cover some of the near-term events that we find very exciting for our overall business and the future of CytoSorb® in the world.

Slides 11-12:

Next week, CytoSorbents will host its Third International CytoSorb® Users Meeting in Brussels, Belgium on March 14th. This is the third such conference in a year. Currently, there are more than one 100 people registered to attend the meeting from a total of 22 countries. The agenda includes 12 clinical and pre-clinical presentations, as well as one panel session. The talks cover a wide variety of topics including sepsis and septic shock, cardiac surgery, liver failure, burn injury, acute pancreatitis, and trauma.

In addition, immediately following our users meeting will be the 36th International Symposium of Intensive Care and Emergency Medicine, also called ISICEM, in Brussels, Belgium from March 15th through the 18th. This conference is one of the largest, most prominent critical care conferences in the world attracting more than 6,200 professionals from all over the world.

CytoSorbents is a gold sponsor and will exhibit and host a research symposium on Thursday March 17th led by session chairs, Dr. John Kellum from the University of Pittsburgh Medical Center and Dr. Antonio Pesenti from Milano, Italy. The sympsosium will feature talks from three major thought-leaders including Dr. Detlef Kindgen-Milles, Dr. Zsolt Molnar, as well as Dr. Axel Nierhaus.

Slide 13:

Fresenius Medical Care, the largest dialysis company in the world and one of our strategic partners, will also be exhibiting at ISICEM next week. Fresenius will initiate the marketing push behind CytoSorb® at the ISICEM conference ahead of the forthcoming launch. This is a very exciting event because it represents a coming out party, so to speak, of the partnership between Fresenius and CytoSorbents to the European critical care community.

CytoSorb® will be featured in the Fresenius exhibition booth on the multiFiltrate Acute Therapy System. Fresenius will use the event to introduce CytoSorb® therapy broadly to its customers, particularly those from the six countries where they have exclusive distribution rights including France, Poland, Denmark, Norway, Finland, and Sweden. Fresenius is also sending approximately 18 people to our CytoSorb® Users Meeting on March 14th.

Slide 14:

Switching gears to Biocon and potential cardiac surgery partners, Biocon and CytoSorbents recently completed a four city week long trip in India and Sri Lanka with Professor Zsolt Molnar, Chairman of SepsEast, the Central and Eastern European Sepsis Forum who is also an experienced user of CytoSorb® for critical illnesses. Through that trip, they introduced CytoSorb® to more than 250 key opinion leaders in that part of the world.

In cardiac surgery, we have ongoing partnership discussions with multiple cardiac surgery partners, who have expressed strong interest in CytoSorb. Interestingly, at our CytoSorb® Users Meeting, key clinical data from the cardiac surgery evaluation study led by Prof. Christophe Baufreton, MD, PhD, cardiothoracic surgeon and Vice Dean of Research from C.H.U - Angers, France - in a patient population that was very similar to those being treated in our REFRESH I U.S. study - will be presented there as well and we're very interested to see how the cardiac surgery community responds to that data.

Slide 15:

That provides a nice segue to our REFRESH I trial update. Again, REFRESH stands for the REduction of FREe Hemoglobin. This trial is 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 expected to last longer than three hours. This includes many complex

cardiac surgery procedures such as aortic reconstruction, CABG redos, multiple valve replacements, and other types of surgeries.

The goal of the study is to show safe reduction in free hemoglobin and other inflammatory mediators that can cause post-operative complications. Again, the therapy has been used intra-operatively in many more than 1,000 cardiac surgeries to date in Europe.

Slide 16:

We are working with major cardiac surgery centers in the United States, which includes Baylor and Texas Heart, Baystate Medical Center, Columbia, Cooper University Hospital, University of Kentucky, University of Maryland, University of Pennsylvania as well as the University of Pittsburgh Medical Center. Currently seven of eight sites are active in the trial.

The trial currently is 35% enrolled with several additional patients already consented for the study and those surgeries are expected to take place this month. We expect to complete enrollment by mid-2016 to be followed by discussions with the FDA on the direction for a potential pivotal trial, which we call REFRESH II that is intended to support application for U.S. approval for CytoSorb® for cardiac surgery.

Slide 17:

I also wanted to give a registry update. The CytoSorb® registry is intended to collect treatment data from all over the world. It is funded by CytoSorbents, but is managed independently by the Center of Clinical Studies at the University of Vienna led by Professor Frank Brunkhorst. Now the analysis of the data is governed by an independent scientific steering committee composed of leaders in critical care and cardiac surgery. Currently we have 103 institutions that are registered to submit data to the registry. I'm pleased to say that the first interim data analysis from the registry is expected to be finalized soon and once we know the results of that study, we will share them with you.

Slide 18:

One last update before we discuss a couple of very interesting case reports is the recently published new sepsis definition. The Third International Consensus Definitions Task Force recently published the new guidelines for the definition of sepsis in the Journal of the American Medical Association, also called JAMA. Sepsis was defined as "the life threatening organ dysfunction caused by a dysregulated host response to an infection".

Now the reason this sounds familiar is because it aligns very well with the message that we've been communicating with key opinion leaders around the world for the past many years about what CytoSorb® is designed to do. As one of the only therapies designed to target the underlying causes of both organ dysfunction and failure in sepsis, as well as a host of other life threatening conditions, we believe we are strategically positioned to be a leading therapy to save lives and change the way critically-ill patients are treated today.

Slides 19-20:

Now I would like to transition to a couple of short case reports. The first one I would like to cover is the study that we recently issued a press release on concerning patients with refractory septic shock. This study was presented at the 26th Symposium for Intensive Care Medicine and Critical Care Conference in Bremen, Germany. Dr. Sigrun Friesecke, Senior Intensivist in the Greifswald University Hospital, medical intensive care unit (MICU), reported on a prospective, single-arm study in 22 patients with refractory, late-stage septic shock.

When we say refractory shock, we are talking about patients where nothing is working to help keep their blood pressure above a critical threshold level that is required to pump oxygenated blood to vital organs. These patients had refractory shock despite the use of high doses of vasopressors. They also had respiratory failure, requiring mechanical ventilation or ECMO (extracorporeal membrane oxygenation). The patients also had anuric kidney failure requiring dialysis. This is one of the worst forms of kidney failure, because the lack of urine production leads to serious fluid overload, and the inability to adequately regulate blood pH and electrolyte composition. These patients also had an average lactate greater than 8 mmol/L, indicating poor tissue perfusion and metabolic abnormalities. To put this into perspective, to qualify for the recently published new definition of septic shock, patients not only had to have shock that required vasopressors to keep the mean arterial blood pressure above 65 mmHg, but they also had to have a lactate greater than 2 mmol/L. Those who meet this new definition have a risk of death of 40%. So 8 mmol/L is very high. Clearly, this patient population in the Griefswald study were very sick with refractory septic shock and multi-organ failure.

A similar population refractory shock population (n=16) was reported by Conrad et al. last year. These were patients who received standard of care but also had refractory septic shock, on mechanical ventilation with an initial lactate level of 6 mmol/L with 75% requiring renal replacement therapy. These patients had a mortality of 100% at 28 days.

In this context, the results of the Greifswald study demonstrating 41% survival, a 30% to 40% absolute improvement over what was expected in this moribund patient population, which is typically 90-100%, was quite impressive. Also, CytoSorb® was able to resolve shock in 68% of the patients. And in terms of the reduction of inflammatory mediators, CytoSorb® led to a reduction in IL-6, one of the cytokines that is most closely associated with severity of illness and mortality in sepsis, from an initial average of 87,000 pg/mL to below 10,000 pg/mL within 24 hours of treatment. To put this into perspective, all of us on the phone should have an IL-6 of about 10 pg/mL and patients with community acquired pneumonia that gets better with outpatient antibiotics may have IL-6 levels of about 200-300 pg/mL. So the levels observed in the Greifswald study were extremely high. So this was a very exciting study…the ability to bring people back from the brink at all was quite remarkable.

Slide 21:

In this second case report, we report on a case of severe burn injury. This involves a 51-year-old man, who was admitted to the hospital and acutely treated for severe burn injuries due to an accidental explosion. He had burns over approximately 60% of his total body surface area. If you look at your palm, that represents 1% of your total body surface area. So imagine your body covered with severe burns on 60% of those palm areas. You can see that this patient is very severely burned. He also had serious inhalation trauma. So it was no surprise that he had massive inflammation and developed acute kidney failure requiring dialysis. He's subsequently developed

shock, requiring high doses of three vasopressors, and was very close to being called refractory shock.

Due to his massive burn injuries, he also developed severe rhabdomyolysis with myoglobin in his blood. Myoglobin is an oxygen carrying molecule that gets released from burned or injured muscle cells that can crystallize in the kidneys and cause kidney failure. His levels were very high, almost 16,000 ug/L with severe inflammation as measured by a number of inflammatory parameters. The patient underwent continuous CytoSorb® treatment for 72 hours using a total of three devices. With treatment, he regained hemodynamic stabilization with significantly decreased need for vasopressors. His renal function also improved, though still required dialysis. His myoglobin levels decreased to approximately 8,000 ug/L and his inflammatory markers also dropped dramatically. In this case, CytoSorb helped to stabilize this patient and he was ultimately weaned from both mechanical ventilation and dialysis before he was successfully discharged from the hospital to physical rehab.

That ends my formal comments and we can now take questions.

Lee Roth

Operator, we're ready to poll for questions now.

Question-and-Answer Session

Operator

Thank you very much. [Operator Instructions] We'll take our first question from Jonathan Aschoff from Brean Capital.

Jonathan Aschoff

Hi, guys. Congrats on the progress, I had about four questions. I was wondering could you elaborate on what exactly Fresenius will be doing initially perhaps in some sort of quantitative way, headcount for sales, detail like that?

Phillip Chan

Hi Jonathan. Fresenius is planning on launching CytoSorb® in six countries, specifically for the area of critical illness. They will be marketing the technology heavily to intensivists for the treatment of many different illnesses, such as the ones that we've talked about today. In terms of the magnitude of those sales, we can't predict that right now. What we do know is that France is the second largest medical device market in Europe. Poland is a very large market, I believe with 30-40 million people in that country, and then the Scandinavian countries are excellent markets due to their very high per capita spend in healthcare with very good insurance. These were some of the important reasons why these six countries were selected. When Fresenius launches, we have limited information on how CytoSorb® will be received in marketplace, but today we do know that there are major key opinion leaders in those countries who are very eager

to use the product and a number of them will be attending many of the sessions that we will be holding next week.

Jonathan Aschoff

Okay. You gave a little bit of CytoSorb® directional sales guidance for the first quarter of 2016, and said that it will be higher than 4Q 2015. Will the quarter also be an uptick sequentially from last quarter, since the first quarter of 2015 was kind of a low hurdle.

Phillip Chan

Historically, we have not given guidance while the quarter is still underway and for the near-term that would be our preference.

Jonathan Aschoff

All right, how about guidance for 2016?

Phillip Chan

While we haven't quantified or given guidance on the magnitude of an increase in sales for 2016, there are many reasons why we believe that 2016 will be a much stronger year than 2015. In particular Fresenius will turn on soon and bring six countries online. We're waiting for final registration in Russia. We are waiting for registration in other countries outside of Saudi Arabia, in the Middle East. We're waiting on Israel, Canada and a number of other countries that we believe will turn on in 2016.

In addition, we see a lot of momentum as we discussed in our letter to stockholders in January about moving toward an inflection point and about how we're reaching a critical mass of awareness, usage, clinical data, and others things that we believe are helping to drive our direct sales, which again, have tripled from the year ago fourth quarter on a doubling of our customers. We believe that a lot of these things will be kicking in, in 2016, leading to substantial growth. But we have not yet provided guidance on what that might look like.

Jonathan Aschoff

Okay, and then lastly, I was just curious – do you see anecdotally much CytoSorb® use in patients that that you don't think were reasonable candidates to possibly benefit from it?

Phillip Chan

We have seen CytoSorb® being used in all sorts of different situations both late as well as early. I think the value of having a broad indication for usage is that it can used, technically on label, really for any situation where cytokines are elevated. I think the original strategy of having such a broad indication is paying off because we are seeing a lot of reports on usage in applications that we never really thought were going to be major markets for us, but have turned out to be very promising areas.

We are also dealing with the sickest of the sick. These are critically ill patients, whose major systems in their bodies are failing around them and are very difficult to treat. When used too late in patients, where cells have died, organs have been damaged, and other things, it has been much more difficult to bring those patients back. This is one of the reasons why the study in refractory septic shock that I talked about earlier is so exciting. In that particular study, they used CytoSorb® much more aggressively than others have been treating these patients in the past, using CytoSorb® twice a day rather than once a day, which was associated with improved outcomes in that study.

Now, obviously that is a single-arm study and we have to approach the interpretation of that study in context. That being said, I think the results were quite remarkable and, based on reports, so did many people in the audience at the conference where the data were presented. So we're very excited by the potential impact of CytoSorb® here, but we will still need to demonstrate that in a true randomized controlled study. Given the magnitude of the effect, however, the interesting thing could be that such a pivotal trial, if you will, could be actually very small, which would be very exciting.

Jonathan Aschoff

Great, thank you very much.

Operator

We'll take our next question RK Ramakanth with HC Wainwright.

Sean Lee

Hi, good evening. This is Sean Lee standing in for RK. Congratulations on the solid quarter and thank you for taking my questions.

Phillip Chan

Hi Sean.

Sean Lee

I see the very encouraging data from the German refractory shock study. Given the new data on 28-day mortality, and given that 28-day mortality is the regulatory hurdle, how does this new data impact your plans for an IDE sepsis study in the U.S.?

Phillip Chan

These data have just been presented, but given the results, it would make sense to do a sepsis study in refractory shock patients, either here or in Europe. If we can do a small trial in sepsis in the United States, and have a strong result, that would be to our advantage clearly.

Sean Lee

Okay, thank you and the REFRESH I study, you mentioned that it's expected to complete enrollment by mid-year. When can we expect major results of this trial?

Phillip Chan

Sometime shortly thereafter – most likely in the third quarter of this year.

Sean Lee

And if all goes well with this plan, do you expect to start REFRESH II towards the end of the year?

Phillip Chan

If everything goes well, we expect to submit the IDE to run REFRESH II before the end of this year.

Sean Lee

Great. And okay one final question for you on the international registry. In terms of the interim results, is that going to be published or presented at a scientific meeting somewhere?

Phillip Chan

I think that is going to be up to the discretion of the scientific steering committee for the International CytoSorb® Registry. But, yes, the intention of setting up the registry was to make these data publicly available to help better educate and inform CytoSorb® users all over the world on how best to use CytoSorb® and in which applications.

Sean Lee

Okay, thank very much. That's all my questions.

Phillip Chan

Thank you.

Operator

[Operator Instructions] We'll go next to Andrew D'Silva with Merriman Capital.

Andrew D'Silva

Hi, good afternoon. Thanks for taking my call, just a couple of quick questions for you.

Phillip Chan

Hi, Andrew.

Andrew D'Silva

Hi, guys. First off, can you give us a quick update on how the Fresenius sales team is ramping up? Are you really engaged right now educating them on the product applications and do you believe they are up to speed with the product's capabilities?

Phillip Chan

Yes. For that one, I'll turn it over to Chris Cramer, our VP of Business Development, he's been working very closely with Fresenius. Chris?

Chris Cramer

Sure, thanks, Phil. Hi, Andrew, thanks for the question. I would say, as you know, we've been working very hard together with FMC to establish the right structure to support a successful rollout for CytoSorb® across all six countries. And it's been, I would say, a big effort, but all the pieces are now coming into place. To answer your question directly, I'd say that we've been doing a lot of training over the last quarter of FMC's sales, marketing and clinical support specialists. I don't have the exact number off of hand, but I would say we're close to 30 or 40 people and I would say it's going well. They understand the products, they get the value proposition and I would say they're very enthusiastic. So, I think that all signs are very positive on the people that would be supporting the product in the field.

Andrew D'Silva

Got it, all right, thanks for that, and then maybe as it relates to your expectations this year, I asked this on the last call and I just wanted to see if your thoughts have changed as now we're a little bit into 2016 already. This year, do you anticipate the majority of your sales should be derived through direct internal sales initiatives, or would you anticipate at this point that sales from distributors and strategic partners will be able to overtake direct sales and may account for the lion's share of things going forward, as there are a lot of regions that should be up online this year that weren't in 2015?

Phillip Chan

Yes – I think that as we've discussed before, our direct sales territories in Germany, predominantly Germany, but also Austria and Switzerland, were started about a year before we had any distribution partners or strategic partners. So from a market development standpoint, they are roughly about a year ahead. That being said, what we've seen is an acceleration of sales in our direct territories, due to greater awareness and usage of CytoSorb®, an increase in clinical data, and a progression of usage from an episodic to a more regular basis, particularly with certain disease states where CytoSorb® has been used almost as a standard of care at select hospitals.

So going forward, in 2016 we believe that direct sales will play a major role in our overall sales growth this year. We anticipate that direct sales will likely be more than half of our sales this year. That being said, we will wait to see how that turns out, because our distributor channel is actually coming on nicely and as we move to additional territories, the contribution of the distributors and

strategic partners will become more important. I think if we could keep that balance at a 50/50 split, that would actually be a very positive thing overall.

Andrew D'Silva

And then for this past year, 2015, do you know what the split was direct versus external?

Phillip Chan

Again, we haven't broken that level of detail out historically; but direct sales were a very important part of our overall sales in 2015 and we continue to expect that to continue in 2016.

Andrew D'Silva

Fair enough, and then as far as regions where you have approval and have received registration, have you had success in establishing reimbursement in those areas and do the investigator initiated studies as well as the product registry data help you in this regard?

Phillip Chan

The reimbursement of CytoSorb® is typically accomplished in different ways. As you know, unlike the United States, the European, as well as the world, markets are very fragmented. In these countries, you typically need to obtain reimbursement or some other type of payment, for example through a DRG, or diagnosis-related group, reimbursement in each country.

We continue to work on reimbursement in most of our territories. In fact, this year, we have a specialist that we brought into the company that will be focused on that as a full time position. In many different countries they have ways of obtaining payment or reimbursement for CytoSorb® and at a very basic level, it is through a sort of a lump sum DRG payment. In other countries like Germany, for example, it's a dedicated payment. We continue to work on reimbursement and that will only help to accelerate sales growth in the future.

Andrew D'Silva

Yes, last question for you. Obviously it was nice to see the positive data related to the refractory septic shock study. Are there any investigator-initiated studies that you're aware of today that are looking to use CytoSorb® earlier in sepsis versus being used as a salvage therapy? Your comments suggest that treatment at an earlier stage could be a larger market and be more efficacious in helping to save lives.

Phillip Chan

Absolutely, we have 50+ investigator-initiated studies that are being planned, with about 17 of those actively enrolling patients, with four that have been completed to-date. Of those that are ongoing or being planned, there are absolutely a number focused specifically on the early and aggressive use of CytoSorb® in septic patients as a means to try to prevent organ failure from happening in the first place. We believe that the prevention of organ failure is really what can

lead to the potential to improve overall morbidity and mortality in these patients. After all, one of the reasons why patients remain in the intensive care unit is because they are on machines or life support that are needed to keep them alive.

So absolutely, early treatment with CytoSorb® is a major focus for both the company and in these investigator initiated studies, and is one of the types of company sponsored trials that is being considered for the U.S. or European markets.

Andrew D'Silva

Thank you for the color. Good luck going forward this year. Take care.

Phillip Chan

Great. Thanks, Andrew.

Operator

We'll go next to Brian Marckx with Zacks Investment Research.

Brian Marckx

Hi, Phil. Congratulations on the quarter. I'm wondering if you can talk about the bigger picture view in terms of the U.S. and your thoughts about pursuing a sepsis trial in the U.S.? Does the updated definition of sepsis potentially influence your strategy in terms of trial design or in terms of pursuing or not pursuing it?

Phillip Chan

Thanks Brian. We know that sepsis is a massive market. It is a top 10 killer around the world and accounts for approximately one million cases admitted to the intensive care unit in the United States every single year. There are about 27 million cases of severe sepsis and septic shock every year worldwide. The United States is no exception, even with the higher standards of medical care that you will find in this country.

Now the incidence of sepsis is being driven by a number of different factors. The first one of these major factors is the aging baby boomer generation. These are patients who are at high risk of developing an infection due to age, but also because of an epidemic in diseases like cancer and diabetes that put them at high risk of developing an infection. Also indwelling implants like artificial hips and knees can get infected and wind up putting the patient at very high risk of developing sepsis; also the increase in hospital-acquired infections and antibiotic-resistant pathogens such as MRSA, or methicillin-resistant *Staph aureus*, which are really driving this.

When the CDC did an epidemiological study on sepsis, they noted that the incidence of sepsis doubled in the ten years ending 2008, due primarily to patients who were greater than 65 years of age, exactly the patient demographic that defines the baby boomer generation.

Sepsis also accounts for approximately 10% to 20% of all ICU admissions. For that reason, it is a market that is very difficult to ignore. We have a lot of data now in sepsis, given that most of our treatments are on patients with sepsis and septic shock, and where CytoSorb® is working in these patients. We are attacking sepsis from a multi-model mechanism that not only involves a reduction in inflammatory mediators, but also involves a reduction of bacterial toxins, a redirection of the immune response, protection of organs against the toxic nature of cytokines, and other mechanisms.

So for many reasons, we absolutely believe that sepsis should be a major target for us in the United States. Now whether or not we pin the hopes and fears of the world on a clinical sepsis trial in United States is a different story. Sepsis is a notoriously risky area to do clinical trials, where no therapy, except for Xigris by Eli Lilly, has succeeded in Phase III clinical trials. And Xigris was voluntarily removed from the market a number of years ago due to a failed post-market study. Because of this, we are initially targeting another large market, cardiac surgery, where there are 1.5 million open heart surgeries performed worldwide, with 500,000 in the U.S. alone, a total addressable U.S. market of approximately $500 million, and where we believe the risk of a trial is lower. We would then pursue a label extension strategy to add on different subgroups of sepsis patients where CytoSorb® can be shown to be efficacious with relatively small numbers of patients. We believe this is a safer and less risky approach to directly pursuing the sepsis market in the United States. Does that help the answer to that question? We've been pursuing a lower risk strategy, focused on cardiac surgery, to obtain U.S. approval first.

Brian Marckx

Yes, if I could just follow-up. So what I gather is from your comments that you expect to go through REFRESH I and then hopefully REFRESH II, assuming REFRESH I is successful. Then at that point evaluate options potentially for expanding the label after cardiac surgery is a successful indication. Is that a fair summation?

Phillip Chan

Well, not exactly because we don't believe that we have to do this in series. Our intent is to pursue sepsis clinical studies in parallel either here in the U.S. and/or abroad, while we pursue the cardiac surgery indication. Although the studies may not necessarily be large scale pivotal registration studies for the application of sepsis, they will help to identify and validate sepsis subgroup populations where the data can then be immediately used to support usage and sales outside of the United States, and either provide the data for label extension in the U.S., or provide the data to help design a pivotal sepsis study in the U.S. So as we pursue cardiac surgery, we absolutely intend to pursue trials in sepsis or septic shock in parallel.

Brian Marckx

Okay. So, in terms of the FDA's requirement for 28-day mortality. How does that fit with what we're talking about here?

Phillip Chan

I think what the FDA has made clear is that they would be looking for 28-day all-cause mortality as a primary endpoint to approve a sepsis therapy in the U.S. The interesting thing about the refractory septic shock study is that with a small number of patients, the therapy showed a relatively robust effect on 28-day mortality compared to a historical control. If the results of the refractory septic shock study hold true, a follow-up study could potentially achieve statistical significance in this endpoint with a relatively small number of patients, which would work in our favor. But again, one of the benefits of having so much experience right now in the treatment of sepsis worldwide is that we have good ideas about where CytoSorb® is being used in a variety of subgroups most successfully. And because of that, we are hopeful that we will be able to pursue smaller studies, where the chance of success is much higher than could be achieved in a large, mixed population sepsis trial.

Brian Marckx

Okay, that's very helpful. I appreciate that. If I could just ask about the cardiac surgery partners, you mentioned that you are having discussions with multiple potential partners. How does that differ from the initial partner that you were talking to and is that company still in the mix?

Phillip Chan

What I would say is that the successes that we've had in the marketplace and the positive feedback from many, many key opinion leaders in the cardiac surgery space have led to a very strong interest amongst the major cardiac surgery players in the world for not only the indication, but for territories as well. This has led to an overlap in what they are asking for and what we can potentially provide. I think that has been the one of the things that has been actually a very positive thing for us. But it's also complicating matters as well.

Brian Marckx

Okay, all right. Are they looking for the top line data at least from REFRESH I as a potential trigger to move things towards a deal?

Phillip Chan

It's interesting, I don't think that's the case. I think that - certainly REFRESH I is very interesting, but the nice thing about working with these major strategic partners is that they have many key opinion leader contacts in a lot of the territories where CytoSorb® is being used today for cardiac surgery. So they're not just taking our word that it is working, they've been talking to their key opinion leader networks. And so I think that's been a very positive thing. Professor Baufreton's data from Angers, France will be presented at the CytoSorb Users Meeting next week which I think highlights the kind of experiences that cardiac surgeons are seeing, particularly in the area complex cardiac surgery which we are focused on in the REFRESH I trial.

Brian Marckx

Great. Thanks, Phil. I appreciate it.

Phillip Chan

Sure. Thank you, Brian.

Lee Roth

Thank you. That's all the time we have today for questions. I would now like to turn the call back over to management for any additional or closing remarks.

Phillip Chan

Thank you very much Lee and thanks everyone for taking the time today for the call. We certainly appreciate your participation. If you do have any questions that were not addressed today, please feel free to reach out to Amy Vogel at avogel@cytosorbents.com and we will try to get back to you soon. In the meantime, we look forward to speaking with you again on the next Q1 2016 earnings call. Thank you very much.

Operator

Thank you. And that does conclude our conference today. I would like to thank everyone for their participation and have a great day.