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AZN.L - AstraZeneca PLC Investor Science Conference Call at the European Society International Congress

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OVERVIEW:

Co. provided an update at the European Society International Congress.

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CORPORATE PARTICIPANTS

Thomas Kudsk Larsen *AstraZeneca PLC - Head of IR*

Colin Reisner *AstraZeneca PLC - Chief Medical Officer of Pearl Therapeutics and AstraZeneca Head of Respiratory Global Medicines Development*

Dr. Mark FitzGerald *Centre for Heart and Lung Health, Vancouver Coastal Health Research Institute, University of British Columbia - Director*

Tom Keith-Roach *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

Dr. Andrew Menzies-Gow *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

Nick Stone *AstraZeneca PLC - Director of IR*

Bing Yao *AstraZeneca PLC - Head of Respiratory, inflammation and Autoimmunity*

CONFERENCE CALL PARTICIPANTS

Richard Parkes *Deutsche Bank - Analyst*

Stephen Scala *Cowen and Company - Analyst*

Sachin Jain *BofA Merrill Lynch - Analyst*

PRESENTATION

Operator

Good afternoon, good morning, welcome ladies and gentlemen to AstraZeneca's investor science conference call. Before I hand over to AstraZeneca I'd like to read the Safe Harbor statement.

The Company intends to utilize the Safe Harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Participants of this call may make forward-looking statements with respect to the operations and financial performance of AstraZeneca. Although we believe our expectations are based on reasonable assumptions, by their very nature forward-looking statements involve risks and uncertainties and may be influenced by factors that could cause actual results to differ materially from those expressed or implied by these forward-looking statements. Any forward-looking statement made in this call reflects the knowledge and information available at the time of this call.

The Company undertakes no obligation to update forward-looking statements. I would now like to hand over to Thomas Kudsk Larsen.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you operator and good afternoon to our European attendees and good morning to US participants and a warm welcome to the AstraZeneca conference call from the European Respiratory Society meeting that took place in London this past weekend.

I am Thomas Kudsk Larsen from the Investor Relations team at AstraZeneca and we are very pleased to have the opportunity to share an update on our respiratory medicines, in particular our first biologic, Benralizumab, and the new phase III trial results presented at the meeting.

This conference call is being webcast online and the presentation is also available for download at AstraZeneca.com. We plan to spend up to about 45 minutes on presentation and interview and then we should have around 30 minutes for Q&A.

Before we get started I would like to thank Nick Stone from the IR Team for organizing this conference call today including all of the preparations. With this, slide two has the usual Safe Harbor statement and please now turn to slide number 3.

The agenda today is as follows. After a short introduction I will hand over to Dr. Colin Reisner who is Chief Medical Officer of Pearl Therapeutics and AstraZeneca Head of Respiratory Global Medicines Development. Colin will cover the unmet medical need in asthma and an overview of the benralizumab phase III program called Windward.

After Colin, Dr. Mark FitzGerald a primary investigator for benralizumab will review the data presented at the ERS meeting, which includes of course the SIROCCO and CALIMA Phase III trial results.

After this Tom Keith-Roach our Head of Respiratory Global Product and Portfolio Strategy will interview Dr. Andrew Menzies-Gow about the current medical practices in severe asthma and finally Tom will also provide a summary of next steps for benralizumab and the commercial outlook.

Special thanks to our two external participants today, Dr. Mark FitzGerald and Dr. Andrew Menzies-Gow for their time and commitment today for our conference call. At the end of the call we have good time for Q&A and questions can be asked either directly on the call via the webcast or also submitted by email using IRteam@AstraZeneca.com and we will then make sure to include them all in the Q&A session.

Please turn to slide number 4. Now taking a step back benralizumab is one of 14 new medicines in late stage development or under registration and one of the medicines we listed as having a larger potential. Further, benralizumab is likely to be the first AstraZeneca biologic medicine to be approved and help patients with respiratory diseases.

It is also the only medicine in development with the mode of action of targeting IL-5 receptor and induce rapid depletion of eosinophils. As we will see later in today's presentation, benralizumab has other unique features we believe including the potential to be dosed once every eight weeks which is half as frequent as currently available potential other treatment options.

Further benralizumab comes in easy to use prefilled syringes for subcutaneous injection and does not require any reconstitution. As such we think that benralizumab is a very good example from AstraZeneca of what science can do.

With this I will now hand over to Colin.

Colin Reisner - *AstraZeneca PLC - Chief Medical Officer of Pearl Therapeutics and AstraZeneca Head of Respiratory Global Medicines Development*

Thank you, Thomas. Hello everyone. Please turn to slide 6.

Asthma is a common disease affecting approximately 315 million people worldwide. Severe asthma is a term applied to asthma that requires treatments with high dose inhaled steroids combined with other asthma medications. Severe asthma is estimated to be present in approximately one in every 10 asthma patients. The consequences of uncontrolled severe asthma are highlighted in the middle panel.

Frequent symptoms result in significant limitation in the patient's daily activities and quality of life. Importantly, poor current control places the patient at risk for future asthma exacerbations that may be life-threatening if untreated. From an economic perspective, patients with severe asthma account for more than half of the costs associated with asthma and patients with uncontrolled severe asthma generate annual costs almost three times that of matched patients with controlled disease.

Please turn to slide 7. Asthma is now understood to be a heterogeneous disease with eosinophilia emerging as a clinically relevant phenotype. Severe eosinophilic asthma is indicated by persistent airway eosinophilia despite a high dose inhaled cortico steroid based treatment regimen.

Indirect markers of airway eosinophilia such as elevated peripheral blood eosinophils also indicate an eosinophilic asthma phenotype. Elevated airway and blood eosinophils have been associated with an increased risk of asthma exacerbations and poor lung function. Thus patients are less able to breathe normally leading to frequent symptoms and reduced quality of life.

Please turn to slide 8. This table depicts the current treatment recommendation from the global initiative for asthma also known as the GINA Guidelines, where medications are stepped up or stepped down based on the patient's current level of asthma control. Steps four and five relate to severe asthma where higher doses of existing medication or the addition of new medication may be required.

Please turn to slide 9. The recommended options at the more severe end of the asthma spectrum are highlighted in this slide. For step four, inhaled corticosteroid long acting better agonist preparations also known as ICS LABAs are effective for most asthma patients. However a substantial number of patients remain inadequately controlled by ICS LABA alone.

Add-on therapy to an ICS LABA is indicated when asthma is inadequately controlled as evidenced by a assistant symptoms and a tendency to exacerbate despite compliance of high doses of inhaled steroid in combination with additional treatment.

Guidance based add-on options are shown here as step five therapy. Oral corticosteroids are frequently used for patients who are not otherwise controlled by an ICS LABA preparation, but this non targeted approache is associated with significant adverse events.

If you look to the right-hand side of the slide the selected attributes of the two anti-IL-5 products are shown as a reference. Dr. FitzGerald will discuss the results of add-on benralizumab in this population. An ideal product would result in improvements in exacerbation risk, lung function, patient reported control and the promise of reducing oral corticosteroids in oral corticosteroid dependent asthma patients.

Please turn to slide 10. Interleukin-5 or IL-5 is the predominant cytokine responsible for eosinophils maturation in the bone marrow and eosinophil activation and survival in tissues. With these insights into the role of eosinophils, AstraZeneca began developing benralizumab a monoclonal antibody that depletes eosinophils via antibody-dependent cell-mediated cytotoxicity in the process in which natural killer cells are activated to target eosinophils.

Unlike the anti-IL5 modalities that bind the cytokine, benralizumab attaches directly to the eosinophil through the IL-5 receptor. When this happens, the eosinophil becomes visible to the body's immune system and natural killer cells bind to them and cause apoptosis or programmed cell death which efficiently removes them.

Early clinical trials demonstrated that eosinophil depletion by benralizumab happens very quickly with essentially all eosinophils removed from the blood within 24 hours. In addition, these early clinical trials also showed that eosinophils are almost completely depleted in the airway and in the bone marrow, the predominant source of circulating end tissue eosinophils. This gave us an early indication that benralizumab may be able to be dosed relatively infrequently once the possibility of dosing once every eight weeks.

Please turn to slide 11. The direct anti-eosinophil activity may confer certain advantages over anti-IL-5 directed therapies. As we learn more about eosinophils we have found that other mediators beyond IL-5 can play a role in their survival, including cytokines like IL-33 and GM-CSF.

This redundancy may limit the degree of eosinophil depletion in tissues that can be achieved by targeting anyone specific cytokine. Consequently, elimination of eosinophils from the tissue using an anti-IL-5 modality may be incomplete with residual cells still being active. In contrast, benralizumab targets the IL-5 receptor which sits on the surface of the eosinophil causing more complete elimination of the eosinophilic inflammation and that represents a new treatment option for severe asthma patients.

Please turn to slide 12. We are currently in phase III trials for benralizumab in asthma under a program called Windward. Windward is the largest known phase III clinical trial program of any respiratory biologic in asthma. It is comprised of six phase III studies in over 3,000 patients across almost 800 sites in 26 countries. The program was designed to support the efficacy and safety of subcutaneous administration of benralizumab across the spectrum of asthma severity with a focus on the subset of patients with severe eosinophilic asthma where there is the greatest unmet medical need.

The program includes the two pivotal safety and efficacy trials in patients with severe asthma, SIROCCO and CALIMA. The results from these studies were published in the Lancet earlier this week.

Results from a study in mild to moderate asthma called BISE were presented earlier this morning at the European Respiratory Society International Congress. Other studies including ZONDA which is our oral corticosteroid sparing study; BORA, the long-term safety extension and GREGALE, the patient youth study.

The focus of the presentation today is on the two pivotal studies SIROCCO and CALIMA. As Dr. FitzGerald will discuss the phase III results demonstrate that in severe asthma patients with an eosinophilic cyanotype administration of 30 mg of benralizumab subcutaneously every eight weeks significantly improved multiple methods of asthma control.

Please turn to slide 13.

Dr. Mark FitzGerald - *Centre for Heart and Lung Health, Vancouver Coastal Health Research Institute, University of British Columbia - Director*

Thanks, Colin, and hello everybody. I am going to spend the next few minutes taking you through the results from the phase III SIROCCO and CALIMA trials in severe asthma.

Please turn to slide 14 and you can quickly turn to slide 15 and these are my conflicts of interest, then you can turn to slide 16. So these SIROCCO and CALIMA trials were designed to assess the effect of benralizumab 30mg subcutaneous in severe asthma patients within eosinophilic phenotype who were uncontrolled on high dose inhaled corticosteroids plus a LABA preparation.

Primary and key secondary efficacy variables that were controlled for multiplicity included the annual rate of asthma exacerbations, lung function as assessed by the prebronchodilator FEV1 and asthma symptoms based on daily diary. For analysis purposes, severe eosinophilic asthma was defined as patients on high dose inhaled corticosteroid LABA with a blood eosinophil count of at least 300 cells per microliter.

In the study and asthma exacerbation was a worsening of asthma symptoms or signs that resulted in use of systemic corticosteroids or temporary increase in stable corticosteroid background dose for at least three days, an emergency department urgent care visit due to asthma that also required systemic corticosteroids or an inpatient hospitalization greater and equal to 24 hours due to asthma and you also see in the figure some key secondary endpoints and other secondary endpoints. The primary analysis population was patients receiving high-dose inhaled corticosteroid LABA with blood eosinophils greater than 300 cells.

Please turn to slide 17. This slide shows the key inclusion criteria. The study population comprised of males and females with the age range of 12 to 75 although the bulk of patients were not in the adolescent range. The patients had to have had physician diagnosed asthma requiring entry-level treatment with a high dose inhaled corticosteroid and LABA. They needed -- in a subset of patients in CALIMA there was patients who had medium dose inhaled corticosteroid LABA. Patients had to have two or more asthma exacerbations in the previous 12 months and also patients had to be symptomatic during the run-in. We also entered criteria based on the previously mentioned blood eosinophil levels.

Please turn to slide 18. These studies were both double-blind randomized placebo-controlled trials with a common fundamental design. The treatment period for CALIMA was 56 weeks which was slightly longer than Sirocco at 48 weeks. All patients received an injection of study drug every four weeks via prefilled syringe. Patients were randomized to receive either benralizumab 30 mg every four weeks, benralizumab 30 mg every four weeks for the first eight weeks and then receiving benralizumab every eight weeks alternating with the placebo to maintain the blind nature of the study.

The subjects in the placebo arm of the study received injections every four weeks with placebo medication and as you can see from the diagram, the patients were followed over a one-year period, predominantly 56 weeks in total and the primary endpoint was asthma exacerbation rate in patients to eosinophil levels greater than equal to 300.

Please turn to slide 19. This is a rather busy slide but it indicates that it was a female predominant population with a mean age of about 50. Patients had airflow obstruction with a modest FEV1 in the range of about 60% predicted. Patients were symptomatic. The ACQ score defines the patient with poorly controlled asthma or uncontrolled asthma with a score of 1.5 or greater which was also an entry criteria. And you can see that entry criteria ensured the patients were quite symptomatic coming into this study.

In addition patients in the prior year to their entry into the study had a history of significant exacerbations and also per protocol the patients had eosinophil levels greater than 300.

Please turn to the next slide. So we are on page 20 now. In the study, as you can see the two primary endpoints are displayed here. The benralizumab significantly reduced annual exacerbation rates in both the SIROCCO trial and the CALIMA trial.

The placebo exacerbation rate is shown by the green bars, the placebo exacerbation rate in CALIMA at 0.93 events per patient per year was lower than expected. This differed significantly from other studies of therapies in this therapeutic domain and it would suggest that the patient population was milder than the intended target population. This may have contributed to the smaller effect size.

Analyses has revealed substantial regional heterogeneity with respect to background exacerbation rates across countries in CALIMA relative to SIROCCO. Such variability is often seen in large clinical trials. Just to reemphasize the point at the top, these differences in both SIROCCO and CALIMA were significant statistically as well as clinically reaching the primary efficacy endpoints for the study.

Of note it should be mentioned that in this program of research, unlike the MAPLE program of research, patients received their maintenance treatment as opposed to other trials which have been completed where patients were not provided with their maintenance treatment.

Please turn to slide 21. In a subsequent analysis the graphic shows the result of a post analysis of asthma exacerbation rates in a subgroup of patients with at least three historically exacerbations in the prior year. The green bars again depict the annualized asthma exacerbation rates for placebo patients and as you can see the background rate increased to approximately two events per patient for SIROCCO and 1.6 for CALIMA indicating that the future risk of exacerbations is higher in patients with more frequent historical exacerbation. Of note benralizumab administered every eight weeks reduced asthma exacerbations by approximately 50% in these higher risk CALIMA patients and this number is similar to SIROCCO.

Please turn to slide 22. This slide shows the standard Kaplan-Meier survival curves for exacerbations over time and the result indicates that the probability of experiencing an asthma exacerbation was significantly reduced by benralizumab for both dosing arms.

Please turn to slide 23. In this graphic it depicts the effect of benralizumab on lung function as assessed by pre-bronchodilator, pre-dose FEV1 compared to placebo. Statistically significant improvements in FEV1 were observed in both trials and for both dosing regimens. These improvements range from 116 to 159 mLs for Q8 dosing which is represented by the blue bars. These would be considered not only statistically significant but clinically significant in the ability of a patient to appreciate an improvement in their symptoms when you see this measure of improvement.

Please turn to slide 24. Here you see the improvements in FEV1 after the first dose of benralizumab at the first four-week assessment. This improvement was sustained throughout the treatment period and was most consistent for the Q8 dosing regimen. These results are important in terms of predicting who might respond to this treatment because if we get a signal at this stage where a patient feels symptomatically better, it is possible to make more accurate predictions about their overall responsiveness particularly in terms of exacerbation which, as you have just seen, is well characterized by their prior history of exacerbation.

Please turn to slide 25. This graphic shows the change in FEV1 using the same post-hoc analysis in patients with three or more prior exacerbations and here we see that the change in FEV1 in patients with three or more exacerbations was numerically larger than the overall population with treatment effects of more than 200 mL for Q8 dosing in both SIROCCO and CALIMA.

It should be mentioned that these patients by definition are on long acting beta agonists which traditionally we have failed to have achieved maximum bronchodilator effect to see an additional bronchodilator effect consistently in both trials above and beyond baseline levels in the severe patients is quite an important clinical attribute.

Please turn to slide 26. The other key secondary efficacy endpoint was total daily asthma symptoms score. Patients were asked to grade their asthma symptoms in the morning and in the evening on a scale of zero to three. Asthma symptoms could include but were not limited to shortness of breath, wheezing, coughing, and/or chest tightness. The total symptom scores are shown here. Q8 dose regimen showed a significant improvement compared to placebo in both studies and these are shown here in this graphic.

The note now to safety. Both benralizumab -- we are now on slide 27. Now to safety. Both benralizumab dosing regimens were well-tolerated and had an overall adverse event rate similar to placebo in each study. The frequency of serious adverse events was similar to that of placebo within each study and there was no clustering or pattern regarding type of events. Injection site reactions for benralizumab were all mild to moderate with similar frequencies between the Q8 week dosing arm and placebo.

Adverse events that resulted in discontinuation were more common in benralizumab treated patients than in placebo treated patients but this imbalance was primarily due to single events without apparent clustering or pattern regarding the type of events. It should be noted that these events numerically were very small.

Some patients on benralizumab developed an anti-drug antibody response, some of which were characterized by neutralizing antibody activity invitro. This is consistent with phase II experience. There was no apparent impact of these antibodies, the development of these antibodies on the safety or efficacy results. Studies which were done to assess the potential for this event.

Please turn to slide 28. In summary with the data presented at the ERS International Congress and published in the Lancet earlier this week, we now have much greater insight into the potential benefit of adding benralizumab to standard of care therapy for patients with severe uncontrolled eosinophilic asthma. We observed a reduction in asthma exacerbation rates of up to 51% compared to placebo. There were also significant improvements in lung function and asthma symptoms key secondary endpoints. In the case of lung function these improvements were observed after the first dose and sustained throughout therapy.

In addition these results were obtained with every eight week dosing of benralizumab and using a prefilled syringe for subcutaneous injection which may be more convenient for patients than currently available IL-5 options. This is very important data for healthcare professionals working in this area. As we continue to see patients who continue to ensure significant limitations to their daily lives and remain at risk for severe asthma exacerbations even with the very best of current standard therapy.

Please turn to slide 29. I am going to hand over now to Tom Keith-Roach to take the next section.

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

Thank you, Mark, and hello everyone. This is Tom Keith-Roach and I am very pleased to be joined by Dr. Andrew Menzies-Gow.

Andrew, alongside your research work you are also a real doctor in the sense that you see severe asthma patients every day in your clinic as a consultant of respiratory medicine and as the director of the lung division at the Royal Brompton Hospital. So, if I may, I would like to start by asking you about current practice.

In your clinic, how do you identify patients with severe asthma? How are they treated typically today and what do you see as the most important remaining unmet medical needs beyond current standard of care?

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

Thank you, Tom, I will take those questions in turn. Defining a patient with severe asthma is still difficult. Colin talked us through very clearly the GINA treatment guidelines, patients who remain symptomatic despite taking GINA 4 or GINA 5 therapy are classically defined as having severe asthma.

I think it is very important to remember that some patients are uncontrolled despite all of our currently available therapies. Some patients can be controlled with the treatments that we currently have. But many of the treatments we have, we have had for many years and although they can be effective, they have significant side effects.

In terms of what I think are the greatest unmet needs, you are absolutely right I see people with severe asthma every day and they tell me that they do not like the treatments that they have to take. In particular they do not like taking oral corticosteroids. These drugs have significant side effects.

From a doctor perspective, I am worried about long-term consequences which includes diabetes, osteoporosis, weight gain, nonalcoholic fatty liver disease, cataracts, and I could go on and on. From a patient perspective these drugs change people's moods, cause them to not be able to sleep at night and give them a huge appetite and cause them to gain weight very quickly.

From a payer perspective, as Colin has already alluded to, this relatively small percentage of patient consume a large amount of healthcare because they are chronically unwell, who because they are having hospital admissions and unscheduled healthcare utilization and also there is a significant indirect cost to the economy.

Certainly within the UK we recognize that the indirect cost to the economy is actually greater than the direct healthcare costs as people have to take time off of work because they are sick or because they having to look after their children that are sick.

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

That is great, thank you.

During this weeks ERS, I heard you from the platform describe yourself as an eosinophil geek. Certainly there was a huge amount of excitement and discussion amongst the community about the role of the eosinophil. How do you see the relationship between eosinophil levels on patients who are suffering from asthma and the severity of their disease?

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

Yes. Thank you for describing me as an eosinophil geek. That is completely fair.

I think we're in a journey within respiratory medicine and as an area, therapeutic area, it's far behind some of our other areas, we're only finally -- eosinophils were initially discovered in 1879 and it is now only really at this conference and recent conferences that we realize they are important. There have been some lovely publications from primary care studies demonstrating that patients with a higher blood eosinophil level are at increased risk of having asthma exacerbation in the next 12 months and their asthma control tends to be lower.

We now know by doing a relatively simple blood test we can help predict response to therapy. For a long time I have had to almost take a wait and see approach and try a treatment with a patient and hope that the benefit is better than the side effects. We're finally starting to get to the point we can use a simple blood test to predict response to treatment.

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

You saw the benralizumab phase III study data for the first time on Monday and I guess the key question, I would like your perspective on is, how does this data run and how do you think benralizumab compares to current alternative therapies?

I guess, as a second question, there was some discussion through the meeting around whether or not benra might be almost too effective in eliminating eosinophils. Would you have any concerns about the speed and extent of eosinophil depletion that we saw in the phase II and phase III programs?

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

Just a touch on our current standards of care from a doctor and a patient perspective it is just not good enough. Significant side effects associated with the treatments and many patients despite maximum therapy are uncontrolled and so that means daily symptoms, increased risk of an asthma attack, increased risk of unscheduled healthcare utilization. I'm glad we're moving towards targeting eosinophils and I was pleased to see the positive results from the phase III studies.

One thing that jumped out to me straight away was the possibility of eight week dosing. I have many, many, hundreds of patients already receiving other biologics and they can be transformational for the correct patient. For the moment patients are having to come up to my unit every two or four weeks. Any option to decrease the frequency of dosing is very well taken.

Also, I think it is very important in terms of drug administration, when I talk to my patients they would much rather have a subcutaneous injection than an intravenous infusion on a regular basis. That is a very big positive.

Now from my perspective having spent many years studying the eosinophil and looking after people with other eosinophilic conditions such as eosinophilic vasculitis. In the wrong patient those can be very dangerous. I think that rapid onset of action and the potential of eosinophilic depletion is actually very important, a very positive step. Certainly if I was using to use a drug to target the eosinophil I would want a drug that worked very quickly and had a very significant depletion of cells from the [organ] and the lung.

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

Finally, it would be great to get your perspective on healthcare systems. Now that we see more effective and more convenient therapies to severe asthma, some of them biologic emerging, how do healthcare systems need to evolve to now most effectively use them?

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

Tom, that is a very good question. They're going to have to change. For a long time within respiratory medicine, we've had one biologic that is available for a small percentage of our patients. With these new anti-eosinophilic compounds that are coming online and other potential drugs further downline, the vast majority of our patients will be able to receive a biologic. That means a massive upscaling of resource.

One of my major concerns is that many patients with severe asthma are not being identified. They are in primary care, they are not getting through to the experts and I think there is a significant potential to treat many more patients with an effective therapy that does not have the side effects.

Key first issue is identification. The key second issue is how -- who delivers the drug and where it is delivered and how frequently it is delivered.

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

Andrew, thanks very much for taking those questions.

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

A pleasure.

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

This is Tom Keith-Roach and I lead the respiratory franchise at AstraZeneca and in this final session I would like to share some forward guidance on the key future milestones for benralizumab. But also along the lines which Andrew just outlined. How we AstraZeneca see the respiratory biologics market evolving. If you could please go to slide 35.

As Colin described earlier, CALIMA and SIROCCO are part of the Windward program. In asthma, Windward includes the BISE study, this was a lung function study in mild moderate asthma presented today at ERS, the SIROCCO and CALIMA studies that we have just covered, will make regulatory submissions in the US and Europe before the end of this year with that data. The ZONDA program which is an oral steroid sparing study, the results of that we will present in the first half of 2017 next year and BORA and MELTEMI. These are the safety extension studies for SIROCCO, CALIMA and ZONDA. In COPD in green TERRANOVA and GALATHEA are also two pivotal studies in COPD with data expected in 2018.

In addition to these you can see GREGALE, this is a study assessing the potential of at-home administration. We expect data from that program to be presented again in the first half of 2017 and ALIZE and ARIA, these are the influenza vaccine and allergen challenge studies respectively.

Collectively, the Windward program represents a strong commitment to strengthen the clinical understanding and profile of benralizumab and also explore its benefit in new areas. Your reference we have a strong patent portfolio covering benralizumab which includes data exclusivity until 2029.

Go to slide 36 please. Here I would like to cover a little bit about how we think about the marketplace. I suppose there are two messages here. Firstly, that we see severe uncontrolled asthma and COPD as very well-defined patient populations, which as a company we understand well. But we also see very significant future headroom for growth.

Firstly, I saw in the top panel of this slide at launch in asthma we will be focused on a very tight group of patients which we estimate to be around two million severe, uncontrolled asthma patients in the top 12 countries around the world. Those numbers were assessed in 2015 and are all externally validated sources.

Similarly, when we look at the bottom panel in COPD, this is a well-defined population that we also estimate around about two million patients that are severe and uncontrolled in the top 12 countries around the world. Just as an aside on the COPD, I have to say even we were a little surprised when we looked at the eosinophil levels of patients in our COPD studies because up to 55% of those patients also have eosinophil levels above 150.

So, by convention, might be considered to be of an eosinophilic phenotype. So while we are starting with severe asthma we also see a very strong rationale for benralizumab also being effective in COPD and this is also a hugely underserved population of patients.

Beyond that, on the right-hand side of this chart, you can see a little bit of why we see headroom for growth of this marketplace and there are a couple of things in there I would just like to call out. Firstly, for reasons that Andrew spoke about, biologic penetration rates in respiratory, last year certainly are very low. Xolair historically have been the only approved respiratory biologic and biologic penetrations being held back by some of the limitations of existing treatment. Slow onset, difficult patient identification, low responder rates, cumbersome dosing, administration, and anaphylaxis have all exerted a significant drag on bio penetration. Again as we see more effective and more convenient medicines becoming available, we expect that to quite rapidly change.

It is interesting to look at bio penetration rates in America in rheumatoid arthritis, and other areas like Crohn's disease, it has taken some time but 15 years after the first biologics were launched we see bio penetration rates in the range of 50% to 60%. Certainly, that is an area where we would see reporting growth, and beyond that, we also expect to see sustained increases in prevalence, in diagnosis and treatment, as Andrew described both in the top 12 countries but also I have not talked about them other rest of world markets. Certainly diagnosis and treatment rates in those countries would be even lower but in some sense also further potential growth.

If you could turn to slide 37 and this is the final one. I am just going to try and summarize what we have covered in this session so far. I want to leave you really with three things. We have had two positive phase III studies in SIROCCO and CALIMA. Benralizumab has demonstrated the efficacy

of Benralizumab in severe asthma. Comprehensive efficacy on exacerbations, lung function, symptoms, quality of life, efficacy that is delivered fast from the first dose.

It is equally effective given every four or eight weeks, we will submit the full data file but we see clear benefits for patients and healthcare systems of a once every eight week dosing regimen. We see even greater benefits in patients who have had a more frequent exacerbation history an a placebo like adverse event profile.

Secondly, you would not be surprised to hear that operationally we are now gearing up for asthma launch. We are going to be very focused on, in the US, making benralizumab fast and easy to access, use and reimburse. This is going to be critical. Understanding and supporting diagnosis and treatment pathways and building out the specialty biologics organization.

In terms of future milestones, Windward is the largest development program of any biologic in respiratory. We expect this to progressively strengthen the clinical profile and support sustained longer-term growth.

That is where I would like to finish, we would like to leave time for questions and I am going to hand back to Thomas to coordinate that process. Thank you.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you, Tom. I think that was very interesting and quite relevant comparison to the anti-TNF use in immunology. Thanks also to Dr. Mark FitzGerald and Dr. Andrew Menzies-Gow. If I may now, our so called eosinophil geek for sharing their data, their experiences and also their insights.

Listening to the real-life experience, it sounds as if the speed and depth of eosinophil depletion and also the infrequent dosing are very important aspects of the profile of benralizumab.

Now we have time for Q&A but we kindly ask that only investors and analysts ask questions on this conference call.

(Operator Instructions)

QUESTIONS AND ANSWERS

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Richard Parkes from Deutsche Bank. Richard welcome to our call.

Richard Parkes - *Deutsche Bank - Analyst*

Hi thanks for taking my questions. I will just limit it to a couple first. First, maybe for Tom and Colin just wondering if I could get your perspective on how you might be able to capture some of the differences in terms of the mechanism, obviously we know about the dosing, but in terms of the potential to overcome cytokine redundancy.

Is there any analysis that you can do to pull that out from the data or can you look at future studies, like at maybe at patients failing, other IL-5 cytokine inhibiting therapies or maybe that is something that you might expect to see emerge with longer-term therapy? So, just wondered about your thoughts on that.

Then, the second question is the mild to moderate study that was presented this morning, there was a death in that trial, due to pencytopenia. I think that was deemed as not drug related but obviously given that this is a self depleting antibody there is likely to be quite a lot of focus on that case. I just wondered if you could talk us through the reasons why that was deemed as not a drug-related incident. Thanks very much.

Dr. Mark FitzGerald - *Centre for Heart and Lung Health, Vancouver Coastal Health Research Institute, University of British Columbia - Director*

This is Mark FitzGerald here, I think I will just address the earlier part of your question in terms of the mode of action and the terms of -- I think there are two opportunities here. One is that these are two very large data sets that will lend themselves to future subgroup analysis and closer analysis in terms of data that could not be included in the already comprehensive reports.

The other likely important study, which I am happy to say that AstraZeneca has agreed to fund, is a study in Canada where we will, in a number of centers that we will induce a mild asthma attack by getting patients to inhale allergens, something they are allergic to and then that will provoke eosinophilic response. In that study we look at what happens in the bone marrow, in the blood, in the airway both in the bronchoscopy specimens and sputum. And I think the novel attributes that you have referred to in your introductory comment and question will be much better elucidated when we look at those compartmentalization and trafficking of eosinophils from those different compartments.

I think we have a lot to learn, the clinical results are very impressive but we need to explore further the biology of how this compound works. I will defer.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thanks [for that]. There was more about how to characterize and maybe capture the differentiating factors for benralizumab. Then there was a question on the mild to moderate I think the BISE study, right? And I will hand it over to Colin to answer that.

Colin Reisner - *AstraZeneca PLC - Chief Medical Officer of Pearl Therapeutics and AstraZeneca Head of Respiratory Global Medicines Development*

Thank you. We have the largest phase III development program with a biologic. We have not seen a signal from a safety perspective relative to placebo. In phase III, unfortunately, SAEs and deaths do occur and the assessment of causality is by the principal investigator. This was the principal investigator's assessment. It also goes through and IRB and they also are involved in the overall review.

Richard Parkes - *Deutsche Bank - Analyst*

Great. Thanks very much.

Nick Stone - *AstraZeneca PLC - Director of IR*

This is Nick Stone, Director of investor relations from AstraZeneca, we have two online questions from James Gordon. The first one being whether you would hope to get a specific claim about fast speed of onset and FEV1 benefit on the label? The second question is would you look to CALIMA subset analyses and would you hope to get those on the label in higher exacerbating patients or would you expect to only have the overall study results from this study?

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

Thanks very much, James. This is Tom Keith-Roach. Obviously in answering those questions I need to be clear that both would be subject to regulatory review. We have not made the submissions in Europe and US. As I said earlier we would expect to do that before the end of this year.

Certainly the answer to whether we would hope to, as you articulated it would be yes. I think we just need to be clear, on the first question, benralizumab on both doses demonstrated at four weeks, after the first dose, both a clinically and statistically significant improvement in lung function. That was a secondary endpoints on a study why we were positive on the primary endpoints. We would not only hope to, we would expect to see that included in the label and support of promotional claim. Obviously subject to regulatory review.

Similarly on the subgroup analysis, this was a prespecified analysis and it was also included in both of the primary publications in the Lancet that were published at nine o'clock in the morning this Monday. Both subject to regulatory review I would both hope and expect to see both of those included somewhere in the label.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you for that, Tom. Now we go to Boston and Steve Scala of Cowen. Welcome to our call, Steve.

Stephen Scala - *Cowen and Company - Analyst*

Thank you. I have two questions. First for Tom, you mentioned that benralizumab would be fast and easy to access. That implies price might be one lever, is that the conclusion we should draw or might there be another conclusion we should draw?

The second question I would like to ask the independent physicians what they think of the other novel targets in the AstraZeneca pipeline in the area of respiratory. Let me just mention a few: the inhaled SGRM, the P38 inhibitor, inhaled beta interferon, TSLP, TLR9, and DPP1. Which is most interesting and which holds the least promise in your opinion? Thank you.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you, Steve. The first question was for Tom, about fast and easy access and if price is a component there?

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

Great question. You should not make that inference, no. I am not commenting on price, that is obviously subject to conversations initially regulatory and then with pricing and reimbursement authorities.

What I was referring to is if you look at some of the things which have held back, biologic penetration in the past, those have been associated with the fact that it is time-consuming and complicated for physicians and patients to use biologics in terms of prior authorization, difficulty getting reimbursed because of plan coverage, but also how effective the specialty pharma distribution model is, particularly in the US in terms of how long physicians and patients need to wait to receive their medication. These are things we're focused on now as a company to make sure that all of those kinks, as far as possible are ironed out by launch to allow patients to quickly benefit from this medicine.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Steve's second question was about other targets in development at AstraZeneca, for instance P38, those inhaled interferon, and I will first hand over to maybe Dr. Andrew Menzies-Gow for your view.

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

There is a very extensive pipeline and I am not just saying that because I'm sitting in a room full of AstraZeneca employees, I think they have a good pipeline and a clear vision of changing the way that we manage respiratory disease from being reactive and trying to manage symptoms to being

far more proactive and dealing with the drivers underlying the immunology and hopefully eventually getting to the point of disease modification remission and maybe one day cure. Certainly every single asthma patient that I see wants and cure and they don't want to have to take therapy for the rest of their lives.

Of all the different molecules many have significant potential. In no particular order is the inhaled seagram and inhaled anti inflammatory that is not a corticosteroid is very exciting to me. I think this has a potential to change the paradigm. Even though inhaled corticosteroids are very effective, patients across the globe are worried about the side effects and if we can deliver the same level of anti-inflammatory effect without the perceived side effect profile. That could be very exciting for the future.

To me what is more exciting is going away from trying to chronically treat patients and decrease inflammation to trying to get to a point where we can induce disease modification and remission. So the two compounds for me particularly interesting the concept of targeting the alarm at the top of the inflammatory cascade so I think slight TSLP which we think are activated very early on whether it is through allergens or viruses and blocking everything downstream of that. That might be very exciting in the future.

Then, the concept of switching away from the T2 high to more of a balanced endotype using an inhaled TLR9 agonist also I think has significant potential.

Nick Stone - *AstraZeneca PLC - Director of IR*

Thank you, Andrew. We have a question from Sachin Jain from Bank of America.

Sachin Jain - *BofA Merrill Lynch - Analyst*

Thanks for taking my questions.

A couple please. Firstly on the label. Could you comment on the breadth of eosinophils you are looking to pursue, the existing mepolizumab label is fairly broad. Are you pursing a similar broad label or just greater than 300? And related, what comfort do you have that 300 is the right cut off given that phase III was not powered to discuss that.

Second question on a comment that Dr. FitzGerald made, if I understood it correctly, I think you said the FEV1 benefit was prediction of exacerbation, can you just give just some color as to how you might use that clinically and do you believe what you're seeing here on that predictive benefit is different versus the other competing IL-5s.

And then thirdly for Tom, just as you have looked at the Nucala launch, are there any learnings from that as you think about ironing out kinks or any specific factors that have done well or poorly that you think you could do differently. Thank you.

Nick Stone - *AstraZeneca PLC - Director of IR*

Thanks, Sachin. First question with regards to label breadth and specifically the greater than 300 cut off? A second question with regards to comment from Dr. FitzGerald with regard to FEV and prediction of exacerbation and then finally, Tom, a question for you in respect to the Nucala launch.

Colin Reisner - *AstraZeneca PLC - Chief Medical Officer of Pearl Therapeutics and AstraZeneca Head of Respiratory Global Medicines Development*

Thank you. While we cannot speculate about the specifics of the future regulatory outcome or what the label is going to look like, our data showed benefit in patients with eosinophils greater than 300 and as was also included in the Lancet articles, there is benefit in eosinophils below 300. So, we believe there will be a labeling that will be consistent with allowing the use across the spectrum in patients within eosinophilic phenotype.

Dr. Mark FitzGerald - *Centre for Heart and Lung Health, Vancouver Coastal Health Research Institute, University of British Columbia - Director*

I could just bridge to the question that was asked directly of me, to just add to that point that one of the unique characteristics of both of these two large phase III trials is that we will have the ability to merge these data sets and provide a much better predictive value around eosinophil levels. The values that have been taken in this and other studies have been relatively arbitrary where we will be able to construct ROC curves and better define.

To the specific question, just to give you an example. Omalizumab the generally clinically relevant discussed point of decision-making with omalizumab is to look for efficacy at six months and that is generally considered. My predictive comment was a cautionary comment that it has the potential, and the reason it has the potential is because these patients are quite symptomatic and the levels of bronchodilator improvement that were shown, it is quite significant. Sometimes you see in large trials a statistically significant improvement to the measurement. But what you see here is both statistically significant but also very clinically relevant.

The other potential for future analysis of this data set is that if we look at measurements of lung function which have not yet been reported such as peak flow, symptom scores, at the very beginning of treatment initiation, it may also give us a signal. I think ultimately with these medications that are relatively expensive we will end up with a composite of eosinophil level, a history of exacerbations and a lung function, it is sort of a scoring system. I think that would be very much appreciated by clinicians, certainly by patients and also by payers.

Tom Keith-Roach - *AstraZeneca PLC - Head of Respiratory Global Product and Portfolio Strategy*

Firstly thanks for the question. Because normally the question I get asked is do I see any disadvantages to coming to market after mepolizumab, by inference what you are suggesting is, what I believe which is frankly we have the advantage in coming to the market slightly later with such a robust clinical profile.

Actually if you look at the US market, the impact of mepolizumab has not just been to take share, it's been to accelerate the penetration of biologics. I think we are going to be entering a market which is somewhat more mature and moving fast relative to the one that we see today.

I think that there are different learnings across European markets and the US. I touched on the access and specialty distribution kinks in the US and that is really why we are very focused on addressing those issues across the next 12 months.

I think in European markets you look at somewhere like the UK, really back to the slide I presented on who we see this drug as being relevant for, we need to be very precise. This is a precision medication in terms of mechanism and I don't think we should be looking at a market like the UK and initially believing that it should be used everywhere.

That is why you see us within some of this analysis starting to think through sub populations and identifying places where the absolute clinical benefit is greatest. You should take that as a signal for what we have learned from Nucala and how we are thinking about addressing some of these HTA countries.

Sachin Jain - *BofA Merrill Lynch - Analyst*

Thank you.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you for those insights, Tom. Just to remind everyone on the call that it is star one to ask questions.

We have a follow-up question from Richard Parkes at Deutsche Bank.

Richard Parkes - *Deutsche Bank - Analyst*

Hi. Thanks for taking my follow-ups. I just wondered whether, -- first of all you could talk about, maybe Dr. Fitzgerald and Dr. Menzies-Gow, from what you have learned about the proportion of patients, severe asthmatics that are responding to some of the new biologic therapies.

I'm just wondering ultimately if we have got maybe three mechanisms, what proportion of patients do you think would ultimately be eligible for biologic therapy and how much overlap is likely to between the eligibility and responsiveness to the different mechanisms that are coming through?

Then, one for Dr. Menzies-Gow given his expertise in eosinophilic disease. You mentioned other diseases where the differentiated mechanism of benralizumab could be even more important. I just wondered if there are any specific disease areas where you would like to see the drug used or where you might potentially use it off label when available?

Then third final question, I just wondered if someone could speculate over the lower efficacy with the eight week dosing regimen and the CALIMA study in terms of times to first exacerbation that lung function symptom data look comparable and maybe with some geographic differences. I'm not sure if you covered that. So just if you could speculate on that. Thanks.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thanks a lot, Richard, for those questions. There is one first maybe we want to start with Mark FitzGerald, to cover learnings from the current biologics and who is responding to what mechanism. Then maybe then when we hand over to Andrew Menzies-Gow we can then also cover the eosinophil question and maybe talk about what different sub population may be relevant for that. Then maybe Colin want to cover the eight-week dosing.

Dr. Mark FitzGerald - *Centre for Heart and Lung Health, Vancouver Coastal Health Research Institute, University of British Columbia - Director*

Thanks very much for that question, Richard. My perspective is actually from two ends of the spectrum as it were. One is that I am a real doctor that sees patients and I am a clinician and a clinical researcher. The point that I make about that is that this is anecdotal evidence-based medicine but it is a prelude to my broader response to your question.

We have been very fortunate to have patients enrolled in pretty well all of the current biologics and development and it has been really gratifying when you get the right patient and they respond as they do. In fact in the news release that came out from my own research institute earlier in the week in response to the CALIMA data we had a respiratory therapist in our hospital who is a poster girl for this type of personalized medicine and that in her little bio that we included, she basically has stopped requiring prednisone. She is breathing, in her own words, for the first time in years, normally and not requiring as much maintenance treatment. And I know that is a skewed response to your question.

But I am going to skip to the fact that I am also very much involved at a pharmacoepidemiology level and I constantly analyze a data set of over 400,000 patients, so every patient with asthma in British Columbia. What we have shown in that data set is that we are talking here about 5% to 10% of patients or 20,000 to 40,000 patients, many of whom are languishing in the community, not being referred by resp GPs. A lot of them being seen by community respirologists who do not really have an interest or an expertise in this area.

So there is a huge unmet need in terms -- although the numbers are proportionately not as big as the total population. When you get down to the smaller subset of patients the issue is there.

I will conclude by saying that in a paper published by David Price in Lancet Respiratory Medicine from a primary care perspective, within that broad population there was a signal for elevated eosinophil levels and a risk of exacerbations. I think the unmet need is there and the patients are there that we identified and treated with these treatments.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

We will go to you for both question one and question two.

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

Just to come back to question one slightly. As physicians, we are starting to see multiple different biologics with similar mechanisms of action and broadly patients frequently fall into a gray area where they could have one or another. So what would determine which ones we use, some of it would be around frequency of dosing, speed of onset of action.

I do not think it should be underestimated that a very rapid response is very important from a patient perspective. They want to go into the right drug first time. From a physician perspective if I find out after four weeks I have got them on the right drug I can relax and move forward.

From a payer perspective clearly they don't want to be providing a drug that is not going to be efficacious. For instance with omalizumab we have to trial for 16 weeks before we know whether or not it is being effective.

Coming on to your very good question around other areas eosinophilic areas of interest. I have written down three that I think there is definite attraction. The largest areas around nasal polyps.

Nasal polyps are frequently eosinophil driven and patients associated with a significant morbidity for them. From a health economic perspective these patients often have frequent and recurrent endoscopic sinus surgery to clear the polyps out. I look after patients that may have four, five, six previous surgeries and they are miserable because of the side effects and the complete loss of smell and continual nasal blockage associated with that. Nasal polyps would be a clear area of interest.

From areas of severe eosinophilic disease that I particularly worry about, I look after patients with what we used to call Churg-Strauss syndrome and we now call it EGPA. This is an eosinophil driven vasculitis that can affect any organ in the body, but particularly the heart and can be rapidly fatal.

Certainly in this patient population at the moment I have to use very high doses of steroids and toxic drugs that we would normally use for chemotherapy such as [sylofloconide] to a drug that acts rapidly and targets the eosinophil and depletes the eosinophil very quickly, I would definitely want to use in this sort of condition.

Then finally there is the broad hematological condition of hypereosinophilic syndrome and that can be driven by many different things. But again this is an area where there are not that many good therapies that a subset of patients can already have one specific targeted therapy but the vast majority again ended up using corticosteroids. So at least three areas where I can see that a targeted therapy that depletes the eosinophils quickly would be of significant benefit.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you, Andrew, and the last question was for you, Colin, on the 8-week dosing.

Colin Reisner - *AstraZeneca PLC - Chief Medical Officer of Pearl Therapeutics and AstraZeneca Head of Respiratory Global Medicines Development*

So, overall, importantly we saw a benefit in both the Q4 and Q8 week dosing across the profile for asthma exacerbations as well as improvement in FEV1. In the Q8 week dose we also saw the benefit in symptoms. So we are very excited about the overall profile, especially since there is the opportunity to give fewer doses per year by a prefilled syringe. This will be really important to both patients and physicians.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you. I hope that covers your question, Richard.

Nick Stone - *AstraZeneca PLC - Director of IR*

We have a further online question from Steve Scala at Cowen. And the question is; what is your view of the IL-13 target particularly after the failure of a competitive drug? Why will AstraZeneca be successful when Roche failed? And fortunately we're joined by Bing Yao Head of Respiratory, inflammation and Autoimmunity. Bing, I would like you to answer this question.

Bing Yao - *AstraZeneca PLC - Head of Respiratory, inflammation and Autoimmunity*

Steve, we continue to believe that our IL-13 are important therapeutic target for asthma. And also we are confident of our programs in here. Certainly this week at ERS we learned a good deal about the competitors program, lebrikizumab . There are quite a few important differences between their program and our program. In particular the patient population that we are targeting.

Just to give you a couple of examples, one is that based on our learnings from our phase II program, we were required the patients to be [reversable] not on oral corticosteroids and more importantly the patients have to have prior exacerbation. A documented the history of two or more prior exacerbations. I think that is really one of the important differences between our program our also [which] program.

Additionally, we have also, have a novel biomarker. We think that is more predictive of a response to IL-13. So, in fact this week, we presented the data to show that DPP4 is predictive of IL-13 response. That has been incorporated into our phase III program.

So in addition to periostin we also have DPP4, for the Phase III program. Our Phase III is currently on track and we will have the data in the first half of next year.

Nick Stone - *AstraZeneca PLC - Director of IR*

I was just wondering if Drs. FitzGerald and Menzies-Gow if you have any perspectives on this IL-13.

Dr. Mark FitzGerald - *Centre for Heart and Lung Health, Vancouver Coastal Health Research Institute, University of British Columbia - Director*

I would just build on Bing's comment that actually from the podium, this week when this data was represented that if you picked the wrong patient it is a classic example, if you picked the patients without an exacerbation history which was the case for this compound you are not going to see efficacy.

I think the story around periostin is maybe not as robust as people thought in the past. And I think the fact that you have got a novel biomarker, again, which is representative of true personalized medicine, the right patient with the right history with the right biomarker that you have the potential to be more successful.

I actually, both in public and private told Roche that I think it has not been good contribution to the scientific and patient communities to have backed off and so I think it is unfortunate. But I would not give up on the IL-13.

Dr. Andrew Menzies-Gow - *Royal Brompton Hospital - Consultant in Respiratory Medicine and Director, Lung Division,*

I would just like to add to that, this is a clear signal from the Phase IIb studies of significant improvement in FEV1 with anti IL-13. So the drugs do have an effect and I actually agree with the two previous comments. If we are going to look at exacerbations as the primary outcome we need to select patients with a past history of exacerbations at study entry.

Thomas Kudsk Larsen - *AstraZeneca PLC - Head of IR*

Thank you very much for those insights. At the current time we do not have any further questions. So thanks for this last question, Steve.

Thanks to all our presenters today for making today's call really interesting and insightful. Thanks also for the general interest in AstraZeneca and for the opportunity to share the data and the update for benralizumab in particular. We will now close the call. Have a nice day all.
