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<<Robert Forrester, President and Chief Executive Officer>>

So, welcome everybody. Thank you very much indeed for joining us this evening. I just want to remind you that this event is being webcast. So try to keep your language to be not too colorful. I know that some of you who can get riotous after a fizzy water. So please try to contain your enthusiasm.

So, thank you all for coming. This is a huge moment for us as a Company. We're seven years old, founded out of Harvard, MIT, the Broad, the Whitehead. And today to be here at ASH and presenting, thanks to Dr. Flinn, some fantastic positive Phase 3 data in CLL/SLL, is a huge moment for us. And we are absolutely thrilled and delighted that we'll be able to help another whole wave of patients in different lymphomas and leukemias. So this is a very exciting moment for us.

As one of our patients said a few years ago, "cancer sucks," but it challenges us to be our best. And cancer does suck, and what I think we show today is that duvelisib was living up to everything that we hoped it could be. And it's going to make a difference for a lot of patients. So, we're delighted to be here today, and to talk a bit more about duvelisib and talk about where it is today, where it's going, and where it could go in the future as well.

So, today what we're going to do is we're going to start with a few slides but then we're going to really open up to questions. We want this to be very, very interactive. We want to get the panelists engaged in conversation. We want to get you engaged with us and ask any questions that you feel that you would like to ask and get into a conversation about duvelisib.

And so this is really for everyone's benefit here, so please, please prepare questions. I've got a few questions here too of course but I really want to get you the audience involved. This is very much for your benefit.

So we're very, very lucky. We got Dr. Kunkel, who has joined us, and she comes from former Chief Medical Officer of Pharmacyclics and is on our clinical and scientific advisory board. We've got Steve Bloom, who is our Chief Strategy Officer at Verastem. And then we've got Dr. Steve Horwitz here who is from Memorial Sloan Kettering, and he's the Principal Investigator on the T-cell program that's going to be presented tomorrow night at 5 o'clock. It's an oral presentation, and I think one of your colleagues is going to do that. And we're looking forward to seeing that tomorrow night. And the data is good, I think we get a sort of slight preview of it this evening. And Dr. Ian Flinn, who was the star this afternoon at 4:30 in presenting the DUO data, he's going to do a short reprise of some of those slides in a few moments.

And he also was the Principal Investigator on the DYNAMO study. So, we could talk about not just the CLL/SLL, but also FL. I think we need to spend a little bit time talking about that as well. So with that, maybe Ian, I think you're first up, just talk a little bit about some of the slides from this afternoon.

<<Ian Flinn, Director of the Blood Cancer Research Program at Sarah Cannon Research Institute>>

Sure, thanks Robert. It's really been a very good day. We've been working on this drug for a number of years now. Just very recently we published the Phase 1 results in *Blood* and so to see that this now, this pivotal trial be presented with a combination of a number of years of work. And so thought may I just walk you through in sort of abbreviated fashion.

The results of the study, so now you know, this is a randomized Phase 3 trial in patients with relapsed and refractory chronic lymphocytic leukemia or smaller lymphocytic lymphoma. There are 319 patients on this study, and they are randomized receive either duvelisib at 25 milligrams given twice a day continuously or ofatumumab at the standard dose.

Now, the important part of this study is the crossover design. There is an optional crossover that allow patients who progressed on one of the arms to crossover onto the other arm. And in fact, many patients did crossover from ofatumumab to duvelisib - 89 patients crossed over. The primary endpoint of this study was progression-free survival and key secondary endpoints included overall response, duration response and overall survival. And of course, we also collected safety data.

Eligibility for this study was very similar to most studies in this space. Patients had to have - of course had to have disease that required therapy - they had to have one or more prior anti-cancer treatments. Patients could have pretty lenient cytopenia, so hemoglobin of 8 and platelet kind of 10,000. This could be with or without transfusion support. There is no minimum absolute neutrophil kind of required. And we did exclude patients with prior BTK or PI3-kinase inhibitors.

Now, from prophylaxis all patients in this study were required to receive new assistance prophylaxis and while it wasn't required, it certainly was encouraged for patients to receive prophylaxis for CMV. This is sort of the cut-to-the-chase. This is the primary endpoint of the study - progression-free survival.

And as you can see, these slides are – these curves are highly divergent and there is a significant improvement in progression-free survival - 13.3 months versus 9.9 months with ofatumumab with a hazard ratio of 0.52 is a highly statistically significant value. This was per an independent response committee. We also - the investigators - also looked at response and they saw an even greater difference that was progression-free survival of about 17 months for patient for the investigator assessment.

So, I'll just skip through this. This is – we look at a bunch of different subgroups, one of the most important subgroups in chronic lymphocytic leukemia is patients who have 17p deletion, this is a very poor prognostic indicator for CLL and in this patient population, the data also held out. So I mean in progression-free survival of 12.7 versus 9.0 in ofatumumab, hazard ratio of 0.41 again highly statistically significant.

We also looked at key secondary endpoints, including overall response. The overall response was about 74% in patients with duvelisib and about 45% on patients on the ofatumumab arm. The lymph node – the decrease in the masses of the lymph node was even greater diversion. So 85% of patients treated with duvelisib had more than a 50% decrease in their lymph node areas compared with just about 16% of patients treated with ofatumumab.

So very, very encouraging results. If we looked at the overall response rate in patients who had a 17p deletion, it was essentially the same - 70% versus 43%. So, the data held up in those – in that patient population. Of course, we also looked at adverse events. This is the adverse event profile of duvelisib, compared with Ofatumumab. In general, this is very consistent with what we saw in the publication of the Phase 1 patient population. One thing to keep in mind when interpreting this data is that the median observation period for patients treated with duvelisib was over twice that of Ofatumumab - 50 weeks versus 23 weeks. This of course is for the trial design.

We did see – and if we looked predominantly at Grade 3 or greater adverse events - there was greater neutropenia in the patients who received duvelisib compared to Ofatumumab and from hematologic toxicity standpoint, 30 versus 17 now, now on the non-hematologic toxicity the leading Grade 3 or Grade 4 non-hematologic toxicities were diarrhea, colitis and pneumonia for patients with duvelisib. These events were actually rare on the patients treated with Ofatumumab.

If you follow the PI3-Kinase space, you will know that there's a set of adverse events that are common with these inhibitors. And so we spent some special time looking at these events, and they are listed here. I think one of the important things is that they're very – that infrequently that these adverse events lead to discontinuation of duvelisib. And we did see a 6% opportunistic infection rate including two patients who developed Pneumocystis pneumonia - I'd like to point out that that these two patients in fact weren't taking their PCP prophylaxis. And so perhaps they could have been prevented if they were taking their prescribed or their protocol mandated PCP prophylaxis. There were four patients who died on this therapy. These were predominantly from infectious complications.

So, I mean in conclusion, DUO met the primary endpoint, which was an improvement in progression free survival we saw improvement across the Board in other secondary endpoints, including progression free survival in the high-risk 17p population. We saw improvement in overall response rate compared to over Ofatumumab. We saw improvement in the lymph node sizes and masses. We did also see, from an adverse event profile, the – this median – with median exposure of 15 weeks - we think that this adverse

event profile was very consistent with what we saw in the Phase 1 study and is manageable.

Finally, I think that these results of the DUO trial as oral monotherapy support the notion of this being a potentially new therapy for patients with chronic lymphocytic leukemia or small lymphocytic lymphoma. That's the end of my slides.

<< Robert Forrester, President and Chief Executive Officer>>

And so, Dr. Horwitz maybe you could go through your slides quickly. Then we can go into a Q&A session.

<<Steven Horwitz, M.D., Memorial Sloan Kettering Cancer Center>>

Okay. Thank you. Thanks for having me. This will be super fast. So, I'm Steve Horwitz from Sloan Kettering in New York, and I'm just going to show a little bit about the T-cell lymphoma program. So, you probably know that T-cell lymphoma still represents a pretty high area of unmet need in the lymphoma space with the exception of ALK-positive anaplastic large cell lymphoma, where the cure rates are about 60% or so with combination chemotherapy. Most of the other subtypes of systemic T-cell lymphoma patients do more poorly with the relatively few patients cured with current frontline therapies.

In the relapsed/refractory setting there are four drugs that are approved: pralatrexate, romidepsin, and belinostat of course are approved across all subtypes. And they have, you know, what would I say, modest reasonable response rates. But the majority of patients either don't respond to those drugs or don't have long-term disease control. The one outlier, of course, is Brentuximab Vedotin in relapsed anaplastic large cell lymphoma. So, that high CD30-expressing lymphoma has very high response rates. So for many of our patients, particularly relapse patients they need additional therapy, so there's lots of room for improvement there.

This is the data that I'm impressed about from the T-cell subset from the Phase 1 study, which is also in *Blood* now, and this one should be out of line hopefully pretty soon now. So, in that large Phase 1 that Ian led, we treated 35 patients with T-cell lymphoma, cutaneous T-cell lymphoma and peripheral T-cell lymphoma and saw reasonably good response rates. So again, this was in the Phase 1. The patients in the T-cell subset here primarily got 75 milligrams BID, which was the MTD, one or two got 100, a couple got 60, which is a little different than the indolent lymphoma patients who predominately got lower doses of duvelisib.

50% response rate in peripheral T-cell lymphoma, again it's only 16 patients, but that would certainly put in the ballpark of what we see with a good single agent activity, a little lower response rate in CTCL .We've kind of hoped that there would be some sort of predictive or cell activity. So you could sort of identify who was more likely to respond to enrich that population, but at least if you look at the subtypes of T-cell lymphoma –

and and kind of “nerd out” too much for you guys here. But we see like responses here and there across all the different subtypes there wasn't like consistently was cytotoxic T-cell lymphomas. There wasn't really a sense that like this subtype is really where we're hitting this target makes the most difference.

So, based on that a strong desire to do better, we did have some patients with durable responses. This guy here actually is out at four-and-a-half years still in remission. So that was the big winner from the single-agent study with relapsed peripheral T-cell lymphoma is still in remission. But by and large the remissions were either partial, not complete, and didn't last years, which was what we'd like.

Based on some preclinical synergy with romidepsin, Alison Mosk, one of my colleagues will talk more about this tomorrow, as well as some genetic data from Stanford, and some myeloma data we borrowed from suggesting that combinations with proteasome inhibitors might make sense, we embarked on a really parallel Phase 1 looking at combination with the idea that we could develop a higher response rate, more complete responses and have a greater impact on our patients. So, this was investigator-initiated study initially supported by Infinity, now Verastem-supported through the Leukemia and Lymphoma Society grant that we have with some of our collaborating sites.

And it's basically two parallel Phase 1s, and Alison presents much more data on this tomorrow. Duvelisib in combination with romidepsin, dose escalation; duvelisib in combination with bortezomib, and then based on what we would see in the Phase 1s some expanded cohort in PTCL and CTCL, neither both or either arm depending on how the data looks. There is also a lead-in arm, which was added to try to get better on-treatment biosites to try to better sort of sort out predictors of response or resistance that data is not going to be presented at this meeting.

So, this is in the *Blood* paper Dave Weinstock, Raphael Koch are some of our collaborators at Dana-Farber - were looking at PI3-kinase signaling and T-cell lymphomas and they looked at a number of cell lines and saw which duvelisib didn't see activity in cell lines with T-cell lymphoma, which was unusual because at that time, we already had a 50% response rate.

Clinically, so I started thinking about some off-targets in microenvironment effects but then they looked at a number of cell lines here and I won't do justice to their figure but the cell lines where there's elevated Phospho-Akt here, here duvelisib, which is the red bar, was very potent in those cell lines.

So, it looks like in the lab at least certain cell lines Phospho-Akt may predict - not that surprisingly - some of the more responsive patients. This is a complicated assay to do in people because it's fairly unstable but it's something that we're trying to add into the studies and hopefully, we'll have some more data on that.

Just very quickly preliminary data, Alison will really show you this tomorrow but in the combinations with particularly romidepsin, we've seen some nice early responses. She'll

show you some updated data on this tomorrow and the responses have been, a few more complete response that we saw in the single agent study and across at least the two most common subtypes of peripheral T-cell lymphoma. So, we're encouraged with that early result.

So, just to conclude and then happy to talk about questions. We have preclinical studies that sort of capitalized on the Phase 1 response rate of 50% that kind of gave us some clues as to who might be your better responder or longer responder to this drug. We are unpacking that a little bit more in the Phase 1 we can give duvelisib with romidepsin or bortezomib safely and there's some different doses, different MTDs from those two arms, that Dr. Alison will talk about.

I didn't really get into this. She'll show you some interesting data tomorrow on the transaminitis and how that's different between the two arms and a little different than what we see in the single-agent study. And we think there's some interesting data there and again response rates of at least 50%. So, we think that certainly puts them in the ballpark of a pretty active drug for this disease.

I'll just conclude there. Thank you.

<<Robert Forrester, President and Chief Executive Officer>>

Go ahead, thank you. Dr. Horwitz. So just a reminder this data is going to be more, going to be more of this presented tomorrow at 5 O'clock, and so we're going to go to sort of now a group discussion. So again really want to encourage you all to ask questions. There are microphones around, Jonathan if – I'm going to ask one question first though.

And then Jonathan you can have the next question. So what is this solving for patients? I mean this is great, it's very, very encouraging and maybe each of you could talk a little about the different areas of expertise but Ian, maybe you should start?

<<Ian Flinn, Director of the Blood Cancer Research Program at Sarah Cannon Research Institute>>

I think I got that question today on the podium.

<<Robert Forrester, President and Chief Executive Officer>>

Oh, you did. That is where I got it from.

<<Ian Flinn, Director of the Blood Cancer Research Program at Sarah Cannon Research Institute>>

Hopefully my answer is consistent. I think that it's an option for patients. Ibrutinib is moving earlier and earlier in the course of therapy for patients with CLL, and so then the question comes up, what are we going to do with patients after that. And I think this is a

very good and potential option for those patients. There's also a lot of people - even patients - who are getting Ibrutinib in second or after and at least in my clinic there's probably 25% of patients said can't tolerate it. So it's an important option for those as well.

I'm excited about that for patients with CLL, I'm excited about that we're talking – I was talking earlier to someone in the hall about the potential in follicular lymphoma - we didn't talk about that tonight, but I think that's a kind of probably where I'm pretty excited. I am most excited in the B-cell malignancies and I'm actually really excited about the potential in T-cell.

<<Steven Horwitz, Medical Oncologist-Memorial Sloan Kettering Cancer Center>>

I'll take T-cell because that's all I do. So I mean I think T-cell lymphomas have high unmet need, if you look at the drugs we have in the relapse setting, right, on average you're going respond to one out of those three, and on average, that's going to last for about a year. So, that doesn't get you very far down the road if you're a patient. So, we've just basically need more active drug.

So, I think as a single-agent this has a lot of promise particularly though, I think this is a drug that may work well in some of the combinations. We showed you some of the data, there's other combinations that we've been thinking about, too.

So, this might be a really good partner for other active drugs and if we can get more patients in a complete response. We get more patients to transplant in curative therapy and I think that's for us where you have a real chance to really impact sort of the course of the disease and not a temporary response for a short period of time. So, very early data but we've not been two-sided with this drug and we have some confidence that there's real activity there.

<<Robert Forrester, President and Chief Executive Officer>>

Thank you. Dr. Kunkel - obviously you know this place very well - I mean what's your impression?

<<Lori Kunkel, Verastem Clinical and Scientific Advisory Board>>

Well, I think when we met a year ago - I mean I see a lot of agents and when you look at this agent, the things that Ian mentioned - you have consistency of response across multiple tumor subtypes. Now, we have been in a randomized setting and there's no surprises about safety. The safety was predictable, manageable, we have large numbers that are holding up. And we know that the way that the oncologists will treat patients is that they will cycle through something that's convenient for the patient, something that they can manage and something that is predictable, especially in the community.

I mean we can look at these four drug combinations at Memorial, but when you get out to the community and you have nurses said or seeing patients every 10 minutes, you want something that is going to be a little bit easier to manage. So I think this will have a role and I think people will use it.

<<Robert Forrester, President and Chief Executive Officer>>

So you obviously have done a lot of market research in the company, anything you'd like to add?

<<Steve Bloom, Senior Vice President, Corporate Development>>

Yeah, I would echo all of the comments. I think the market research supports what we're hearing, the drug will – it's an active drug, the market is changing as Ian said, you've got Ibrutinib moving front-line, as Zydelig sort of flattening out, venclexta difficult to use because of the titration schedule. So, I think this becomes a convenience play, right.

And when you have patients that maybe are elderly and they relapse they're 75 or 76 years old. They're 37 miles from their infusion center or the hospital. I mean might as well change the pill and not the routine and give them another oral agent, where they can sort of sequence and maintain their quality of life. And I think that's really the value proposition for the drug as you said just now this afternoon.

Q&A

<Q>: That was very, very helpful. Maybe we should get to some questions from the audience. I see there is a lot of them on. I think Joti put his hand up, so maybe we'll give him the first question.

<Q>: Thank you. Dr. Flinn, I just wanted to start the questions back exactly where they left off during the oral session earlier. And I think the question was having become better at maybe managing or just dealing with events associated with PI3 kinase. So, I guess, given that it's a smaller group and perhaps you can take more time to with that question of being more qualitative about it. I was going to say even as you look at the distribution of events in that light, in that slide, are there may be different proportions of what you see in infections versus colitis, et cetera that might give you a sense that yes, we have become they're being handled differently or really there's just no qualitative good way to see, yeah.

<A – Ian Flinn>: I had some time to think about that question after Dr. Kauffman asked me that earlier. And I guess I still think it's a combination of what he was getting at which was what you're talking about education. First is perhaps there is just maybe an easier drug to use. I think that if you look at the centers that were part of the study, there was a mix of people centers that were pretty good at, and then I've seen a lot of never PI3 kinase inhibitors. But there was also a fair number of ex-U.S. and ex-Western European sites, and I don't think they have a huge experience with the PI3 kinase inhibitors.

So, I don't think it's just that we're smarter about doing this is why this led to this discontinuation. And that's part of it, but not the whole story, maybe it is that this is a drug is, maybe we did a better job in the trial of teaching people, but I don't think it was because they – I don't know all these things - but they came in a priority and knew how to use PI3 kinase inhibitors.

<Q>: Dr. Horwitz what's your experience on working in Duvelisib?

<A>: In terms of managing side effect?

<Q>: Yeah, managing side effect.

<A>: Yeah. I mean this is hard, because to answer that in a general way, because I work at one place that we have a lot of experience. So I think we know a lot about it now. I don't think we had damaged so, but I think in the Phase 1 - Ian correct me if I'm wrong - we had some in fact it seems very early on institute of prophylaxis and then we didn't really have them. So we all either duvelisib sort of toxicity came out. I mean I think at that time we were more surprised and hadn't come out sooner because we thought early in the Phase 1 with duvelisib and then it mostly went away with prophylaxis and paying attention.

So, I think in that sense maybe there was a learning curve, we recognized that. I think we were pretty familiar with the side effects. So, we don't have a lot of trouble managing those, but my group has a lot of experience. I think we recognized things early. I can't really speak to other centers so much. Your trial was multi-center - many sites. Ours is a few types - sites have really focused on clinical investigators.

<Q>: So what's the patient experience? I mean what is the sort of the patient feedback from being on the drug?

<A>: I mean I think for the most part, as long as they're doing well and then remission and respond to the thing and they have a great quality of life, but they don't really, they – it's all very positive. Unfortunately some – there are some adverse events and they were to patients are to experience sort of course – that's of course an issue for patients. But in general I would say people have a go about a very normal life on this drug, right.

<Q>: Yeah. And I think one of the goals of this drug is to do exactly that these patients to live out the normal life expectancy with a good quality of life. So hopefully we can deliver that. Any other question from the audience, I think Mara, sorry. Where is the microphone? You got the microphone. We'll come back to you.

<Q>: Thanks very much. Two questions if you don't mind. The one of the solution criteria for the trial was prior experience at PTK inhibitors and I'm wondering if you can speak to that in the context of as what treatment is today and why that is? And then

secondarily the – can you just remind us the prophylaxis were patients prophylax to the entire duration of treatment or only through part of their treatment? Thank you.

<A>: They received PCP prophylaxis throughout the duration of the therapy that parts easier. The changing landscape as within when the study was initiated this is really – it was just before the approval of – approved never – just as approved it was being approved. And so the landscape has changed considerably since that time. I don't think that I mean Ibrutinib is coming frontline. There are a variety of other therapies that that might come in play often with venetoclax combinations with these – with therapies might move the way in early and the earlier.

But as I think Steve said there's a difficulty in the community with using venetoclax - we use it at our side successfully, but my partners throughout Tennessee oncology that practice I mean they really don't use venetoclax. And so I think that takes us as to where maybe Duvelisib fits in. I think it's going to fit in and as a second or third line therapy for patients, I think whether they receive chemotherapy or not before. I think there's a great reluctance on both the patients and doctors. So if someone got us – we got Ibrutinib or other target therapy frontline, to then they go to chemotherapy seems like a nonstarter for most of my patients. And so having another option to go to it's important.

<Q>: Any question from the audience.

<Q – Bert Hazlett>: Talk about the patient types and you might consider…

<A>: One second…

<Q – Bert Hazlett>: Bert Hazlett from BTIG. Could you talk about the patient types that you might consider initially for this therapy. And are there any particular patients you might exclude or at least a reserve to you maybe get more experience with molecule, both of you would be helpful.

<A>: So the people – so the CLL patients that come in – there's sort of several different experiences. One they may have already had chemotherapy might be bendamustine, rituximab, it might be FCR. There's certainly in Tennessee a huge drop off in the use of the FCR and more of bendamustine, rituximab is being used. And so the question is what do you do when someone relapses after that you could. It's hard to keep cycling through the same chemotherapy because of the damage to the bone marrow. You get these drugs are stem cell poised in the cytotoxic chemotherapy.

So, the question is what you do next. I think for most patients Ibrutinib is probably the most appropriate second line therapy. It has – we have a good track record of its efficacy, it has a good safety profile for the most part. But there are some patients that either after they've progressed or there's about 25 patients that are – 25% of patients that are intolerant they get these bad arthrologist that they could impossible to treated with Ibrutinib or they may have one of the other things like atrial fibrillation. There already have atrial fibrillation, they already on an anticoagulant and makes it harder to teach

people that in which case you might consider PI3 kinase inhibitor like to give a list of instead of Ibrutinib. And then if the other Ibrutinib then of course having Duvelisib at that time is a real bonus.

<A>: I think the patient, am I saying this right - I mean they – if they're in that relapse setting and your choices again back to what we were talking about earlier. Do I want to go on oral IV, the seven week titration in the hospital or just stay in an oral agent. I mean the nurse may present options to the patient and their family. And maybe the patient has a choice here, because of their lifestyle and what do they want to get next. And knowing that these are active drugs and they're approved, hopefully we will be approved and I think there's some element of that. Is that fair to say.

<A>: Yeah, I mean I think that – I mean to be fair I think it's – well, hopefully as the doctor presenting these options to – but I think the Internet that that venetoclax doesn't get if anyone your point of view, doesn't get presented often to patients in the community as an option, because of some of the logistical barriers to using it. I think it's a great drug. But it's not used as calmly as it could be for all the reasons that Steve just outlined. Maybe that will change, but that's why it is today.

<A>: I think I mean you look at drug and if you have a patient, I mean, there's a lot of qualities they get varied, they've come to expect them that it's got a rapid onset. I mean that's important if the patient symptomatic works in del(17p), which is most of – a large majority of the relapse. And you can put them on bed now are FCR. It doesn't work in del(17p).

So there are a lot of the areas where this becomes more attractive and as Ian mentioned I mean Ibrutinib isn't perfect, right. We did not enroll patients who are on an anticoagulant. That's an area that definitely this drug would have a role. And the cytopenias aren't that profound, quite honestly. So there is some real strong points to this.

<Q>: And one of the things that we saw which we thought was very encouraging with patients expected, it is the rapid onset of the response I mean, I would say a couple of months. I think it is encouraging. And also the ability to stop treatment a few example you have some example of colitis, treat the colitis and be able to re-challenge. But also it seems to be helpful as a drug for the patient compared to Ibrutinib what it seems like some cases you get a sort of BTK rebound which maybe a little bit more challenging, but Dr. Flinn have you seen examples of that.

<A>: Restarting on for the colitis…

<Q>: Yes, restarting on Duvelisib.

<A>: Yeah, I mean, I think the data from the trial suggests that you can put people back on it and restart it. It is a – I think at that point if someone's had a very difficult case with colitis then you have to reevaluate the options about whether that's really the right thing to do or perhaps try one of the…

<Q>: Dr. Horwitz, would you like to move with that from the T-cell perspective?

<A – Steven Horwitz>: Yeah. I think, we have a very different landscape. We don't have an oral low toxicity drug that's available for T-cell lymphoma. So, who are your competitors if you're making a decision. In the relapse setting, our drugs that have or either IV and or have a higher rate of day to day toxicity. So I think if this drug was available as a single agent and T-Cell Lymphoma with say comparative data to the currently available agents, I think the idea that it was oral would probably move at pretty high in the list as the first thing to try.

With our patients, often the decision point is, are we trying to get a remission in the relapse setting to go to LA transplant which is the select group of patients, and then we're looking mostly at CR rates, but a large number of our patients were looking for sort of pay lead of long-term durable therapy. And in that case a low toxicity oral agents would certainly be a high consideration. I think, we're going to present like right now, is the who would we not give this to I think because it's something inflammatory side effects, we have some thoughts about in patients who are immediately post checkpoint inhibitor, which I mentioned, it doesn't really come up in CLL too often we have some of our patients on clinical trials, but coming off that. But I can't think of another profile right now that I would say in our patients who know go on this drug. Because I think our competitor have higher toxicities than in some of the CLL available agent – some CLL agent.

<Q>: And then we can talk about follicular lymphoma from a movement, and then we go through the CLL and you speak through about the FL and the patient opportunities though.

<A>: And I think, if you think about it, we haven't really move the bar very much in follicular lymphoma, perhaps since the introduction of rituximab frontline therapy for patients with follicular lymphoma in the U.S. is most commonly in the communities, most commonly then the muscular rituximab there are some academic institutions that still favor our shops by enlarge its ORR, if someone relapses with after frontline therapy, they're either going to get the other chemotherapy they had or look for a novel agent.

And I think this is where duvelisib has its tremendous opportunity. We saw in the DYNAMO that there were good response rates that were durable and very terrible patients. Right, double the refractory patients was – that you probably couldn't come up with the worst population of patients for that trial. And we saw very good responses in that were durable. So I think there's a tremendous potential there, overall it's not in that patient population. Hopefully, it's giving people earlier where we hope we can maybe make a difference than waiting for the very the variant.

<A>: It was something that fell it's for the five years behind where CLL is going, so CLL move to this chemo free, increasing the chemo free, all the targeted therapies, maybe

duvelisib could be part of that sort of starting that wave for the follicular lymphoma patients. Maybe…

<Q – George Zavoico>: Thank you, George Zavoico from B. Riley FBR. So Robert, you guys just finished successful Phase 3 trial. And you are probably the sort of think about exactly what to put in the product label, which – what the panel just said is going to be way too much to put all that into a product label. So could you speak perhaps to what you'd like to see in the product label and having said that when do you think you might be submitting at NDA.

<A>: So I can answer the second part, relatively easily, the goal is to submit the NDA in the first quarter. And we're going to find the CLL/SLL and also for accelerate the approval in follicular lymphoma. And in terms of the label, now clearly, we're going to try to get as broad a label as possible and that's a negotiation, we'll have to have with the agency.

<Q – George Zavoico>: And there is follow-on. Did the Phase 3 was a crossover, so do you foresee doing a west trial, post marketing, perhaps to get in the U.S. Did that plays on the…

<A>: Comments on the crossover study – part of the study, and whether overall survival something that is important to the agency.

<A>: I think it's unlikely that I mean – so many patients on that trial and crossed over to receive duvelisib that though I imagine there ever be a difference on that trial with overall survival. Many, many agents have been approved in CLL without an overall survival benefit. So I don't see that as a likely, necessary study to do. More I do I think it's really practical for most of what we're seeing in CLL today.

<A>: Yet, she has given guidance that in CLL, I'll put in a chronic disease that PFS is necessary endpoint to not overall survival.

<Q – Chad Messer>: Chad Messer from Needham and Company. Maybe if you could just spend a little bit more time on sort of a likely initial patient population in CLL that makes sense to target. So Ibrutinib failures whether they had my Ibrutinib first or second one makes a lot of sense. But what about this Ibrutinib refractory population that you says up to 25%, have these patients could have started to take it and seen effects? Are there certain contraindications, maybe it split-off the larger groups there? That make sense and how big they are and when we would maybe be able to target that?

<A>: So I think it's all the above what you just said and that's from the patients, I have got patients that first to second dose, who have can't take Ibrutinib. They get tremendous of arthrologist recently had so much more rare side effect. But I recently had someone who had just a rash that was, it was like – my nurse practitioner called me and said, we can't treat this patient. He got – general rash I think you've got to be kidding I never see anybody.

And we tried again once again just an overwhelming rash. There's a lot of – the lot of research, Anthony Mato at the University of Pennsylvania has done a lot of research into discontinuation rates with the rudiment, I mean it's actually quite high, because of all this. The other thing that commonly comes up is atrial fibrillation, but need for any coagulation for patients who have atrial fibrillation can be a difficult thing.

And so in my experience, the major – the number one group is the patients that just don't tolerate it from pain or other immediate side effect that they can get. That usually happens relatively quickly with it's not usually a late side effect. So I'd say within the first month that's the biggest group that I see. Probably less is the patients that develop atrial fibrillation although in one series of that, I saw that was presented from the MD Anderson, it was 9% of patients on the trial developed atrial fibrillation. The problem isn't so much if they're in AFib, the problem is that you would – you generally need to anticoagulate them and then that makes people nervous including ibrutinib with that.

And then the largest that there's a tremendous as we're talking about aging population, there is a background rate of people that have had either a clot or already have atrial fibrillation and need to be on anticoagulation to begin with. I think if you add that all up, I think, it's fairly conservative to say that that's 25% of patients in that second 9%.

<Q>: Who's presenting or maybe how is it presenting, at ASH is 24% or intolerant within the first six and half months, so you're right, Dr. Flinn this seems to happen really quite quickly.

<A>: Yes, I just want to add something. I mean I know that there was a lot of new BTK inhibitors coming for – they're claiming less toxicity. But I'll tell you one thing we learned from development of carfilzomib is that people will change – they're going to – they would rather change to a new agent than to try to work through it. So that's just the way people practice.

<Q – Bin Lu, Raymond James>: Hi, this is Bin Lu on behalf of Reni Benjamin from Raymond James. Question for the panel is, just to follow-up on the prior topic, I think Dr. Flinn you mentioned that about 25% of the patients in second line would be eligible for destruct. So I was wondering as Ibrutinib is being moved early and earlier in the frontline, probably let's say essentially target like 50% or 60% of the frontline patients and would that percentage go up? And then the potential usage of destruct would be much higher than what it is right now?

<A – Ian Flinn>: Maybe, Mr. Bloom would you like to take the first stab of that?

<A – Steven Bloom>: Yes, I think it's fair to say, I think you're right. I think we've heard from KOLs that we've interviewed that this ibrutinib push is happening and the shadow will sort of disappear overtime. And as you get to 60% or 70% frontline, now you've got a huge white space in that relapse setting for drug like Duvelisib to come in and take share. So that's also again what I said earlier consistent with what's happening in that

relapse setting right now, where Zydelig sort of flattened out a bit and VENCLEXTA sort of struggling to get out of the gate. As that happens over the next two or three years, that's where our market opportunity is, and that's what we saw in the drug is the value proposition from a revenue perspective was that dynamic that was developing in the in the relapse setting.

<A – Robert Forrester>: Only respect for everybody's time, and we know at 9:00 o'clock. Maybe we got time for maybe one maybe two more questions. Who's got the microphone currently? Okay, you were trying to ask the question earlier.

<Q – Swayampaukula Ramakanth, H.C. Wainwright>: Hi this is R.K. from H.C. Wainwright. Just a question on discontinuation and some of the reasons for discontinuation, there seem to be about 80% discontinuation in the treatment that Duvelisib are isn't a competitive there were like 100%. I just trying to understand what do you think was going on in those patients that we had seen this kind of discontinuation rates?

<A – Ian Flinn>: In the duvelisib arm there were 22% of patients that remained on treatment at that time of the analysis with the median exposure rate of about 50 weeks. The 35% of patients discontinued therapy because of an adverse event. So 20% or 22% of patients discontinued because of progressive disease. And then there were sort of smattering of other reasons, but originally no dominant reason other than those listed.

<A – Lori Kunkel>: I think actually one thing that's kind of buried in the data is about a 30 of the patients are still on it two years. If you look at that curve or they're progression free at two years. So there's a substantial part of patients who still remain on…

<Q>: So you're also bringing up an important point to sell this in the Phase 1 study and earlier on that even when people discontinue they didn't necessarily progress.

<A – Lori Kunkel>: Yes, yes, which is different than some of the other agents in their study right now.

<Q – Mara Goldstein, Cantor Fitzgerald>: Just a follow-up question, and do you have a sense of just the dynamics behind discontinuation and the team to occur around the same time from a temporal perspective for treatment or whether it was more random?

<A – Ian Flinn>: I actually don't know the answer to that question. My senses it's more like – and this is just from personal experience that sort of between five, between six and 12 months is when we see that lot of the discontinuations from adverse events. I don't know of anybody that's branding that differently, I think, that's my sense of it. But it's – I have to say that's more of an anecdotal description of things than we know in the hard data.

<Q – Robert Forrester>: So just one final question. I personally was quite encouraged from the crossover study and seeing the level response rate, but what did you think Dr. Flinn?

<A – Ian Flinn>: Yes, I as well. I mean it didn't – it didn't look like that the people were on necessarily harmed by going on Ofatumumab into Duvelisib and had basically the same weight of responses as the patients that received Duvelisib upfront. So I think that was encouraging.

<<Robert Forrester>>

That was encouraging. Well, I just want to reiterate that we're absolute thrilled to be working with each of you even you Mr. Bloom. And this is really exciting, it's exciting for patients, it's exciting for us as a company. So I just want to thank each of you very much, indeed. Thank you very much indeed. And thank you all for coming this evening. Thank you.