

GlaxoSmithKline

Analyst Call

Accelerating our priorities and building capabilities in Oncology

GSK to acquire TESARO

Monday, 3 December 2018

Cautionary Statement

This communication is neither an offer to purchase nor a solicitation of an offer to sell securities. The tender offer for the outstanding shares of TESARO's (the "Company") common stock described in this communication has not commenced. At the time the tender offer is commenced, Adriatic Acquisition Corporation and GlaxoSmithKline plc will file, or will cause to be filed, a Schedule TO Tender Offer Statement with the Securities and Exchange Commission (the "SEC"), and the Company will file a Schedule 14D-9 Solicitation/Recommendation Statement with the SEC, in each case with respect to the tender offer. The Schedule TO Tender Offer Statement (including an offer to purchase, a related letter of transmittal and other offer documents) and the Schedule 14D-9 Solicitation/Recommendation Statement will contain important information that should be read carefully before any decision is made with respect to the tender offer. Those materials will be made available to the Company's stockholders at no expense to them by the information agent for the tender offer, which will be announced. In addition, those materials and all other documents filed by, or caused to be filed by, Adriatic Acquisition Corporation and GlaxoSmithKline plc with the SEC will be available at no charge on the SEC's website at www.sec.gov.

Sarah Elton-Farr: Thank you. Good morning and good afternoon, everyone and thank you for joining us to discuss our announcement today of our agreement to acquire TESARO. You should have received our press release and can view the presentation which is located on the Investor Section of the GSK website.

Cautionary statement

Before we begin, please refer to slide 2 of our presentation for our cautionary statement.

Agenda

Our speakers today are Chief Executive Officer, Emma Walmsley, Luke Miels, President of Global Pharmaceuticals, Dr Hal Barron, Chief Scientific Officer and President of R&D and Simon Dingemans, Chief Financial Officer.

Following our presentation we will open the call to your questions and with that, I will hand the call over to Emma.

Emma Walmsley: Thanks very much, SEF, and hello to everybody.

Delivering on our strategic and capital allocation priorities

When I became CEO last year I set out three long-term priorities for the company; Innovation, Performance and Trust. These priorities are designed to improve the competitive performance of our global businesses and deliver long-term sustainable growth. Strengthening our Pharma business is of critical importance when it comes to ensuring GSK's long-term growth outlook and we have been consistent in putting it at the top of our capital allocation priorities.

The proposed transaction will present a compelling opportunity to deliver long term sustainable growth

Today's announcement is a significant step in building not only our pipeline, including late stage, but also in our commercial capability in Oncology which is becoming a key area of focus. It is accelerating the path forward for our R&D approach that Hal laid out at Q2 this year.

Today's announcement of the agreement to acquire TESARO, supports our aim to deliver long-term sustainable growth and value to shareholders. As a Boston-based oncology group, TESARO will strengthen the building of both GSK's pipeline and our commercial capability in Oncology.

We believe that the potential of Zejula, which is currently approved and marketed in the US and Europe for the second-line maintenance of platinum-sensitive ovarian cancer, is under-appreciated and that there is significant upside potential from use in first-line maintenance therapy as monotherapy, where we can see potential beyond the *gBRCA* mutation population.

There is also the potential to expand Zejula's use into other tumour types, including breast and non-small cell lung cancer and TESARO also brings us a pipeline of early-stage immuno-oncology assets.

This transaction will allow us to harness the significant Oncology experience of both our senior Commercial and R&D leadership, to optimise the potential of TESARO's broader portfolio and together with our existing portfolio of novel Oncology assets, we will have the opportunity to develop wholly-owned combination therapies in multiple tumour types.

The transaction supports the ongoing expansion into specialty pharma reinforcing our existing team with some great talent.

This acquisition of TESARO will also bring us a US and European commercial footprint in Oncology and strengthen our capabilities in clinical development, medical and payer engagement.

Upon completion of the transaction, we will be delighted to have a new world-class Boston team that will continue to be a magnet to attract and collaborate with the very best, so we believe this transaction creates compelling long-term value for our shareholders and supports our goal of delivering stronger long-term growth.

Let me turn you first of all over to Hal who is going to talk you through why we are so excited about this opportunity.

Hal Barron: Okay, thank you, Emma and for those who have the slides, I will be speaking first now to slide 6 called PARP inhibitors.

PARP inhibitors: wider application than has been appreciated

Although TESARO brings much more than just one asset, it's probably worth spending a bit of time on Zejula. It's an approved medicine that is already in the clinic helping many women with ovarian cancer.

We are excited by the partnership because we think it demonstrates a very big opportunity for this under-appreciated class of medicines. I would like to just step back to show you how this fits into our overall R&D approach, by highlighting some of the comments we made in July.

First, we highlighted that human genetics was going to be an important part of our discovery engine and hence did the deal with 23andMe but we also highlighted the incredible importance of functional genomics to understand the cell biology and to understand how to identify new targets. And one of the most important components of functional genomics is to be able to identify things like synthetic lethals which are ways of identifying targets that make the cancer cell in particular very sensitive to new treatments.

So we are very excited about that strategy because it allows us to identify more effective therapies such as PARP inhibitors which were the first synthetic lethal targets identified that have made it into the clinic.

Let me explain to you just for a second how PARP inhibitors work. Women who carry the mutated *BRCA* gene, which many of you have probably heard of, are at risk for developing cancers because *BRCA* is an important protein in healing DNA damage. When women with this mutation develop cancer, they are very dependent on the PARP protein because it is the second protein that is involved in DNA repair.

The reason that the PARP inhibitor class has been so effective, particularly so far in the *gBRCA* population - those women with the mutation, is because the inhibition results in the inability to heal the DNA that's been damaged and therefore results in the cell dying.

So today we know that PARP inhibitors have transformed the treatment of ovarian cancer, particularly as I mentioned in this population of women with the mutated *BRCA* gene. It's known in ovarian cancer that there is about 15% of the population with ovarian cancer that harbour this *BRCA* mutation.

Prior to the publication of TESARO's NOVA study, PARP inhibitors were really thought to only benefit those *gBRCA* patients, but what the NOVA study identified due to the outstanding development work of TESARO, is that there are other genes that cause the same defect and induce a *BRCA*-like state in other patients. In fact, it looks like almost half of all patients with ovarian cancer have some kind of mutation that makes them vulnerable to the PARP inhibition and therefore PARP inhibitors are effective at treating their cancers.

So evidence is really mounting that with this HRD test which is now available and I will talk about in a minute, we can expand the opportunity to help patients dramatically and that's why in particular we are so excited about this opportunity.

NOVA study: designed to assess outcomes in distinct biomarker populations

Moving to the next slide, I want to show you the data from the NOVA study, which really brought the concept of treating these other *BRCA*-like patients to life.

The NOVA study was designed to assess outcomes in two distinct populations, as you can see on the slide: those carrying the *BRCA*-1 mutation where they were randomised in a 2:1 fashion to receive Zejula 300mg or placebo but, more importantly to some extent, randomising and exploring those patients who do not carry the *BRCA* mutation. Those patients were subdivided into those patients who had this Homologous Recombination Defect, so called HRD positive where they had a *BRCA*-like state, or those who didn't.

NOVA study shows efficacy beyond *gBRCA*

If you look at the next slide, you can see the results which are pretty striking. As expected, Zejula had a pretty dramatic effect in those women with the *gBRCA* mutation with as much as a 73% improvement in their progression-free survival. What is particularly

interesting is that in those women who had no germline *BRCA* mutation but had the HRD positive signature, the benefit was almost as striking - a 62% improvement in progression-free survival hazard ratio 0.38.

In the HRD negative patients, those who had neither the *BRCA* mutation nor were identified as being positive by this HRD test, the benefit was still present but significantly less with a hazard ratio of 0.58, giving the overall non-*gBRCA* mutation group a hazard ratio of 0.45. These data give us a lot of confidence that Zejula is working in a patient population beyond the *gBRCA* as just described.

Monotherapy versus combination therapy in 1LM

For women with ovarian cancer, the largest impact that patients will have is if PARP inhibitors are moved more into the first line; the prior data have been demonstrated in second line and beyond. We see this big near-term opportunity both for Zejula and for the women with ovarian cancer, because there are approximately twice as many patients in the first line as in the second line, as well as the duration being quite a bit longer.

There are three different studies that will clarify the role of PARP inhibitors in first line ovarian. The first study, which read out recently, is SOLO-1 which explores Lynparza in the 15% of women who have the *gBRCA* mutation. This study showed a pretty dramatic benefit in those women. Our study PRIMA is looking to explore whether Zejula is active beyond the *gBRCA* population. There is a possibility, given the data from NOVA, that the benefit will be extended not just to *gBRCA* but to all HRD positive patients - again, increasing the market quite substantially in the number of patients who would benefit. There is even a possibility - again given the data from NOVA - that all-comers might benefit, which would be a substantial increase of almost six-fold over those with the *gBRCA* mutation.

Importantly, Lynparza is also being explored in combination with Avastin, which is used in roughly 25% of patients and they are exploring whether the combination of Lynparza and Avastin might be beneficial. We are excited by the PRIMA study which is very important for patients and for us, because we believe that we can move into the front line and benefit many more patients. We believe that the drug is likely to be safe and interim safety data from ESMO show that starting with a dose of 200mg in a selected group of patients - those with low body weight of less than 77kg or low platelets - can be done very safely and without any impact on efficacy.

We believe that daily once-a-day oral dosing will also be a competitive advantage and we are looking forward to this because these data are expected soon, in the second half of 2019. That is really why we are excited about the opportunity as presented.

HRD status likely to identify non-*gBRCA* patients who will benefit from PARP inhibitors

The next slide really highlights something about the HRD test that I believe is also important. I have mentioned several times already that HRD status is likely to identify patients who are non-*gBRCA* mutants who will benefit from PARP inhibitors. Currently, the test that is used and is commercially available is from Myriad called myChoice, and it was originally developed to identify patients most likely to respond to platinum therapy but it has been used to identify patients with this defect that would make them sensitive to PARP inhibitors. We believe it is possible that this HRD test, designed by Myriad, may underestimate the true number of HRD positive patients, because we believe that other genetic mutations, such as ATM, ATRX, Rad50, the FANC proteins, could all be captured if one were to do a more sensitive test.

In addition, there are ways that are beyond genetics like promoter methylation: you can hypermethylate the promoter of *BRCA*, for instance, and result in reduced expression of the protein leading to an HRD-like state. There is one other unidentified cause such as gene-to-gene interactions or even therapies that might induce an HRD state. We believe, as I mentioned, that there is a possibility that not only does it work in HRD positive but beyond that, potentially in all-comers, which shows the importance of optimising this HRD test.

HRD testing could enable further development opportunities for Zejula

This next slide shows another reason why we are very excited about Zejula. If one is to explore HRD testing beyond ovarian cancer, one might imagine that we can identify other patients who would benefit from PARP inhibitors. There is a very interesting study from Marquard that was obtained from data from the TCGA dataset looking at the HRD score in a number of cancers. As you can see on the left of this figure, ovarian cancer comes to the top but, interestingly, a close second is lung cancer: there is a very high degree of HRD abnormalities in bladder, neck, breast, melanoma, gastric, colon, GBM and prostate. We believe that this test could identify, as depicted here, other patients who would be sensitive to PARP inhibition.

In addition to identifying other patients in the sub-groups within those cancers who would benefit, we believe that while monotherapy is likely to be very beneficial in ovarian, there is also the possibility of exploring combinations and Zejula plus anti PD-1, as well as Zejula plus Avastin is being explored extensively in ovarian cancer, and particularly interesting is the Zejula plus anti PD-1 antibody for lung cancers, described before in a study called JASPER.

There are other indication studies as well, including triple negative breast cancer, metastatic castrate-resistant prostate cancer and even Ewing's sarcoma that are currently underway, and as you can see on the left, the potential is quite significant for other indications.

I should also point out, just to get a little bit more into the science that when you have a defect in homologous recombination, you rely on non-homologous end joining to repair your DNA, and that's a very insensitive method for repairing DNA, and what it does is it causes insertions and deletions in the DNA that result in very, very abnormal proteins, and oftentimes these proteins are presented as neoantigens on the cell surface, and we think this might increase the probability that a cancer becomes immunogenic and responsive to PD-1, so there is some possibility that PARP inhibition in certain cancers might induce a more immunogenic state, and, therefore, be synergistic with immuno-oncology drugs, such as PD-1, increasing the opportunity of some of these combinations.

Additional pipeline assets will provide upside potential

On the next slide it shows that in addition to Zejula, we are inheriting an additional pipeline of assets that we think will provide significant upside.

As I just described, the value of PD-1, particularly in combination with Zejula, but also as monotherapy, will be a particularly useful thing for us to have to help patients.

There is an on-going registrational study, called GARNET, which is in MSI-high tumours for endometrial cancer, and there was some encouraging data presented at ESMO, and the BLA is planned for second-line treatment by the end of 2019. The combination studies, as I have mentioned, of Zejula plus PD-1 (TSR-042) in ovarian cancer are interesting for the reasons I have described, as well as in lung cancer.

There are two earlier stage assets, TSR-022, an anti TIM-3 antibody, which we can discuss, which is also looking at whether the combination of 042, that is anti PD-1 plus anti TIM-3 can be beneficial. In early data, the dose response is indicative of some activity, and TESARO also has an antibody called TSR-033, or anti LAG-3 antibody that is being evaluated and has potential.

That is really why we are so excited about the many opportunities we have to help patients with Zejula, both as monotherapy in ovarian in the frontline, as well as many other indications, as well as combinations, and this exciting early-stage pipeline.

With that, let me turn it over to Luke, who can tell you more about why he is excited.

Zejula well positioned in an evolving market

Luke Miels: Thanks, Hal, and it really is great to be talking about this product today. The title of the slide, as you can expect, is very deliberate. This is, from my perspective and from our perspective, a very interesting class, and Zejula is a very competitive asset when explored in depth.

Within ovarian, following the introduction of PARP inhibitors we have seen several trends start to emerge, and, increasingly, on the back of compelling data in second line, and now first line, we see maintenance therapy being used in up to two-thirds of patients, depending on the market, in second line plus. We anticipate that this will grow over time, and would extend into the much larger first-line maintenance setting.

We think this will be initially driven by the SOLO-1 data, placing some short-term pressure on Zejula. However, the opportunity flowing from this for Zejula is two-fold. Firstly, this data will accelerate the creation of a first-line maintenance market for PARP inhibitors; and, secondly, SOLO-1 is limited to a minority of patients who are *gBRCA*. Therefore, assuming the PRIMA study with Zejula reads out positively, as Hal has explained, this approach will be adopted in HRD positive patients, and potentially all comers.

In HRD negative patients, we also see a potential role for PARP inhibitors in combination with a VEGF inhibitor such as Avastin, so looking at the on-going and planned studies, we think Zejula is a very well-positioned asset to take advantage of these trends.

Ovarian cancer opportunity offers significant potential

Referring to the bar graph, the ovarian market is one that offers significant upside potential for PARP inhibitors. Today, the bulk of use, as you know, is within this blue segment of the market, i.e., the second-line platinum-sensitive, representing around 5,000 patients a year in the US.

TESARO has initiated a number of further studies, which could allow for label expansion into other parts of the ovarian market, highlighted in orange on this chart. We can see potential for use in fourth line, from the on-going QUADRA study, which we expect to be filed shortly, and adding access to a further 2,000 patients in the US. The study could also lead to use in the second-line platinum-resistant setting.

However, much more significant is the first-line maintenance market, which is about 10,000 patients in the US alone. The PRIMA study, looking at Zejula mono is well advanced, and we anticipate results being available in the second half of 2019. Zejula could be the first approved monotherapy in this market for use beyond *gBRCA*. The SOLO-1 data was striking, but limited to *gBRCA*, which is about 1,500 patients.

With PRIMA the potential exists to address the HRD-positive group, and even potentially all comers at first line.

Well positioned in a competitive market

The next slide gives you a sense of how dynamic the class is in ovarian. Further opportunities exist or can be created in breast and lung.

In the short term, we do expect some revenue pressure, and I want to be clear about this so that you factor this into your models. We need to bridge to the readout of PRIMA in first-line maintenance, and also to a lesser extent, OVARIO.

In parallel, we want to focus extra resources in areas where we think we can unlock more value in the mid to long-term.

Moving beyond this phase, Zejula is well positioned in ovarian, where it could be, as mentioned before, the first class monotherapy in first-line maintenance in non-*gBRCA*, and the first also with the combination data in ovarian with a PD-1. There is also potential that it could be the first PARP/PD-1 combo in lung.

The proposed transaction will accelerate GSK's oncology presence

From a commercial operations perspective, this deal creates value for shareholders beyond the acquisition of a competitive on-market product in an exciting class.

We also get an immediate critical mass in oncology, a critical mass in terms of a group of talented and competitive sales people, a critical mass in terms of capability like regulatory, market access and medical that can directly benefit BCMA costs and others, and critical mass to drive a cultural change in approach to specialty care, late-stage lifecycle management, and it also helps us attract and retain the right people.

With that, I will now hand over to Simon.

Transaction details

Simon Dingemans: Thanks, Luke, and just a few details on the transaction. We have agreed to acquire TESARO for \$75 per share, representing an aggregate consideration of \$5.1 billion, or £4 billion at today's exchange rates. This includes refinancing TESARO's net debt and assuming the conversion of their convertible notes.

We will commence a tender offer for the shares in TESARO within the next ten days but we have commitments already to accept from shareholders representing over 25% of the share capital.

This price represents a premium of 110% to TESARO's 30-day volume weighted average share price.

The transaction represents a significant long-term investment in GSK's Pharmaceutical business and we plan to resource it appropriately to ensure we have the right clinical data and commercial capabilities in place to support the growth of Zejula as well as investing in the pipeline we are also acquiring.

Given that driving faster revenue growth will take time, the investments we believe are necessary will result in short-term dilution over the next couple of years and we expect this to impact adjusted earnings per share by mid to high single digit percentages in each of these years. This is after some contribution from our ongoing R&D portfolio prioritisation and other restructuring savings.

There will also be an impact to the Pharma operating margin in the short-term during this investment phase. As a result, we now expect the 2020 Pharma margin to be about 300 basis points lower than our previous guidance of around 30% at 2015 exchange rates.

As the returns from these investments build, the dilution is expected to diminish rapidly with the acquisition becoming accretive to adjusted earnings per share by 2022 and increasing thereafter. The transaction will be funded through a combination of existing cash resources and new debt and facility is already in place. There is no change to our current dividend policy as a result of this acquisition and we continue to expect to pay 80 pence a share in dividends for 2018.

Finally, we expect the transaction to close in Q1 2019 pending regulatory approval. Overall, we believe this transaction represents a compelling opportunity to accelerate the build of our pipeline and commercial capability in Oncology ultimately to improve our performance and generate long-term sustainable growth for GSK.

And with that, I'll hand the call back to Emma.

Emma Walmsley: Thanks very much, Simon. Perhaps we will now move to Q&A and can I ask the operator to please outline the protocol.

Questions and Answers

Graham Parry (Bank of America Merrill Lynch): Thanks for taking the questions. The first question is just positioning of Zejula versus other PARPs in the space, so the compounds behind Lynparza in first-line ovarian, could you highlight where you could see room for differentiation either in that indication or others, perhaps just an appraisal of its market position overall, therefore?

Secondly, Clovis's Rubraca patent I think has a European hearing tomorrow. I just wonder what assumption you have made around protection of that patent and the risk of generics in this class over time.

Then thirdly on dividend, you reiterated the 2018 dividend. It would be useful to hear your thoughts on cash dividend cover from '19 through to 2020. I think previously you talked about potentially being able to raise dividends in the mid to the long-term based on a 1.25 to 1.5 times cash dividend cover. Thanks.

Emma Walmsley: Thanks very much, Graham and I'll ask Luke to pick up on Zejula's competitiveness within the PARP class and reiterate our confidence around the patent situation, remembering that as well as relative differentiation, we fundamentally believe that the overall PARP class as a whole is underestimated.

And in terms of dividend, as Simon mentioned, our policy and expectations are unchanged. We still are holding a dividend policy which will be distribution as a function of free cash flow within that range of 1.25 to 1.5 cover before we increase the dividend and we've consistently said that the pace of the rebuild of cash flow cover will depend on our investments in growth. At the same time we continue to improve our operating cash flow conversion and that's also why the growth in our base business including progress in both Vaccines and Consumer is important for the contribution to cash flow.

With that, Luke, do you want to comment on the PARP class and patent?

Luke Miels: Sure, thanks Emma. Graham, thanks for the question. The first one, we assume patent expiry at 2030 in the US. When we valued things we also took a pretty aggressive erosion curve beyond that, but as you know in oncology the pattern tends to be a little bit different.

In terms of competitive positioning and Hal, feel free to jump in here, I think the SOLO-1 data was striking but the key thing we need to keep anchoring ourselves in is that it's limited to the *gBRCA* population and that's a consistent and very deliberate strategy that was taken there.

TESARO, in contrast, of course took a broader approach and as Hal has reinforced in terms of the data we've seen so far, we have a high degree of confidence that that would

then be translated into the first-line setting. It is certainly very consistent with the market research and the perception we see about it.

The other dimension is when you look at the profile of the product, particularly with the 200 mg dose, which is around 50% of patients now, if you look at the tox profile it's very competitive versus Lynparza so we think this combination is compelling and then when you add in other various combinations that we have looked at, we think that there is opportunity to carve out areas not only in ovarian but potentially in lung and breast as well.

I think the key thing as well is the alternative physicians would have is the combination with Avastin and we think if physicians are provided with compelling data in monotherapy in contrast to a combination, remember, in a maintenance setting with an infusion and with a relatively complex tox profile, then monotherapy is going to be very attractive for these patients and their physicians.

Emma Walmsley: Okay, thank you Graham. The next question, please.

Kerry Holford (Exane BNP Paribas): Thank you very much. A couple of questions, please. Firstly, just interested to understand how much of the valuation, that £4 billion that you put on TESARO represents the underlying value to drugs and how much relates to your anticipated expectations for cost avoidance around infrastructure build and so on that you mentioned earlier, Luke.

On Zejula specifically I wonder if you can talk about the expected patent life, any royalties or pay-aways on that product that we should be aware of.

And then coming back to the Consumer India deal and the divestments there, clearly the announcement today involves a large proportion of equity and I am wondering if you can talk there about how quickly you might be able to sell that stake post deal closure and realise cash and also whether, tied into that, there are any other divestments that might be on the table for you at this point? Thank you.

Emma Walmsley: Thanks, Kerry. I'll ask Simon first of all to comment on the final phasing around the India equity sell-down that we announced. We were delighted with the announcement of that deal which we expect to be able to sell-down in around a year and he can also comment on the valuation, although we are not going to get into detail about the breakdown within that.

But first of all, Luke, perhaps you would like to follow up on the point on patent protection as well.

Luke Miels: Yes, sure. Kerry, you may not have heard before but we've looked at this extensively and we've taken the assumption of 2030 in the US as the expiry point for the patent. There are royalties to Merck and AstraZeneca. I don't know, Simon, if you wanted to go into those, but they have been disclosed by TESARO so there's nothing new there.

Emma Walmsley: Simon, do you want to pick up on the other question?

Simon Dingemans: Yes, just to confirm on the royalties, that's factored into our valuation. Kerry, as you would expect, we are not going to breakdown the valuation into its component parts but you highlight an important point that we are not just buying Zejula, we are buying a pipeline, we are buying commercial teams, we are buying medical regulatory and a platform that we can build around here. There are many different elements that come into the valuation that we have paid here and the prospects that we see.

On India, will probably take up to a year to close. Anything in India tends to take a bit of time, so of the various different alternatives that we looked at, all of them had a relatively long fuse on it. However, we are very pleased with the valuation we have and we believe that the time it takes to monetise that is well worth the premium that we have achieved in the disposal. Remember that the shares we are taking in Hindustan Unilever are a little over 5% of the total against a company with a market cap in excess of \$50 billion, so we feel very comfortable in being able to monetise those efficiently.

Emma Walmsley: Both of these deals we have announced today are about reshaping the Group and accelerating the changes that I outlined in July 2017, and that Hal emphasised when he outlined his R&D strategy, and we shall continue to do that at pace as you say, Kerry, while being thoughtful about other portfolio opportunities. Luke, I think you want to make another point?

Luke Miels: Kerry, you make a really important point around talent and building a core, particularly in Commercial when we are trying to attract people who are extremely excited about BCMA and ICOS etc. When we try to bring people in, if you have an in-market product it is further reassurance for them and it enables us to bring these people in faster, which is, ultimately, reflected in success and a better uptake with BCMA.

Keyur Parekh (Goldman Sachs): I have three questions please - two financial and then a product question. First on the financial side, the guidance you are giving of mid to high single digits, on the high single digit side would imply an operating loss of this

asset of about \$700 million or thereabouts, which compares to a consensus loss for TESARO of \$350 million in 2020. How should we bridge the gap between those two?

Secondly, and more philosophically, as we think about GSK being more proactive on various transactions in the future, should we think of those as potential for the downside to your already issued guidance, or should we think of those as operating efficiencies filling up the hole that dilution may cost from those transactions?

Thirdly, from a philosophical perspective, Hal, most people would think of this asset as neither being first-in-class or best-in-class. Luke, you are on record as saying you think all the PARPs are the same. Can you help us understand again why did you think this was worth \$5 billion of GSK capital?

Emma Walmsley: Thanks very much, Keyur, and we'll come to Hal and then perhaps Luke on your last question. To your first point, just to be clear, this is a significant investment for GSK and it is all about doing what we said we were going to do, which is to reorient the prioritisation behind innovation, the Pharma business, strengthening the pipeline, including with some near-term catalysts, building out a commercial capability and accelerating all of that. When we are making this acquisition, we are going to invest in this pipeline, which is why we have updated on the guidance to 2020.

However, that said, you should be reassured that, having made this major move, we are going to be very focused on executing against this deal successfully. As I said last year, and as Hal said in the summer, we shall continue to do some work on BD but that is factored into our outlook. We shall look at BD that might continue to accelerate Hal's strategy, being very disciplined on returns whether that be early stage assets, platforms or partnerships but that is factored into the outlook with which we have updated you today. Hal, would you like to comment on why Zejula?

Hal Barron: Thanks, Keyur, and the key thing here is about defining best-in-class. To me, best-in-class is defined by the molecule that has the most thoughtful and aggressive development programme. It is important to realise that one of the biggest opportunities for this class is in front line ovarian and in the monotherapy setting, which we believe is likely to be the most attractive for patients and clinicians to use the drug, TESARO is ahead and by the end of 2019 we shall have data to suggest - and I believe it is likely - that the benefit is not just in the *gBRCA* patients, which, as you point out, has already been identified, but in a population that could be as large as three-fold larger - the HRD positive.

It is also possible that, because HRD testing is less sensitive than ideally we would like, it might even work in all-comers, giving us somewhere between six and seven-fold higher number of patients who can benefit. That would be first-in-class in terms of that

opportunity. I believe that is just the tip of the iceberg of this class and the combination potential is significant. You heard about Lynparza combining with Avastin in the 20-25% of patients in the front line who will get that, but we don't believe that Avastin combination is likely to dominate the front line. Avastin has been approved for the front line for a couple of years but its adoption has been somewhat limited. The benefits in PFS aren't huge and there are significant side-effects, as well as the logical burden of infusions every three weeks and the financial burden. Therefore, we believe that in front line ovarian, if it is to work in HRD positive, this is a substantial improvement which will be best-in-class and it could be useful in all-comers, which would be even further upside. Even that probably underestimates the true potential that a great development programme can elucidate, which is that this drug could be very effective in lung cancer.

One of the things that people have probably missed is the fact that a biomarker of where PARP inhibitors work might be patients who benefit from platinum therapy. That is one reason why it potentially works in ovarian cancer because response to platinum therapy might be a biomarker. Interestingly, lung cancer is the other tumour type where the platinum benefit is most dramatic. Not only do we have potential benefit in the HRD positive, but with PD-1 inhibition with TSR-042, we have the potential of being first and best in combination therapy in lung cancer, which would be a really significant advantage both for the class, in particular for Zejula and most importantly for patients. Again, there are probably a number of other tumour types, when we get the HRD testing optimised, that we'll identify as being HRD positive with both TESARO's pipeline of IO re-agents as well as our own. We believe there are some very exciting combinations that could lead us to be first or best-in-class in those combinations, including things like epigenetic modifiers or STING agonists. There are a number of very interesting scientific observations that point us towards combinations that could be very beneficial for patients.

I believe that best-in-class is quite likely for Zejula and it will result from outstanding and aggressive development work, which is why we are excited about this and about the class in general.

Luke Miels: Keyur, as you know, I have some history with this area. I want to reinforce Hal's point that it is going to be the label, it is going to be the development plans and, ultimately, where these are positioned. It is an interesting class that continues to surprise us and I don't believe that the story is over yet.

If you go back to the original molecules, they failed and then you had it resurrected through Study 19 and the strategy pursuit around Lynparza. Then, of course, TESARO came through with their initial study in a broader population. There has been a lot of

attention paid to immuno-oncology in other areas and I believe this is a class that people have been looking at less intensively so, coming in and looking at this in depth, I became very excited about the opportunity that Zejula offers here, and it is very interesting, when you look at what physicians say they do, versus what they actually do, if you look in second-line maintenance, for example, if you look at cancer data, they say they use Avastin in 35% of patients. The reality is it is between 14 and 11%, depending on *BRCA* status, so there is not a lot of usage there.

If you look, however, even at early data now, it is small numbers with Flatiron, but the trends are quite interesting. In *BRCA* positive Lynparza is used around 12% of time in second-line maintenance, and 2% of the time in *BRCA* negative.

Zejula is used 14% of time in *BRCA* positive, and around 20% of the time in *BRCA* negative, but what is very striking, actually, is when you look at the number of watch and wait, it is around 50% in *BRCA* positive, even in *BRCA* positive, and 60% in *BRCA* negative.

Therefore, I think when you look at the sequence of data readouts coming, more intensively focused resources around education and on particular individuals in the community, I think there is a real opportunity for us here to be competitive.

I think on the tox side, as I mentioned earlier, it is more of an even fight now with the 200 mg, and if you look at withdrawal rates, AEs, etc., in terms of percentages they are very similar, and I think the other thing with Zejula, of course, is these things tend to manifest themselves in the first four weeks, so it is something that physicians can prospectively manage with patients.

Therefore net/net, the conclusion that we came to, looking at this systematically, is this is a competitive asset in a class that is likely to continue to expand in multiple tumour types.

Emma Walmsley: Thanks, Luke, and thanks, Keyur. Next question, please.

Andrew Baum (Citi): Thank you, three questions, please. First, can you remind me of the royalty rate that TESARO agreed to when they licensed prostate indications to J&J, and Japan rights to Takeda?

The second question, I completely understand, Luke, the point about market expansion, but thinking about market share, if the PAOLA-1 data with Lynparza replicates what the Phase 2 cediranib combination trial is raising, the benefit in the wild-type patients, isn't that going to be problematic for you?

Finally, in relation to the on-going first combination trial with PD-1, in terms of the risk of timelines, I lose track of how many PARP sponsors are running combination trials with PD-1s, there must be four or five. Is there a risk that there is slippage here, given the competition and enrolment of patients within these trials?

Emma Walmsley: Thanks, Andrew. Simon, maybe you can just comment quickly on the Janssen royalties on prostate, and then we will come to Hal and Luke on the trial questions.

Simon Dingemans: Yes, sure. Andrew, it is a tiered royalty, low-to-mid single digits, remembering, though, that we will book them as royalties rather than as revenues when we consolidate the numbers.

Hal Barron: Yes, thanks, Andrew, for your question. Let me just try to address that. When we looked at potential Avastin combinations used in front line, we looked at the cediranib data, and it is important, I think, to note that this is first of all, a dirty kinase and has other effects besides VEGF TKI.

The trial was relatively small numbers, and so I think drawing conclusions is a bit problematic, and I think it is important also that one looks at the GOG 218 data, particularly at this subgroup analysis from Swisher et al, looking at the effect of Avastin as a function of *BRCA* status, where Avastin use in the upfront plus maintenance setting in patients who are *gBRCA* positive was trivial. I think the hazard ratio was 0.95, so that's inconsistent in some respects with it being particularly synergistic with platinum or potentially subsequently predicting response as synergistic with PARP inhibition.

However, it is an interesting combination and for the 15 to 30% of patients, depending on where you are, who do get Avastin, if the trial is synergistic there will be use, but, again, we get back to the belief that in frontline setting, monotherapy is going to be much better tolerated. It is simply a pill. It is financially less expensive, and from a toxicity perspective, much more attractive, and given the hesitancy, in general, for a maintenance therapy to be given in the frontline, we think that this approach of using monotherapy and then looking for combinations that will be more likely to be synergistic, such as PD-1, and better tolerated is a better approach, and so we are excited and confident that we will be the leaders in frontline ovarian soon.

Emma Walmsley: On the PD-1 question?

Hal Barron: On the PD-1, I think TESARO's development organisation has been outstanding in executing on trials, and we are pretty confident in the timelines and that resulted in our assessment of the value.

We are particularly excited about the combinations in lung. There are, as you say, many, not just PD-1 in combination with PARPs, there is PD-1 in combination with a lot of things, so it is always challenging, but we think the data will speak for itself and probably help with enrolment, so we are optimistic that the timelines we have will be met.

Emma Walmsley: Thanks, Hal. The next question please.

Emmanuel Papadakis (Barclays): Thank you for taking the questions. I have a couple of follow-ups.

The first one, if I could try and pin you down a little bit on financials, the question asked earlier about the delta between the opex levels, you are implicitly guiding to relative to what people had been previously modelling standalone for TESARO? Should we assume that will come more in R&D and SG&A, or across the board? That would be helpful to know if you are planning, for example, to accelerate the clinical development costs there versus other things.

The second one was just the differentiation on the safety side. You did mention, Luke, that the 200 mg has looked a bit better on things like anaemia, thrombocytopenia, etc. Should we worry that will come at the compromise of efficacy in the PRIMA study?

Then, the third one I was going to follow up on was if you could just talk a bit about the recent update we had on both the PD-1 and TIM-3. The data looked relatively unimpressive. You have barely mentioned the TIM-3 on the call today. Should we assume that implies you share that view? Many thanks.

Emma Walmsley: Thanks, Emmanuel. Listen, I will ask Simon in a second to maybe give you a bit more colour in terms of the investments we are proposing to make, both in the pipeline and in commercial.

However, first of all, perhaps Hal can talk about the reassurance around tox and thrombocytopenia because the interims were reassuring on that in terms of there not being a trade off, but also the question on the TIM-3.

Hal Barron: Yes, thanks Emmanuel. So in terms of the interim safety data presented at ESMO, I think it was reasonably compelling that by starting off with a lower dose, particularly in the patients who had a lower body weight and who had baseline platelet counts of less than 150,000, that you can minimise to a large degree the safety concerns that were observed when all patients got 300mg.

It should be pointed out that clinicians had sort of figured that out already and approximately 50% of patients used 200mg, so this is more of proving what I think most clinicians had observed clinically through dose reductions.

When you look at the data from retrospective analysis in the previous studies where this was examined, this did not have any reduction in efficacy by doing so and when you think about it, that makes sense because the dose reduction is really for a very short period of time relatively speaking compared to what is used clinically, so the absolute amount of drug that's used isn't reduced that substantially because it's only for the first few weeks that dose reduction would be implemented in a novel way. But, as you say, we will have that data from PRIMA.

When we look at, as I said, thrombocytopenia as well as dose interruptions, dose reductions, discontinuation AEs, etc with the new regimen they all look very comparable so we're reasonably optimistic that this new regimen will be both much safer, and equally effective.

In terms of the other pipeline, most of the value and excitement was, as you say, on Zejula but the PD-1 data is I think quite interesting. It looks at least as compelling as data from pembro. The higher dose that's used could give some interesting potential upside as well as the convenience which starts off every three weeks but goes to a high dose every six weeks to use similar PK, so as an adjuvant, the convenience might be valuable.

But I think the excitement for PD-1 overall is that it gives us flexibility with combination trials and doesn't require us to rely on anyone else, so we'll have these both for Zejula but as well as for our own combination studies.

The data on TIM-3 I think was interesting because there did appear to be a dose response and obviously there was no control arm but having a low dose that was essentially ineffective allows you to see what a slightly higher dose would do in terms of response rates and there was some activity.

It's early days and I think drawing conclusions about how excited to be is inappropriate. There will need to be higher dosing and I think with that we will learn a lot more. It's early stage, but again like many of these IO assets you need to ensure you have a larger dataset before drawing conclusions. The biology is compelling and the combination is very rational so cautiously optimistic that we'll see even more impressive signals with time.

Emma Walmsley: Thanks, Hal. Simon, any comments on the investment?

Simon Dingemans: Just to add I think as Keyur has highlighted, the guidance we've given does signal that we expect to invest more than the current spend rate

that TESARO are putting behind both their Commercial and R&D operations for all the reasons that we've been through on this call. We see on the R&D side significant opportunity to take Zejula into other treatment areas and also to build on the pipeline progress that you've seen already. To remind you there are any number of comments about how TESARO was going to be able to afford to progress the opportunity sitting in front of them, so we want to make sure that we do resource them and advance those as quickly as possible.

Equally on the Commercial side, competing in this space, as I think some of the earlier questions highlighted, is not a small task and we need to build around the Commercial teams and make sure that they are again resourced appropriately. So the increased spend will be both on Commercial and R&D and I think where current street estimates for TESARO are missing an opportunity is that they expect that spend to come down a bit too quickly against the opportunity set that we've expressed and that's why we've highlighted the next couple of years will be diluted to the extent that we've described.

Emma Walmsley: Thanks and I think, Luke, you wanted to add a comment.

Luke Miels: Yes, I think this is a key point. I mean, if you look at TESARO's success so far, if you look at ovarian, you have to exclude breast of course, they've done extremely well with around 50% of the market share with what I think is fair to say a very constrained budget and a very focussed budget and as part of the due diligence when we looked at some of the resource allocation and focussed on that, we reached the conclusion that with a bit more investment and a bit more focus to that investment, we could unlock value for shareholders.

There are a number of areas where the market research is telling us if we can invest more, then we should be able to drive broader adoption and faster uptake, so that's certainly what we plan to do.

Emma Walmsley: Thanks very much, Luke. The next question, then please.

Steve Scala (Cowen): Will GSK adopt TESARO's strategy to convert patients to flat dose independent pricing or will that be revisited?

Secondly, I imagine the answer is no, but does Novartis have first option rights on any TESARO assets? I think they have such rights through 2027 and then lastly, this is more of an observation, but I'm just struck by the comments on footprint and critical mass in Oncology since that was what was sold to Novartis. Why re-enter now instead of with an asset that is within GSK's stated Oncology focus, which is IO, epigenetics and gene

therapy? I know you think that Zejula is differentiated so you probably don't need to respond to the observation. Thank you.

Emma Walmsley: Thanks very much, Steve. I'll let Luke comment in a second on the footprint and the pricing point of view, as much as one does on this kind of call. Just to be clear, Novartis do not have an option on the assets; they have a right to negotiate but not on already marketed assets, which would be the case for Zejula. It is a right of first negotiation in terms of pipeline assets.

As far as why we decided that this move back into differentiated oncology was the right way forward, as a reminder we didn't get out of oncology completely, we kept the early stage pipeline including, as you outlined, BCMA which we have recently accelerated and other specific IO assets and epigenetic assets.

The key here is what Hal was talking about, which is that we believe that Zejula in the PARP class is the first approved asset to demonstrate synthetic lethality. It is completely in line with the functional genomics strategy that he talked about and we believe - and Hal may want to comment on that - that he can bring some of the technology platform capabilities that GSK is building across the broader portfolio. Hal, do you want to add to that on why this specific asset is right as well as being competitive? Then, Luke, you can talk about the commercial aspects.

Hal Barron: Thank you for the question. What is missed about PARPs, to be completely transparent, is that they were developed as a very targeted therapy for women with *BRCA* and with that perspective I don't think it makes that much sense. However, we believe that is wrong and that the PARP inhibitor class and Zejula is taking a lead in showing that it works in a vast number of types of tumours, those that have the homologous recombination defect, and that is a class, for example, of something you learn through functional genomics. Our build-up of this capability we believe will give us a very unique opportunity to see all the different places where Zejula could benefit patients, as well as, frankly, what combinations would be ideal partners.

Without tipping our hand too much, there are data both in the public domain and that we are generating that would suggest some very interesting combinations that we believe will give us an opportunity to be best-in-class from a development perspective. We believe that it fits very well and that is not to mention the fact that, in addition to Zejula, there are three IO assets that we believe are, in many respects, perfect complements to what we had internally. Therefore, when you look at all the different opportunities out there to expand our pipeline, which is our commitment to do, this became the most attractive opportunity.

Luke Miels: Thanks, Steve. What I would say in terms of the flat pricing, there are pros and cons to it. We have some time to land on a final decision but that is probably all I shall say at this point.

Emma Walmsley: Thank you everybody. I am afraid that is all we have time for on this call today. Please do feel free to follow up with the IR team if you have anything else that you would like to discuss, or indeed with us, and we look forward to catching up with you soon. Thank you.

[Ends]