R&D Script Martin Mackay – Half-year results 2011

SLIDE Title slide

Thank you Simon.

SLIDE Agenda

I am going to give you an update today on where we are with our late stage portfolio. My focus will be on BRILINTA, dapagliflozin and late stage trial programs including NKTR-118, our project in opioid induced constipation, which moved into phase 3 in the 1st quarter. I'll finish with a top line summary of upcoming milestones.

In conjunction with this morning's results we also published our half yearly update of the clinical development pipeline – so first, a quick word on that.

We currently have 88 projects in clinical development. This is down 4 from Full Year – and proof that we are following through on the scrutiny I spoke about in January, advancing only those projects that meet the most stringent selection criteria and being prepared to remove those that don't.

Over time, this dynamic will lead to an increase in the overall quality of the pipeline and as you know, I believe that over the long-term a relentless focus on quality leads to lower risk and consequently better returns.

You will also note from the pipeline table that we've continued our practice of guiding to future filing dates on a much broader geographical basis.

SLIDE Portfolio movement January-July 2011

So far this year, we've seen 7 product approvals in the major regions and BRIC markets including BRILINTA in the US last week, ONGLYZA in China in May, and NEXIUM in Japan in July.

Our pain medicine VIMOVO continues its launch rollout and to receive additional marketing authorisations.

CAPRELSA – for the treatment of advanced medullary thyroid cancer – was approved in the US in April. In Q1, high dose FASLODEX got approved in India and our flu vaccine FLUENZ was approved for the first time in Europe.

In both the US and the EU, ONGLYZA received label enhancements for patients with renal impairment.

We have submitted BRILINTA in further markets including China, our quadrivalent flu vaccine MEDI-3250 in the US, as well as dapagliflozin and CAPRELSA in BRIC markets.

SLIDE Brilinta – Regulatory status

Clearly the highlight of the year so far has been the progress we've been making around the world with BRILINTA, most notably with last week's US approval.

Since the EU marketing authorization in December, we have significantly expanded BRILINTA approvals beyond Europe – covering 41 countries now, including the European Union, US, Australia, Canada and Brazil.

SLIDE Brilinta – Reimbursement

Where we have achieved pricing reimbursement already, it is broad – in that the product labels reflect the full extent of the PLATO data and government authorities are showing a willingness to reimburse for the broad ACS patient population studied in the trial.

We are also happy with the pricing we are achieving, with governments and other payers seeing BRILINTA as superior to branded clopidogrel and willing to reflect that superiority in a premium price, despite the availability of generic clopidogrel in these markets.

Health economic data from PLATO show BRILINTA to be cost effective even compared to generic clopidogrel, which help further demonstrate the compelling value proposition of BRILINTA versus a widely used generic. This is of interest to payers looking to lower overall healthcare expenditures.

SLIDE Brilinta – Regulatory status

There's more work to be done, both in completing the 'step wise' launch process David talked about and also in completing the Regulatory reviews ongoing in a further 43 markets including China, Russia and India.

And we've already turned our focus to future lifecycle management. With the PEGASUS-TIMI 54 study we are working on extending the scientific knowledge about the benefits of BRILINTA 1 to 3 years following an ACS event.

And we've recently started a second, smaller study called ATLANTIC in STEMI patients who are to be treated with an artery opening procedure known as PCI. Current treatment guidelines recommend initiation of antiplatelet therapy as soon as possible, but there are limited data on pre-hospital administration in the ambulance setting. The aim of this study is to determine whether initiation of BRILINTA as early as possible can lead to improved outcomes for these patients.

The Japanese registration program has also progressed to phase 3, with a target submission date of 2013.

SLIDE Brilinta – Label details

Turning briefly to the US approval – I believe the label is a strong one; it fully reflects the patient population and the excellent data from the PLATO trial and gives us a unique CV mortality benefit claim over clopidogrel.

The boxed warning gives appropriate prominence to the data on bleeding and on the impact of higher aspirin doses on the effectiveness of Brilinta.

The warning states that maintenance doses of aspirin above 100 mg reduce the effectiveness of BRILINTA, and should be avoided.

I see this to be in line with the general trend in the US towards a greater use of lower maintenance doses of aspirin. Real-world data from PLATO also suggests that more than 40 % of US patients are already receiving low dose aspirin in clinical practice.

SLIDE Dapa

As you know, on July 19th the FDA's Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) met to discuss dapagliflozin, our SGLT2-inhibitor developed with BMS.

Clearly we had hoped for a positive vote from the Advisory Committee. But in reflecting on the committee's deliberations, I'd make a few points:

There was a clear call for additional information to fully characterise some important aspects of the benefit / risk profile for this compound – as well as general appreciation of the need for new treatment options for this disease, and many of the committee members found aspects of the product profile interesting: oral dosing, novel insulin-independent mechanism, the potential for weight loss rather than weight gain, low potential for hypoglycaemia.

As the agency said at the end of the meeting, the balance of these questions now moves into the hands of the reviewing division, and clearly there is a discussion that needs to take place to find the appropriate way forward.

We remain committed to the broad clinical development program for dapagliflozin and will focus our efforts on working with the FDA between now and the PDUFA date October 28 to address these outstanding questions.

SLIDE Late stage trials

Let's now look at some of our late stage trial programs.

NTKR-118, an oral, peripherally acting opioid antagonist which we are developing with Nektar Therapeutics, moved into phase 3 and is being investigated for the treatment of opioid induced constipation, or OIC.

Opioids are widely prescribed in pain management, with over 250 million prescriptions written annually in the US alone.

And some 50% of patients taking them long term suffer from constipation. Of these, only 40 to 50% gain effective relief with current treatments.

NKTR-118 is designed to block opiate receptors in the GI system and thus alleviate OIC without counter-acting the analgesic effects of opiates in the brain.

The phase 3 KODIAC program started enrolling in March. It consists of two efficacy studies of 630 patients each, which compare two doses of NKTR-118 and placebo. A 52-week long-term safety study assigns patients to open-label treatment of either NKTR-118 versus traditional treatment chosen by the physician. KODIAC also includes one 4-week study of patients with cancer-related pain.

Building on results from phase 2, KODIAC will aim to establish a substantially improved lower GI function by increasing the frequency of spontaneous bowel movements in patients with OIC, while simultaneously preserving opioid mediated analgesia.

The first regulatory filing of NKTR-118 is being planned for 2013.

Other phase 3 clinical programs are on track, too.

The FOSTAMATINIB phase 3 development program OSKIRA in rheumatoid arthritis is progressing well. We expect the first set of data in the 2nd half of 2012 and remain on track to meet the planned US and European filing dates in 2013.

In addition to the three pivotal combination studies, we commenced a further phase 2b study during the first quarter – OSKIRA 4 – which explores FOSTAMATINIB as a monotherapy in RA and will provide important information on the profile of FOSTAMATINIB without concomitant treatment with a DMARD.

In neuroscience, our novel neuronal nicotinic channel modulator TC-5214 licensed from Targacept is progressing through its phase 3 clinical program, called RENAISSANCE. This program investigates TC-5214 as an adjunct to SSRI/SNRI therapy in major depressive disorder.

Readouts from the first completed study will become available in Q4 and all study results will be available by Q2, 2012.

We continue to anticipate the US NDA submission in the second half of 2012, and EU filing in 2015.

The SATURN trial investigates the effects of 40 mg CRESTOR and 80 mg atorvastatin on atherosclerotic disease in patients with coronary artery disease. The last patient visit occurred in June, and we are now awaiting the completion of the IVUS data analysis and expect the first full scientific presentation of the data at the American Heart Association meeting in November.

SLIDE 2011 Newsflow

Let me summarise the key milestones coming up in the second half year.

We expect BRILINTA to be filed, approved and launched in further markets. Final reimbursement decisions are expected by NICE in the UK, the French Transparency Commission, in Canada and in Germany.

VIMOVO is anticipated to continue its launch in over 20 more markets this year.

We are expecting regulatory decisions on AXANUM in the EU – and on high-dose FASLODEX and IRESSA 1st line in Japan in Q3 to 4.

The US PDUFA date for dapagliflozin is October 28.

We're planning to further broaden the SYMBICORT market to reach more patients in Japan, and will submit ZINFORO in several emerging markets.

As regards CAZ104, our β-lactam / β-lactamase inhibitor combination for the treatment of serious Gram-negative bacterial infections, we are discussing with regulators potential trial designs. A decision on phase 3 progress will be taken jointly with Forest Labs.

Depending on the review of all available data and the resolution of certain formulation challenges, OLAPARIB in serous ovarian cancer may obtain a phase 3 decision toward end of this year.

This concludes my portfolio review today.

With the organizational improvements I spoke about in January, our improved rigor in drug candidate selection, and the momentum we have built since, I believe we are on the right track to creating long term, sustainable pipeline value.

Yet I will not rest to continue to adapt the organization to ensure we have the right priorities, the right structure and the right level of investment in place to successfully deliver great medicines to patients and value to our investors.

David – back to you.