Capital Markets Day 2021

Thursday, 11th March 2021

Presentation by

Christian Rommel

Head of Research & Development Pharmaceuticals

(Please check against delivery)

Paving the Way for our Future in Science-based Innovation

Christian Rommel

Head of Research and Development, Pharmaceuticals Division

Ladies and Gentlemen, welcome to today´s presentation about R&D at Pharma. I am Christian Rommel and I recently joined Bayer Pharmaceuticals to lead research and development.

During today´s presentation, I will provide you with my first impressions about the R&D organization, its focus areas and capabilities, some initial thoughts about the key pipeline projects as well as some of my priorities going forward.

When the news became public that I would move on to Bayer, many people were asking me why Bayer? Well, before making the decision to take over this new position, I obviously did my personal due diligence on Bayer´s Pharma division. Let me share with you what I found out.

The R&D team has established highly regarded and respected excellence in small molecule drug discovery. They are fully committed to develop new treatments for areas of high unmet need. This all is founded on a deep science-based understanding of disease mechanisms in the therapeutic areas of focus. Also, beyond small molecules, the organization has begun to expand into new science and new modalities. In my view, especially their investment into cell and gene therapies was a bold and smart move.

On the areas to be strengthened, my first impression is that despite the excellence in drug discovery, there is an opportunity to focus and direct small molecules into the innovation space of medicinal chemistry and disease biology. In addition, success of internal R&D requires external sourcing of innovation. On top, attracting and developing top scientific talent is in my view an area to be strengthened in certain areas as well.

The expertise of our Pharma R&D organization is witnessed by the strong track record of execution as well as innovation during the last decade.

The business delivered really differentiated and first in class drugs to the benefit of the patients. Just to mention a few examples:

- Xarelto, an oral, direct factor Xa inhibitor
- Xofigo, an alpha radiopharmaceutical
- Adempas, a soluble guanylate cyclase - sGC - modulator
- and Vitrakvi, a specific treatment for NTRK gene fusion tumors.

To complete the list, I would also add Nubeqa for treatment of prostate cancer and Verquvo a new drug for the treatment of heart failure.

Based on this track record, we will continue to pursue our patient-centric approach to develop new and better medicines for the future.

Aligned with our purpose “Science for a better life”, we are focusing on areas of high unmet medical need. We are working science-based and patient centric. Our research and development activities are predicated on a deep scientific understanding of disease biology and a diverse range of modalities, complemented by data generation and insights analytics. New product developments

need to deliver scientific and clinical innovation and need to make an impact. We all know that incremental progress will not be rewarded – and it's not on our 'to do' list.

In order to deploy our resources efficiently, we focus on therapeutic areas of high unmet medical need. These are cardiovascular diseases and oncology, which still represent the two "biggest killers" in terms of number of deaths worldwide. In addition, endocrinology, metabolic dysregulation & reproductive health as well as adjacencies like ophthalmology and rare diseases belong to our focus areas in R&D.

In my view, expertise in disease biology and therapeutic areas needs to be supported by a broad and agnostic approach to the modalities applied. Novel drug modalities and integrated platforms are key to state-of-the-art drug discovery.

We already expanded beyond small molecules into protein therapeutics, radiotherapies, cell and gene as well as RNA therapies; complemented by digital technologies like large scale-data analytics and artificial intelligence.

In essence, we are focused on diseases that matter. And we are equipped with a broad modality "toolbox" to drive ground-breaking science to deliver innovative and transformative treatments for patients.

When looking at the R&D pipeline, several assets caught my attention immediately. In the area of cardiovascular diseases these are Finerenone and the Factor XI portfolio. In Women´s Health it's Elinzanetant, the KaNDy asset, and from the mid-stage pipeline, I believe that the P2X3 receptor antagonist may bear significant potential.

I also believe that the early pipeline includes some really appealing projects, especially in the areas of oncology and in cell and gene therapy.

But let´s first look at Finerenone.

Finerenone is a non-steroidal, selective antagonist of the mineral-corticoid receptor. It may become a new treatment option for chronic kidney disease - CKD - in patients with type-2 diabetes.

The impact of CKD in type 2 diabetes is far-reaching. We estimate that about 145 million patients suffer from CKD. While it is critically underdiagnosed it's a major risk factor for the development of end-stage kidney disease and of increased mortality due to cardiovascular events.

CKD-progression in type 2 diabetes is influenced by three major factors: hemodynamic and metabolic as well as inflammatory and fibrotic drivers. Today, physicians are fighting CKD in type 2 diabetes on multiple fronts. But even with well-controlled hemoglobin and blood pressure, many patients are still experiencing disease progression. Recognizing some advancements in the field, there are more opportunities to reduce the residual risk of end-stage kidney disease and death from renal disease.

For these patients unaddressed inflammation and fibrosis can lead to a variety of cellular changes that permanently alter the structure and the function of the kidney. This inflammatory and fibrotic damage is a major consequence of mineral-corticoid receptor overactivation in the kidney.

Finerenone is targeting this over-activation of the mineral-corticoid receptor.

Based on positive phase II data we initiated the largest CKD phase III trial program in patients with type 2 diabetes with more than 13,000 patients enrolled. The first trial, FIDELIO-DKD comes with a composite renal endpoint, while the second trial, FIGARO-DKD has a composite cardiovascular endpoint. Data for FIDELIO-DKD were presented last year. The FIGARO-DKD trial is clinically completed, and we expect to publish the data at a medical congress later this year.

In FIDELIO-DKD, Finerenone demonstrated a significant reduction of the composite primary endpoint of kidney failure, a sustained decrease of at least 40% in the eGFR from baseline, or death from renal causes.

In addition, a significant reduction in the composite of time to cardiovascular death or non-fatal cardiovascular events - a key secondary endpoint - was shown. Finerenone did not interfere with the glycaemic control of the patients. Impact on blood pressure was minimal. Importantly, study results revealed only infrequent discontinuations due to hyperkalemia in patients who received Finerenone. This clearly differentiates Finerenone from older steroidal mineral-corticoid receptor antagonists which typically showed a more pronounced impact on potassium.

Based on these data we filed for approval in key markets. FDA granted priority review and if approved, the drug could be launched in its first market in the second half of this year already.

We believe that the potential for Finerenone goes beyond chronic kidney disease in type 2 diabetes.

Mineral-corticoid receptor over-activation plays also a significant role in heart failure. Blockade of the mineral-corticoid receptor has demonstrated beneficial effects in the treatment of certain forms of heart failure. Based on robust phase II data, we initiated the FINEARTS-HF study, a phase III study to evaluate the effect of Finerenone on morbidity and mortality in patients suffering from heart failure with a left ventricular ejection fraction of ≥40 percent.

Currently, there are limited options available for patients suffering from heart failure with preserved ejection fraction. Given their substantial risk for cardiovascular events, this represents a critical unmet need in cardiovascular disease. FINEARTS-HF is the first trial to investigate the use of a non-steroidal, selective mineral-corticoid receptor antagonist in this setting.

Moving on to the field of anti-coagulation where Bayer has established itself as a global leader with Xarelto.

Venous thrombosis including deep vein thrombosis and pulmonary embolism annually affects several million people worldwide. Furthermore, arterial thrombosis including ischemic heart disease and stroke collectively causes more than 10 million deaths per year worldwide. Thrombosis is the common underlying pathology of these diseases and anti-coagulants are the mainstay to prevent and/or treat thrombosis.

Over the last decade, significant progress has been achieved in anti-coagulation therapy. After decades of use of heparin and vitamin K antagonists, direct thrombin inhibitors and direct factor Xa inhibitor - the so called NOACs - define the treatment standard today.

Commonly used anti-coagulants produce therapeutic anti-thrombotic effects either by inhibiting thrombin or factor Xa or by lowering the plasma levels of the precursors of these key enzymes. However, these drugs do not distinguish between thrombin generation contributing to thrombosis and thrombin generation required for hemostasis. Thus, anti-coagulants increase bleeding risk, and

many patients who would benefit from therapy go untreated because comorbidities may expose them to an unacceptable risk for hemorrhage.

Blood coagulation factor XI has emerged as promising target for new anti-coagulants. As the factor XI pathway contributes to thrombus formation to a greater extent than to normal hemostasis, pharmacological inhibition of this coagulation factor may offer the possibility of anti-coagulation therapies with lower bleeding risk.

Hereditary deficiency of factor XI is known as hemophilia C. It is generally associated with a relatively mild-to-moderate bleeding phenotype compared with hemophilia A or B. In fact, FXI-deficient individuals rarely suffer from spontaneous bleeding. In addition, epidemiological studies suggest that FXI deficiency confers reduced risk of thrombotic disorders. Such epidemiological findings are supported by the fact that factor XI-gene deficient, knockout, mice are protected from thrombosis while no profound bleeding phenotype is observed.

Supported by such lines of evidence, targeting factor XI is expected to inhibit thrombosis but only depress hemostasis. Targeting factor XI may serve as a powerful route to new anticoagulants that may be associated with less bleeding risk than currently available options.

We have a broad and diverse portfolio of factor XI inhibitors which we currently investigate in a comprehensive phase II study program.

In collaboration with IONIS Pharmaceuticals we are developing an antisense oligonucleotide, factor XI LICA, to depress the biosynthesis of factor XI in the liver. This antisense approach uses a short nucleic acid sequence which is specifically designed to selectively hybridize with the mRNA target in the hepatocytes. This hybridization typically results in the degradation of the targeted mRNA and leads to a corresponding reduction in factor XI plasma levels.

A dose finding study with Factor XI LICA in end-stage renal disease patients on hemodialysis is currently underway.

In a second approach we are looking at Osocimab, a fully human monoclonal antibody that binds adjacent to the active site of factor XIa and prevents it from activating factor IX in the coagulation cascade.

Phase II data confirm proof of concept for Osocimab. Among patients undergoing knee arthroplasty, postoperative, single doses of Osocimab between 0.6 mg/kg and 1.8 mg/kg were non-inferior to enoxaparin. The preoperative 1.8 mg/kg dose met the criteria for superiority compared with enoxaparin for the primary VTE outcome.

Osocimab is currently investigated in a further phase II program to assess the safety and tolerability of monthly subcutaneous administrations to end-stage renal disease patients on regular hemodialysis as well.

Our oral therapy is a potent, direct and reversible small molecule inhibitor of FXIa showing strong anti-thrombotic efficacy without increasing the bleeding risk.

It is investigated in a broader spectrum of potential indications. We initiated a comprehensive phase II study program, called PACIFIC, where we test the compound in patients with atrial fibrillation, acute ischemic stroke and in patients following an acute myocardial infarction. In total, we plan to

enroll more than 4,000 patients into the program. First studies are expected to be completed later this year and early next year.

Switching gears to Women´s Health.

Vasomotor symptoms, or hot flashes and night sweats, are the most commonly reported menopausal symptoms linked to declining levels of estrogen. Up to 75 percent of women going through menopausal transition experience these symptoms which can impact both their work and private life and are debilitating for several years for those affected. About 16 million women in the U.S. and another 16 million in Europe suffer from such menopause symptoms.

The current standard of care is hormone replacement therapy. Given its limitations, a non-hormonal treatment for vasomotor symptoms would be a major advancement for women suffering from symptoms of the menopause.

Elinzanetant, formerly known as KaNDy NT-814, is a non-hormonal dual antagonist of both the neurokinin-1 and 3 receptors. Neurokinin signaling increases in response to estrogen deficiency in menopausal women and has been implicated in the etiology of hot flashes. Elinzanetant is modulating a specific group of estrogen sensitive neurons that in menopausal women due to the absence of estrogen, become hyperactive and consequently disrupt the body´s thermoregulation. Inhibition of NK-3 receptor signaling may reduce this hyperactivity and address this dysregulation that is driving hot flash symptoms.

In addition, blockade of NK-1 receptors may result in a lessening of the vasodilatory response in the periphery, thereby contributing to reducing the intensity of hot flashes.

Elinzanetant demonstrated significant and rapid improvement in vasomotor symptoms in phase II. Symptom frequency was reduced in all treatment groups. Reduction was shown as early as the first week of treatment. Improvements in hot flashes were accompanied by significant benefits on sleep, mood and parameters of menopause-specific quality-of-life assessments. Elinzanetant was well-tolerated. Most adverse events were mild or moderate and there were no serious adverse events related to treatment.

Based on these exciting data, we are planning to initiate a pivotal phase III trial this year.

Another attractive pipeline asset that caught my attention is Eliapixant, a P2X3 receptor antagonist.

P2X3 receptors are a family of ion channel receptors that are mainly localized on sensory nerve cells. Studies have shown that P2X3 plays an important role as natural mediator of pain and nerve hypersensitivity in peripheral pain responses, and it functions as inducer of neurogenic inflammation.

Eliapixant is a potent, selective P2X3 receptor antagonist that reduces nerve fiber hypersensitivity and may have multi-indication potential. It was first identified within our strategic research alliance with Evotec in connection to our joint endometriosis research. But P2X3 also seems involved in several other diseases characterized by painful neurogenic hypersensitivity including refractory or unexplained chronic cough, over-active bladder and neuropathic pain.

Proof of concept for Eliapixant has been obtained in refractory chronic cough. This is a poorly recognized condition causing significant morbidity. About 1-5 percent of the global population suffers from refractory or unexplained chronic cough. There are currently no approved treatments

available and off-label pharmacologic treatments typically have limited efficacy and high adverse event rates.

Eliapixant demonstrated a dose dependent reduction in cough frequency of up to 25 percent for the 24 hours cough frequency and up to 36 percent for the awake cough frequency. The rate of adverse events, including taste-related effects, was low across the study participants.

To fully exploit the full therapeutic potential of Eliapixant we expanded the clinical phase II program beyond chronic cough into over-active bladder, endometriosis and neuropathic pain. All these conditions have a significant prevalence and only limited treatment options are available today.

In my previous position I was the Head of Oncology Research and Early Development at Roche. Thus, it should be no surprise for you that I was particularly interested in learning more about Bayer´s pipeline in oncology.

At Bayer, we are mainly focused on three areas in oncology research.

In Precision Molecular Oncology we are exploiting intracellular oncogenic dependencies with small molecules and new modalities. Deliverables from our R&D in this area include most of our marketed products incl. Nubeqa, Vitrakvi and Stivarga.

In the area of Targeted Radio-therapies we are utilizing alpha-particle emitting radionuclides to deliver a high radiation energy to selectively kill tumor cells. Xofigo, or radium-223, is the first approved alpha radiopharmaceutical. It demonstrated improved overall survival among castration-resistant prostate cancer patients with symptomatic bone metastases, with mild side effects owing to its localized dose deposition.

We also have unique access to tumor targeting Thorium-227 conjugates which combine the alpha-emitter Thorium-227 to an antibody to selective deliver the radiation to the target cells.

In the field of Immuno-Oncology, we focus on select next-generation approaches and on the development of allogeneic T-cell-based therapies.

As you can see, an already broad modality spectrum in our oncology research spans from small and large molecules to radio- and cell-therapies.

Let´s talk about some of the highlights of our oncology pipeline.

Activating mutations of epidermal growth factor receptor, or EGFR, play a major role in the development of non-small cell lung cancers. For the majority of patients whose tumors have such mutations, tyrosine kinase inhibitors, such as gefitinib and erlotinib, provide significant clinical benefit. The majority of patients treated with these TKIs experience an objective response, improved progression free-survival, and improved quality of life compared to chemotherapy alone.

However, approximately 2% of all lung adenocarcinoma cases have an in-frame insertion within exon 20 of the EGFR. These tumor types are generally resistant to EGFR tyrosine kinase inhibitors.

Patients with these tumors have a median progression free survival of just 2 months with approved TKIs and of about 6 months with chemotherapy which is currently the standard of care. Thus, a very significant unmet medical need exists for these, molecularly defined patients.

Our small molecule EGFR exon20 inhibitor shows activity against a broad range of Exon20 insertion mutations and demonstrated anti-tumor efficacy in preclinical tumor models. It is a highly potent

compound with excellent selectivity compared to EGFR wild-type which is important for activity and differentiation. In addition, our molecule is also active on HER2 exon 20 insertion mutations which account for about 2-3 percent of patients with non-small cell lung cancer.

Based on the preclinical progress so far, we are planning to initiate phase I clinical development in the second half of this year.

To secure the integrity of the genome, cells have evolved mechanisms termed DNA-damage response, or DDR. This mechanism detects DNA lesions, signals their presence and promotes their repair.

Many cancers harbor defects in DDR pathways, leading to genomic instability that can promote cancer cell growth.

The ATR kinase plays a central role in the DNA damage response. Many tumor cells, but not normal cell, are often reliant on ATR to survive replication stress.

Thus, ATR inhibition may be a promising therapeutic strategy to inhibit tumor cell growth and viability. It may also have a synergistical antitumor effect on cell lines with specific genetic alterations. Genome wide studies identified a number of genes with a synthetic lethal relationship with ATR inhibition. It is suggested, that increased replication stress and impaired DNA repair may increase sensitivity of tumor cells to ATR inhibition which opens up strategies for combination therapies.

These findings may also have the potential to provide new genetic biomarkers for specific patient enrichment in clinical studies.

Our ATR inhibitor demonstrates strong single-agent activity in different preclinical tumor models with DDR defects. We are now investigating this novel, selective inhibitor in a phase I program in several advanced cancer types. It is applied as a single agent or in combination with pembrolizumab, a PD-1 inhibitor or with niraparib, a PARP inhibitor. Study completion is currently expected for the 2023/2024 timeframe.

Radiation therapy is one of the mainstays in cancer therapy. We at Bayer were at the forefront of targeted radiation therapy which delivers systemic radiation selectively to cancer cells. As said before, Xofigo was the first ever approved alpha radiopharmaceutical. The physicochemical properties of the Radium nuclide in Xofigo mimic those of Calcium. As a consequence, the Radium is accumulated in bone tissue. Based on this tissue specifity, Xofigo is used for the treatment of bone metastases in patients suffering from advanced metastatic castration resistant prostate cancer. Xofigo was approved for this indication based on phase III data demonstrating a significant prolongation of overall survival.

Apart from Xofigo, we are pursuing targeted alpha therapies with potential across several tumor types.

Thorium-227 is an alpha radiator as well. Due to its chemical properties it can be complexed to a variety of antibodies which may help directing the alpha radiation to the target tumor cells.

We are investigating Thorium conjugates in phase I in combination with antibodies targeting PSMA in prostate cancer patients and Her2 targeting radio-conjugates in HER2 expressing breast, gastric and gastroesophageal cancer. We expect first trial completions in the 2023/2024 timeframe.

In accordance with our overall cell- and gene-therapy strategy, we are expanding our modalities in oncology into cell-therapies as well.

Chimeric antigen receptor engineered T-cells, or CAR-T cells, have yielded significant efficacy in certain B-cell malignancies. Based on this success, CAR T-cell therapy is now being investigated in several hematologic and solid tumor types as well.

CAR T-cells are generated by removing T-cells from a patient's blood and engineering the cells to express the chimeric antigen receptor, which reprograms the T-cells to target tumor cells. The engineered T-cell are propagated and infused back into the donor patient. This autologous approach is complex, time consuming, and patient specific.

The development of allogeneic, i.e. donor independent CAR T-cells is anticipated to overcome some of the technical and logistical challenges associated with autologous CAR-T cells.

This is why and where we collaborate with Atara Biotherapeutics.

Atara's allogeneic T cells originating from donors are generated from immune cells that have not been exposed to a patient´s conditions that may impair cell quality. These cells are engineered, manufactured and stored in inventory with the goal of being readily available for patients with serious diseases.

The collaboration includes the development candidate ATA3271, an armored next generation allogeneic T-cell immunotherapy, and an autologous version, ATA2271, for the treatment of high mesothelin-expressing tumors such as malignant pleural mesothelioma and non-small-cell lung cancer.

The allogeneic candidate leverages Atara´s novel, proprietary Epstein-Barr Virus (EBV) T-cell platform combined with next generation CAR-T technologies to improve efficacy, persistence, safety, and durability of response.

ATA3271, the allogeneic version of this CAR T, is currently in IND-enabling studies. ATA2271, the autologous version has enrolled the first patient in an open-label, single-arm Phase 1 clinical study in patients with malignant pleural mesothelioma in November 2020.

I appreciated your attention to my update on R&D.

Having talked now about some of the most attractive pipeline projects you may ask what´s on my agenda for the next months to come.

Obviously, after being with the company for about 6 weeks I will not be able to provide you a full picture today. But I set myself a number of key priorities that I would like to share with you today as well.

First, I will learn more about the individual R&D projects and will perform a holistic portfolio review to prioritize the most promising assets.

I will advance the late-stage pipeline to make these innovations available to patients as quickly as possible.

I will have a look at our resource allocation and how we may shift these to sufficiently fund the most promising internal or external opportunities.

I will continue to enhance our focus on external innovation and plan to further strengthen access to new science, technologies and modalities.

And, I will continue to grow scientific talent and leadership within my organization.

This concludes may presentation for today, and I am looking forward to being in contact with you in the future. I am happy to take your questions later on in the Q+A session.

Cautionary Statements Regarding Forward-Looking Information

This presentation may contain forward-looking statements based on current assumptions and forecasts made by Bayer management.

Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at http://www.bayer.com/.

The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.