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GSK profiles innovative R&D portfolio to investors

~40 potential new medicines and vaccines offer significant opportunity to drive long-term performance and deliver new benefits to patients and consumers

At a presentation to investors in New York today, GSK described a deep portfolio of innovation, focussed across six core areas of scientific research and development: HIV & Infectious diseases, Oncology, Immuno-Inflammation, Vaccines, Respiratory and Rare Diseases. Around 40 new potential medicines and vaccines were profiled, supporting the Group's outlook for growth in the period 2016-2020 and the significant opportunity the Group has to create value beyond 2020.

The portfolio represents some of the latest scientific achievements from GSK's R&D organisation and its more than 1,500 company and academic collaborations. The company believes approximately 80% of the medicines and vaccines presented have the potential to be "first-in-class" with novel mechanisms of action. As a result, many of these potential medicines and vaccines may offer benefits beyond current standards of care and, in some cases, could radically transform how patients are treated.

In developing this portfolio, the company's scientists have focussed on:

- Targeting immune mechanisms that could alter the fundamental course of diseases, modifying disease progression and presenting opportunities to achieve remission and functional cures.
- Developing simplified treatment regimens and a new generation of long-acting medicines to provide long-term control and improve treatment outcomes for patients.
- Using next generation technology platforms to increase understanding of fundamental disease mechanisms, to develop new approaches to disease management and control.

At the event, notable advances within the portfolio were outlined, including potential:

- Leading-edge molecules in the field of epigenetics and immuno-oncology for the treatment of cancer;
- The next generation of respiratory medicines beyond inhaled treatments;
- A portfolio of new antibodies for inflammatory diseases including rheumatoid arthritis, autoimmune diseases and osteoarthritis;
- New options for long-term control and prevention of HIV;
- Opportunities designed to cure or induce long-term remission in both Hepatitis B and C;
- Breakthrough cell and gene therapies for treatment of rare diseases;
- A novel maternal immunisation platform for vaccines.

GSK also profiled a number of significant material opportunities in late-stage development, including: *Nucala* (mepolizumab)* for treatment of severe eosinophilic asthma, *Shingrix* (zoster)*, a candidate vaccine for the prevention of shingles, sirukumab for the treatment of rheumatoid arthritis, daprodustat for anaemia, cabotegravir for HIV, a candidate combination vaccine for the prevention of bacterial meningitis and a new inhaled triple therapy for treatment of COPD.

In total GSK has the potential to file up to 20 assets with regulators before 2020. Seven of these assets are in advanced late-stage development (with the potential to launch before 2020) with the remainder, being in earlier development, notably in the areas of oncology, immuno-inflammation and respiratory disease. In 2016/2017 GSK has the potential to start phase II development of ~30 new molecular entities (NMEs) and product line extensions (PLEs) and to start phase III development of ~20 NMEs and PLEs.

* The names *Nucala* and *Shingrix* have not been approved for use by the FDA or EMA



During the period 2021-2025, GSK has the potential to file up to 20 additional innovative assets, now in clinical development.

Commenting on the event, Sir Andrew Witty, CEO GSK said: “Earlier this year we set out our expectations for the Group to generate sustained sales and earnings performance over the next 5 years. With the recent transaction, we have significantly strengthened our Vaccines and Consumer Healthcare businesses.

“Today, we have profiled around 40 innovative potential new medicines and vaccines which will support future growth in our Pharmaceuticals and Vaccines businesses. Several of these assets are in advanced late-stage development and, for the first time, we have also outlined the scale of new opportunities GSK has in earlier stages of development, notably in areas such as oncology and immuno-inflammation.

“The level of innovation in this portfolio is substantial. We believe this is critical in today’s operating environment as payors look to balance pressures of pricing and demand. It also provides us with confidence that this portfolio can generate significant value for shareholders and deliver widespread benefits to patients and consumers.”

HIV and infectious diseases

The burden from infectious diseases continues to grow, presenting significant public health challenges. GSK’s leadership in **HIV** began with the development of the world’s first breakthrough medicine for HIV patients, *Retrovir* (zidovudine), in the 1980s. Successful development continues as demonstrated by the recent launches of new **dolutegravir**-based products, *Tivicay* (dolutegravir) and *Triumeq* (dolutegravir/abacavir/lamivudine). Dolutegravir was discovered through a collaboration between GSK and Shionogi. The next stage of development for dolutegravir is investigating its potential as a two-drug regimen. A phase III study is ongoing as part of a collaboration with Janssen, to investigate dolutegravir in combination with rilpivirine, as a potential maintenance therapy for adult patients with HIV who have already achieved viral suppression with a three drug regimen.

GSK is exploring new therapies for patients that could potentially enable long-term HIV control through infrequent dosing. The long-acting integrase strand inhibitor, **cabotegravir**, is at the forefront of this work and is currently in phase II development. Clinical data supporting the progression of cabotegravir development for both treatment and prevention of HIV was presented and included a positive headline data readout from the LATTE2 trial. Data from this phase IIb trial is expected to be presented at a scientific conference in 2016. Cabotegravir is expected to enter phase III development in 2016.

In a collaboration, the details of which will be announced later this week, GSK will work with the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, to optimise and develop **broadly neutralising antibodies (bnAbs)**, to recognise their potential to enable infrequent dosing in the long acting treatment and prevention of HIV.

Through its collaborations, and by applying the latest scientific breakthroughs, GSK is aggressively pursuing research programmes focused on curing patients with other infectious diseases.

A new collaboration with Regulus Therapeutics will undertake a clinical combination study investigating the potential of GSK’s NS5B polymerase inhibitor, **2878175**, currently in phase I development, and Regulus’ miR-122 antagonist, RG-101, to offer a single treatment cure for **hepatitis C**. The company’s collaboration with Isis Pharmaceuticals, which began in 2010 to develop new therapies using antisense technology, is also exploring use of the antisense oligonucleotide, **GSK3228836**, as a functional cure/long term remission for **hepatitis B**, with a phase II study planned for 2016.

GSK began its research into **antibiotics** over 40 years ago and, while the number of large pharmaceutical companies involved in this area has reduced in recent years, a dedicated research team at GSK continues to focus on discovering the next generation of medicines to treat bacterial



infections. The company's topoisomerase inhibitor, **gepotidacin (GSK2140944)**, has a novel mechanism of action and the potential to address multiple indications. It has been developed in collaboration with BARDA and DTRA. The asset is currently in phase II development with a phase III study planned to begin in 2016.

Oncology

GSK has focussed its oncology discovery efforts to target the fundamental drivers of cancer, exploring new technologies and approaches to stimulate anti-tumour immunity, reprogram cancer cells and improve long-term survival. Development timelines for oncology drugs can be compressed, which offers potential for several of these assets to be filed with regulators in the next 3 to 5 years.

Epigenetics, the 'control system' that helps regulate the DNA of cells and determines cell function – including the initiation and progression of cancer – holds significant potential for future cancer therapies. GSK made a significant research commitment to the field of epigenetics in 2008 and has a number of strategic biotech and world-leading academic collaborations.

GSK has an industry-leading epigenetics pipeline including a potential first in class BET inhibitor, **GSK525762** – currently in phase I clinical development – which has the potential to treat many indications including **solid tumours** and **heme malignancies**. **GSK2879552**, an LSD1 inhibitor, is also in ongoing phase I clinical studies to treat **small cell lung cancer (SCLC)** and **acute myeloid leukaemia**. The phase I studies have shown an early signal of significant progression-free survival for some patients with SCLC.

GSK also has a pipeline of potential **next generation immuno-oncology** therapies to stimulate anti-tumour immunity in patients. Its collaboration with Adaptimmune, is exploring use of **GSK 337794**, a T-cell receptor (TCR) therapy in phase I/II development across multiple indications including **sarcoma, myeloma, NSCLC, melanoma** and **ovarian cancer**.

Monoclonal antibody **GSK3174998**, an OX40 agonist antibody being developed in collaboration with MD Anderson, is one of four OX-40s currently in development across the industry. GSK has begun a development programme in eight **solid tumours** and **heme malignancies**, and announced today that in 2016 a study will commence exploring the asset's potential for use in combination with Merck's anti-PD-1 therapy, pembrolizumab, in **solid tumours**.

A first in class ICOS agonist antibody, **GSK3359609**, being developed in collaboration with INSERM, is focused on enhancing patients' anti-tumour T-cell response and is expected to enter the clinic in Q1 2016, providing a potential universal mechanism across multiple cancers either alone or in combination treatments.

Targeting the key biologic pathways thought to control cancer stem cells is also a key area for the company's oncology research. **Tarextumab**, being developed in collaboration with OncoMed, is a first-in-class anti-cancer stem cell therapy in phase II development for the treatment of **pancreatic** and **small cell lung cancer**.

Immuno-inflammation

GSK's growth of research in this area, and the multiple opportunities being explored, reflect the company's progress in understanding the underlying cause of immune-related disease and the potential for broad therapeutic utility from single pathway interventions.

The company today highlighted a broad portfolio of innovative immune-modulating therapies in clinical development, focused on potentially altering the course of disease and inducing sustainable remission.

GSK3196165, a granulocyte macrophage colony-stimulating factor (GM-CSF) antibody in-licensed from MorphoSys AG and in phase II development in **rheumatoid arthritis (RA)**, has shown a good magnitude of effect with a fast onset of action in this indication and further potential for early use to induce remission. Understanding from this programme has also unlocked a clinical development path



for disease modification and analgesic activity in **hand osteoarthritis (HOA)**. An expedited phase II trial in this indication is anticipated in 2016.

GSK also profiled a portfolio of potential first in class antibodies for inflammatory diseases, with four assets already in the clinic and set to enter phase II in 2016: **GSK2618960**, an anti-IL-7R antibody for **Sjögren's syndrome**; **GSK3050002**, an anti-CCL20 antibody for **psoriatic arthritis** in collaboration with Morphotek/ Eisai; **GSK2831781**, a cell depleting anti-LAG3 antibody for **T-cell driven immunoinflammation indications**, and **GSK2330811**, an anti-OSM antibody for **systemic sclerosis**.

RIP1 kinase inhibitor, **GSK2982772**, is a novel class oral therapeutic with phase I and preclinical data that support the potential for this drug to have activity in multiple potential indications. Phase II studies in **RA, ulcerative colitis** and **psoriasis** will progress in parallel in 2016.

The company also profiled two late-stage assets in this therapy area. **Sirukumab** is an anti-IL-6 antibody currently in phase III development with Janssen Biologics to treat **rheumatoid arthritis** and with potential for further GSK development programmes in **giant cell arteritis** and **asthma**.

When intravenous *Benlysta* (belimumab) was approved in 2011 it was the first treatment for **systemic lupus erythematosus (SLE)** in 50 years and has established itself as a key therapy option. New data presented today from a 3rd consecutive successful pivotal study show efficacy in a subcutaneous formulation of **belimumab**, which has potential to help patients manage their disease. Filing for this subcutaneous formulation is planned for Q4 2015/ Q1 2016.

Metabolic

Daprodustat (GSK1278863), a low dose prolyl hydroxylase inhibitor (PHI) in phase II development for the treatment of **anaemia in patients with chronic kidney disease**, would be an oral tablet to potentially replace the injectable current standard of care (rhEPO), and has potential for improved cardiovascular safety. A phase III study in this indication is expected to begin in 2016 and further development programmes are in phase I for the treatment of **diabetic foot ulcer** and in **muscle injury**.

Vaccines

The company's leadership in vaccines R&D is reflected through its short, mid and long term clinical development programmes.

Shingrix (zoster), GSK's candidate **shingles** vaccine, represents a significant advance in vaccination to help prevent shingles, displaying high and potentially lasting efficacy across all age groups from 50 to above 80 years old. Global filings are expected in 2H 2016.

The company has the broadest portfolio of approved and candidate meningococcal meningitis vaccines. This includes its commercialised **Menveo (MenACWY)** tetravalent and **Bexsero (MenB)** vaccines and a full pentavalent combination candidate vaccine, MenABCWY, which may become the optimal option for disease prevention and is currently in phase II development, with phase III planned for 2017.

The development of a vaccine against **Respiratory syncytial virus (RSV)** is a key public health priority. RSV is a common cause of bronchiolitis and pneumonia in infants and can lead to hospitalisation and an enhanced risk of severe asthma. No vaccine is currently available. GSK has two novel approaches to RSV vaccination in phase II clinical development: a **paediatric RSV vaccine** that uses a genetically engineered recombinant chimpanzee adenovirus (CHAd155) – the same vector that is used in GSK's Ebola vaccine candidate; and a recombinant glycoprotein **maternal RSV vaccine** that, given to pregnant women, may provide infants with protective maternally-derived RSV neutralising antibodies.

Maternal immunisation is now a clinically validated strategy to prevent diseases that afflict very young infants in the first weeks of life. In addition to RSV, GSK is further advancing its new maternal immunisation vaccines portfolio with a vaccine candidate to prevent **Group B Strep (GBS)**, a leading



cause of pneumonia, meningitis and sepsis in newborns. Beyond **GBS** and **RSV**, GSK is also considering this approach for the prevention of **pertussis** and **influenza** diseases using its currently available vaccines, thereby building potentially the most comprehensive maternal immunisation vaccines portfolio in development.

Epidemiological studies show an association between some bacterial infections in the lung and exacerbation episodes in COPD patients. GSK is investigating a candidate vaccine concept currently in a phase II clinical proof of concept study, for the prevention of exacerbations in **COPD** patients.

Respiratory

Following the recent launches of *Relvar/Breo Ellipta*, *Anoro Ellipta*, *Arnuity Ellipta* and *Incruse Ellipta*, GSK's commitment to developing the most innovative inhaled respiratory medicines continues through the ongoing phase III development with Theravance of the unique once-daily closed triple combination in the *Ellipta* device of **fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI)** for patients with **chronic obstructive pulmonary disease (COPD)**. Filings are expected in 2016 (EU) and 2018 (USA).

Building on its heritage as a leader in respiratory research, the company today unveiled a next-generation of treatments for respiratory disease, beyond the current approach with inhaled medicines.

While current options for the treatment of mild to moderate **asthma** enable patients to achieve good control of their symptoms, there remains significant unmet need in severe patients. GSK's diverse portfolio of targeted and extended-duration biologicals offer the potential to alter the fundamental course of disease, with **Nucala (mepolizumab)**, its subcutaneous anti-IL-5 mAb, leading the portfolio – a first in class medicine with a strong profile, significantly reducing exacerbations in patients with **severe eosinophilic asthma**. The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion recommending marketing authorisation for **Nucala** on 24 September 2015. An FDA decision is expected on 4 November 2015. Following **Nucala**, other assets in the asthma biologic pipeline include **sirukumab**, which is expected to enter phase II in 2016, a **long-acting anti-IL-5 mAb**, expected to begin phase I/II studies in 2017 and an **inhaled anti-TSLP domain antibody (dAb)** expected to enter the clinic in 2016.

GSK2245035, an intranasal TLR7 agonist in phase II development, is supported by clinical data demonstrating prolonged suppression of allergic response and reaffirms GSK's continued innovation into **allergic asthma**, exploring the potential to achieve disease remission.

By targeting the underlying drivers of disease, two novel assets offer the potential to delay or halt progression of **COPD**, a disease that affects 329 million people worldwide and is expected to become the 3rd leading cause of death by 2030 – **GSK2269557**, an inhaled PI3K δ inhibitor and **danirixin (GSK1325756)**, an oral CXCR2 antagonist are both in phase II development.

Beyond **asthma** and **COPD**, GSK is using its long-term leadership in respiratory R&D to actively explore new diseases, including **idiopathic pulmonary fibrosis** and **acute lung injury**. **GSK2862277**, an inhaled TNFR1 dAb, is already in phase II clinical development for **acute lung injury**.

Rare Diseases

GSK is developing potential breakthrough cell and gene therapies for the treatment of rare diseases. In May 2015 the company filed for European approval of the gene therapy, **GSK2696273**, to treat patients with **adenosine deaminase severe combined immunodeficiency syndrome (ADA-SCID)**. This is the first autologous stem cell gene therapy product to be submitted for marketing application review worldwide, and represents the first in a set of innovative rare disease programmes from GSK's collaboration with the Telethon and Ospedale San Raffaele Institute in Italy. Further gene therapy products are in clinical development in the rare diseases, **metachromatic leukodystrophy (MLD)**, **Wiskott-Aldrich Syndrome (WAS)** and **beta thalassemia**.



Through this development programme and filing, GSK believes it has a leadership position in this novel and demanding area of drug development. The company believes cell and gene therapy has the potential to be an important additional modality for tackling the underlying cause of serious disease.

Two innovative treatments for **amyloidosis**, a complex multi-component disease with a high mortality burden, are in development through GSK collaborations with a biotech partner and academia, demonstrating the strength and value of GSK's research collaborations.

The combination of a small molecule and a monoclonal antibody, **CPHPC + anti-SAP mAb**, directly targets amyloid deposits that cause disease, and is in phase II development through a collaboration with Pentraxin Therapeutics.

GSK2998728, a transthyretin (TTR) RNA-targeted compound, is in phase III development with Isis Pharmaceuticals to treat **familial amyloid polyneuropathy (FAP)** and **wild-type TTR amyloidosis cardiomyopathy (TTRCM)**.

GSK's clinical research and development projects

Today the company has published on its website an updated pipeline chart, which details more than 90 clinical research projects that GSK is conducting. This, along with further details from today's investor event, including copies of all presentations, is available at www.gsk.com.

2016-2020 Outlook

At its Investor Day on 6 May 2015, GSK outlined a series of expectations for its performance over the five year period 2016-2020. This included an expectation that new Pharmaceutical and Vaccine products, launched in the last three years, together with contributions from current pipeline assets, *Nucala* (mepoluzimab) and *Shingrix* (zoster), are expected to generate sales of at least £6 billion per annum by 2020 on a CER basis. GSK expects core EPS to grow at a CAGR of mid-to-high single digits on a CER basis over the five year period 2016-2020. The introduction of a generic alternative to *Advair* in the US was factored into the Group's assessment of its future performance. For more information see: www.gsk.com/en-gb/investors/investor-event.

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