Innovative Medicines

Our Innovative Medicines Division is a world leader in offering innovation-driven, patent-protected medicines to patients and physicians. The Innovative Medicines Division researches, develops, manufactures, distributes and sells patented pharmaceuticals, and is composed of two global business units:

- **Novartis Oncology**
- **Novartis Pharmaceuticals**
  - Cardiovascular, Renal and Metabolism
  - Immunology, Hepatology and Dermatology
  - Ophthalmology
  - Respiratory
  - Neuroscience
  - Established Medicines

Financial Figures and Product Portfolio

The Innovative Medicines Division reported consolidated net sales of USD 18.1 billion in the first half of 2019.

The product portfolio of the Innovative Medicines Division includes more than 60 key marketed products, many of which are leaders in their respective therapeutic areas.

Key Marketed Products

The descriptions of individual product indications are not always country-specific, and may contain information that is outside the approved indications in any one country.

Novartis Oncology

Afinitor/Votubia (everolimus)

is an oral inhibitor of the mTOR pathway. *Afinitor* is approved in more than 120 countries, including the US, EU member states and Japan, for patients with advanced renal cell carcinoma whose disease has progressed during or after treatment with vascular endothelial growth factor-targeted therapy (in the EU), or after failure of treatment with sunitinib or sorafenib (in the US). Additionally, *Afinitor* is approved in more than 110 countries, including

the US, EU member states and Japan, for patients with progressive neuroendocrine tumors (NETs) of pancreatic origin that are unresectable, locally advanced or metastatic; in more than 45 countries, including the US and EU member states, for patients with well-differentiated, nonfunctional NETs of gastrointestinal or lung origin in adults with progressive disease that are unresectable, locally advanced or metastatic; and in 117 countries, in combination with exemestane, for postmenopausal women with advanced hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer after recurrence or progression following treatment with a nonsteroidal aromatase inhibitor (in the EU), or after failure of treatment with letrozole or anastrozole (in the US). All oncology indications are approved under the trade name *Afinitor* in the tablet formulation. Everolimus, under the trade names *Afinitor* in the US and *Votubia* in the EU, is also approved in more than 100 countries to treat patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) who require therapeutic intervention but are not amenable to surgery, and in more than 95 countries to treat patients with TSC who have renal angiomyolipoma who are at risk of complications not requiring immediate surgery. The dispersible tablets for oral suspension formulation are approved in more than 40 countries – including the US (under the trade name *Afinitor Disperz*), EU member states (under the trade name *Votubia*) and Japan (under the trade name *Afinitor*) – for patients with TSC who have SEGA. Dispersible tablets are also approved in more than 30 countries – including EU member states (as *Votubia*) and the US (as *Afinitor* Disperz) – as adjunctive treatment for patients aged two years and older with TSC-associated partial-onset seizures. Everolimus is available under the trade names *Zortress/Certican* for use in transplantation in the US and the EU, respectively. It is exclusively licensed to Abbott and sublicensed to Boston Scientific for use in drug-eluting stents.

Exjade and Jadenu (deferasirox)

is an oral iron chelator approved for the treatment of chronic iron overload due to blood transfusions in patients two years of age and older, and of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia. *Exjade*, a dispersible tablet for oral suspension, was first approved in 2005 and is now approved in more than 100 countries, including the US, EU and Japan. An oral film-coated tablet formulation that can be swallowed or crushed is also approved in countries including the US and Canada (under the tradename *Jadenu* or *Exjade*, depending on the country). Additionally, the formulation has been developed as granules and is approved in the US, EU and Japan.

Gleevec/Glivec (imatinib mesylate/imatinib)

is a kinase inhibitor approved as a targeted therapy for adult and pediatric patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in the chronic phase. It is also approved to treat patients with Ph+ CML in the blast, accelerated or chronic phase after failure with interferon; to treat patients with metastatic and/or unresectable gastrointestinal stromal tumors (GIST) that are KIT (CD117)-positive (KIT+); and as an adjuvant treatment for certain adult patients following resection of KIT+ GIST. First launched in 2001, *Gleevec/Glivec* is approved in approximately 125 countries. It is approved in more than 80 countries as a post-surgery therapy for certain adult patients with KIT+ GIST. Additionally, *Gleevec/Glivec* is approved in the US, EU and Japan to treat Ph+ acute

lymphoblastic leukemia (a rapidly progressive form of leukemia); in the US and EU to treat dermatofibrosarcoma protuberans (a rare solid tumor), hypereosinophilic syndrome, myelodysplastic/myeloproliferative diseases and other rare blood disorders; and in the US (as *Gleevec*) to treat aggressive systemic mastocytosis.

Jakavi (ruxolitinib)

is an oral inhibitor of the JAK1 and JAK2 tyrosine kinases. It is the first JAK inhibitor indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis, and for the treatment of adult patients with polycythemia vera who are resistant to or intolerant to hydroxyurea. *Jakavi* is currently approved in more than 100 countries for patients with myelofibrosis, and in more than 75 countries – including EU member states and Japan – for patients with polycythemia vera. Novartis licensed ruxolitinib from Incyte Corporation for development and commercialization in the indications of oncology, hematology and graft-versus-host disease outside the US. Ruxolitinib, marketed in the US as Jakafi® by Incyte Corporation, is approved by the FDA for the treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis; and for the treatment of patients with polycythemia vera who have had an inadequate response or are intolerant to hydroxyurea. In May 2019, Incyte announced the FDA approved Jakafi® for acute graft-versus-host disease in the US.

Kisqali (ribociclib)

is a cyclin-dependent kinase inhibitor, a class of drugs that helps slow the progression of cancer by inhibiting two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). *Kisqali* is approved as initial endocrine-based therapy for pre-, peri- or postmenopausal women with HR+/HER2- locally advanced or metastatic breast cancer in combination with an aromatase inhibitor, and also indicated for use in combination with fulvestrant as both first- or second-line therapy in postmenopausal women. Also approved is the *Kisqali Femara Co-Pack* (ribociclib tablets and letrozole tablets). *Kisqali* is approved in more than 75 countries around the world, including the United States and European Union member states. Novartis continues to assess *Kisqali* in the MONALEESA-2 and MONALEESA-3 trials in metastatic breast cancer as well as in the adjuvant setting in the NataLEE trial. These trials are evaluating *Kisqali* in multiple endocrine therapy combinations and treatment settings. *Kisqali* was developed by Novartis as part of a drug discovery collaboration with Astex Pharmaceuticals.

Kymriah (tisagenlecleucel)

suspension for intravenous infusion is a CD19-directed genetically modified autologous chimeric antigen receptor T-cell (CAR-T) therapy. *Kymriah* received FDA approval in 2017 for the treatment of patients up to 25 years of age with B?cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse, and in May 2018 for the treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma, including diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. *Kymriah* is not indicated for the treatment of patients with primary central

nervous system lymphoma. *Kymriah* is also approved in countries including Japan, EU member states and Switzerland for the treatment of children and young adults with r/r B-cell ALL, and adult patients with r/r DLBCL.

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Lutathera (USAN: lutetium Lu 177 dotatate/INN: lutetium (177Lu) oxodotreotide)

is a lutetium Lu 177-labeled somatostatin analog peptide. It is a radioligand therapy and is comprised of a targeting molecule that carries a radioactive component. *Lutathera* has received orphan drug designation from the FDA and the EMA. In the US, *Lutathera* is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut and hindgut neuroendocrine tumors, in adults. In Europe, it is indicated for the treatment of unresectable or metastatic, progressive, well-differentiated (G1 and G2), somatostatin receptor-positive GEP-NETs in adults. *Lutathera* was also approved in Canada and Israel in January and May 2019, respectively.

Piqray (alpelisib)

is approved as a treatment specifically for patients with a PIK3CA mutation in HR+/HER2- advanced breast cancer. *Piqray* is a kinase inhibitor approved by the FDA in combination with fulvestrant for the treatment of postmenopausal women, and men, with HR+/HER2-, PIK3CA mutated, advanced or metastatic breast cancer, as detected by an FDA-approved test following progression on or after endocrine-based regimen. Approximately 40% of HR+ advanced breast cancer patients have a mutation in the PIK3CA gene that encodes the alpha isoform of the PI3K enzyme. Presence of this mutation may activate the PI3K pathway and are associated with resistance to endocrine therapy, disease progression and a poor prognosis.

Promacta/Revolade (eltrombopag)

is a once-daily oral thrombopoietin receptor agonist that works by stimulating bone marrow cells to produce platelets. It is the only approved once-daily oral thrombopoietin receptor agonist and is marketed under the brand name *Promacta* in the US and *Revolade* in most countries outside the US. It is approved in more than 90 countries for the treatment of thrombocytopenia in adult patients with chronic immune (idiopathic) thrombocytopenia (ITP)

who have had an inadequate response or are intolerant to other treatments, and in more than 30 countries for the treatment of pediatric patients one year and older with chronic ITP who have had an insufficient response to other treatments. In the US and EU, *Promacta/Revolade* is approved for pediatric patients one year and older with chronic ITP who have had an insufficient response to other treatments. *Promacta/Revolade* is also approved in more than 40 countries for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow them to initiate and maintain interferon-based therapy. It is approved in the US and Japan for aplastic anemia as first-line therapy and in 30 countries for the treatment of patients with severe aplastic anemia (SAA) who had an insufficient response to other treatments (including in the EU for adults with acquired SAA who were either refractory to prior immunosuppressive therapy or heavily pretreated and are unsuitable for hematopoietic stem cell transplant). *Promacta/ Revolade* is marketed under a collaboration agreement between Royalty Pharma and Novartis.

Sandostatin SC (octreotide acetate) for injection and Sandostatin LAR (octreotide acetate) for injectable suspension

are somatostatin analogs indicated for the treatment of patients with acromegaly, a chronic disease caused by over secretion of growth hormone in adults. *Sandostatin* is also indicated for the treatment of patients with certain symptoms associated with carcinoid tumors and other types of gastrointestinal and pancreatic neuroendocrine tumors. Additionally, *Sandostatin* LAR is approved in more than 60 countries (not including the U.S.) for treatment of patients with advanced neuroendocrine tumors of the midgut or unknown primary tumor location. *Sandostatin* SC was first launched in 1988 and is approved in more than 100 countries.

Tafinlar + Mekinist (dabrafenib + trametinib)

is a combination therapy approved for the treatment of patients with stage III unresectable or metastatic melanoma with a BRAF V600 mutation; the adjuvant treatment of patients with stage III melanoma with a BRAF V600 mutation; the treatment of patients with advanced non-small cell lung cancer with a BRAF V600 mutation; and the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer with a BRAF V600 mutation. Usage in the adjuvant treatment of melanoma was approved in the US, EU, Japan and other countries worldwide in 2018, making *Tafinlar* + *Mekinist* the first targeted therapy approved in this setting. The 2018 FDA approval of *Tafinlar* + *Mekinist* for the treatment of anaplastic thyroid cancer represented the first approval of any therapy in the US for this aggressive form of thyroid cancer. *Tafinlar* and *Mekinist* target different kinases within the serine/threonine kinase family – BRAF and MEK1/2, respectively – in the RAS/RAF/MEK/ERK pathway, which is implicated in NSCLC and melanoma, among other cancers. When *Tafinlar* is used with *Mekinist*, the combination has been shown to slow tumor growth more than either drug alone. The combination of *Tafinlar* + *Mekinist* is currently being investigated in an ongoing clinical trial program across a range of tumor types in study centers worldwide. Novartis has worldwide exclusive rights to develop, manufacture, and commercialize trametinib granted by Japan Tobacco Inc.

Tasigna (nilotinib)

is a signal transduction inhibitor of the BCR-ABL tyrosine kinase. Since its launch in 2007, it has been approved in more than 125 countries to treat patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in the chronic and/or accelerated phase who are resistant or intolerant to existing treatment, including *Gleevec/Glivec*, and to treat newly diagnosed patients in the chronic phase. In June 2017, the EC approved the inclusion of treatment-free remission data in the summary of product characteristics for *Tasigna*. In December 2017, the FDA also approved the inclusion of treatment-free remission data in the US label for *Tasigna*. In November 2017, the EC approved *Tasigna* for the treatment of newly diagnosed pediatric patients with Ph+ CML in the chronic phase (CP), and Ph+ CML-CP pediatric patients with resistance or intolerance to prior therapy including imatinib. In March 2018, the FDA approved *Tasigna* for this pediatric indication.

Votrient (pazopanib)

is a tyrosine kinase inhibitor that targets a number of growth factors to limit new blood vessel and tumor growth. *Votrient* is approved in the US for the treatment of patients with advanced renal cell carcinoma (RCC), and in the EU for first-line treatment of adult patients with advanced RCC and for patients who have received prior cytokine therapy for advanced disease. *Votrient* is also approved in the US for the treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy (efficacy in adipocytic STS or gastrointestinal stromal tumors has not been demonstrated), and in the EU for the treatment of adult patients with selective subtypes of advanced STS who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy. *Votrient* is approved in more than 100 countries worldwide for advanced RCC and in more than 90 countries for advanced STS.

Novartis Pharmaceuticals

Cardiovascular, Renal and Metabolism

Entresto (sacubitril/valsartan)

is a first in class angiotensin receptor/neprilysin inhibitor indicated for the treatment of symptomatic chronic heart failure with reduced ejection fraction (HFrEF). It acts to enhance the protective neurohormonal systems of the heart (neprilysin system) while simultaneously suppressing the harmful system (the renin angiotensin aldosterone system, or RAAS). *Entresto* was approved in the US and in the EU in 2015. *Entresto* is now approved in more than 100 countries, and launched in more than 90 countries. Both the European Society of Cardiology heart failure guidelines and the US heart failure guidelines have given a Class I recommendation, the strongest class of recommendation, for the use of sacubitril/valsartan in patients with HFrEF.

Immunology, Hepatology and Dermatology

Cosentyx (secukinumab)

is a fully human monoclonal antibody that selectively inhibits circulating interleukin-17A (IL-17A), a cytokine involved in the pathogenesis of psoriasis, ankylosing spondylitis and psoriatic arthritis. *Cosentyx* is approved in more than 90 countries, including the US, EU member states and Japan, for the treatment of moderate to severe plaque psoriasis. It is approved in more than 80 countries, including the US, EU member states and Japan, for the treatment of adults with ankylosing spondylitis and psoriatic arthritis. *Cosentyx* is also approved in Japan for the treatment of pustular psoriasis and psoriasis vulgaris. In 2017, a label update for *Cosentyx* was approved in the EU based on data showing long-term superiority over Stelara® (ustekinumab) in moderate-to-severe plaque psoriasis, along with efficacy in the treatment of moderate-to-severe scalp psoriasis – one of the most difficult-to-treat forms of the disease. In 2018, the FDA approved a label update for *Cosentyx* to include moderate-to-severe scalp psoriasis, and new evidence that *Cosentyx* inhibits progression of joint structural damage in psoriatic arthritis.

Ilaris (canakinumab)

is a selective, high-affinity fully human monoclonal antibody that inhibits interleukin 1? (IL 1?), a key cytokine in the inflammatory pathway. *Ilaris* is approved in the US, EU member states and Japan to treat systemic juvenile idiopathic arthritis and various auto-inflammatory conditions, such as cryopyrin-associated periodic syndromes and other distinct periodic fevers (also known as hereditary periodic fevers). It is also approved in the EU for adult-onset Still's disease and the symptomatic treatment of refractory acute gouty arthritis. *Ilaris* is approved in one or more indications in approximately 70 countries worldwide.

Ophthalmology

Lucentis (ranibizumab)

is a recombinant humanized high-affinity antibody fragment that binds to vascular endothelial growth factor A (VEGF-A), a key mediator of intraocular neovascularization. *Lucentis* is an anti-VEGF therapy specifically designed for the eye, minimizing systemic exposure. *Lucentis* is approved for six indications: neovascular (wet) age-related macular degeneration (nAMD), visual impairment due to diabetic macular edema (DME), visual impairment due to macular edema secondary to branch retinal vein occlusion (BRVO), visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO), visual impairment due to choroidal neovascularization secondary to pathologic myopia (myopic CNV), and visual impairment due to choroidal neovascularization (CNV) secondary to other pathologies. *Lucentis* is available in more than 110 countries and the *Lucentis* pre-filled syringe has launched in 37 countries. *Lucentis* is licensed from Genentech, and Novartis holds the rights to commercialize the product outside the US. Genentech holds the rights to commercialize *Lucentis* in the US.

Luxturna (voretigene neparvovec)

is a one-time gene therapy to treat children and adults with vision loss due to inherited retinal

dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells. In May 2019, *Luxturna* was granted an ASMR 2 rating (important clinical added value) by the French Health Authority. Eligible patients have started to be treated in France and Germany while reimbursement discussions are ongoing, with further countries expected to follow over the course of 2019 and 2020.

Travatan (travoprost), Travatan Z (travoprost) and Duotrav (travoprost/timolol)

are indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. Single-agent travoprost products (*Travatan*, *Travatan Z*, *Travatan* BAK-Free and *Izba*) are prescribed as first-line agents and are marketed in more than 110 countries, including the US and EU member states. *DuoTrav* is a fixed-dose combination solution for the prostaglandin analog travoprost with the beta-blocker timolol and is approved as a second line treatment in adults for the reduction of IOP in patients with open angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta blockers or prostaglandin analogs. *Duotrav* is currently marketed in more than 105 countries, including EU member states.

Xiidra (lifitegrast ophthalmic solution)

is a prescription eye drop solution approved in the US for the treatment of both signs and symptoms of dry eye disease with a mechanism of action that targets inflammation. *Xiidra* is also approved in multiple other markets including Canada and Australia, and is under regulatory review in a number of additional markets.

Respiratory

Xolair (omalizumab)

is approved for the treatment for moderate-to-severe, or severepersistent allergic asthma in children (age six and older) and adults. It has also been approved as a treatment for chronic spontaneous urticaria (CSU), also known as chronic idiopathic urticaria (CIU) in adults and adolescents aged 12 years and above. It is available in more than 90 countries, including the US since 2003, the EU since 2005, Japan since 2009 and China since 2018. *Xolair* is provided either as lyophilized powder for reconstitution or as liquid formulation in a pre filled syringe. In December 2018, the European Commission approved *Xolair* for self-administration by patients across all indications. A phase III study assessing the efficacy of *Xolair* in cedar pollinosis allergic rhinitis in Japan was recently completed. Its positive results were communicated in 2019 and the new indication has been submitted in Japan. Two other phase III studies (POLYP 1 and POLYP 2) assessing the efficacy of *Xolair* in chronic rhinosinusitis with nasal polyposis were also completed and positive results were announced in June 2019. In addition, *Xolair*'s efficacy in food allergy is currently being assessed in a phase III study led by the US National Institutes of Health. Novartis co-promotes *Xolair* with Genentech in the US and shares a portion of operating income, but does not record US sales. Novartis records all sales of *Xolair* outside the US.

Neuroscience

Aimovig (erenumab)

is designed specifically to block the calcitonin gene-related peptide receptor (CGRP-R), which plays a critical role in migraine. It is the first FDA- and EMA-approved CGRP-targeted therapy for the prevention of migraine in adults. *Aimovig* received US approval in May 2018 and EU approval in July 2018, and is currently available in 29 countries. *Aimovig* is co-commercialized with Amgen in the US, where Amgen records sales, and Novartis has exclusive commercialization rights for all territories excluding the US and Japan.

Gilenya (fingolimod)

is an oral disease-modifying therapy approved to treat relapsing forms of multiple sclerosis (MS). It has a reversible lymphocyte redistribution effect targeting both focal and diffuse central nervous system damage caused by MS. In the US, *Gilenya* is indicated for relapsing forms of MS in patients who are 10 years of age and older. In the EU, *Gilenya* is indicated for adult patients and pediatric patients aged 10 years and older who have high disease activity despite treatment with at least one disease-modifying agent, or who have rapidly evolving severe relapsing-remitting MS. *Gilenya* is currently approved in more than 90 countries around the world and is the third most prescribed MS treatment worldwide. *Gilenya* is licensed from Mitsubishi Tanabe Pharma Corporation.

Mayzent (siponimod)

is an oral, second-generation sphingosine 1-phosphate (S1P) receptor modulator. It binds selectively to the S1P receptor subtypes 1 and 5, and effectively penetrates the central nervous system. *Mayzent* was approved by the FDA in March 2019 for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Results from the Phase III EXPAND study, the first and only study in a representative secondary progressive MS (SPMS) population and evaluating efficacy and safety, demonstrated that *Mayzent* reduced three- and six-month confirmed disability progression against placebo and reduced relapse rates. Additionally, patients showed improvement in cognitive decline measured via Symbol Digit Modalities Test, and reduction in brain volume loss. The full results from the Phase III EXPAND study of *Mayzent* in SPMS were published in The Lancet in March 2018. EXPAND showed that the efficacy of *Mayzent* on disability was largely dissociated of relapse activity in SPMS, a MS stage where deterioration is less dependent on the usual relapse activity. The safety profile of *Mayzent* is similar to other S1P1 receptor modulators, and first dose observation is required only for patients with certain pre-existing cardiovascular conditions.

Zolgensma (onasemnogene abeparvovec-xioi, previously known as AVXS-101)

was approved and launched in the US in the second quarter of 2019 for the treatment of pediatric patients less than two years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene. Administered as a single, one-time intravenous (IV) infusion, *Zolgensma* is the first and only gene therapy approved by the FDA

for the treatment of all types of SMA, including those who are pre-symptomatic at diagnosis. One-time treatment with *Zolgensma* offers an alternative to lifetime chronic therapy for patients with SMA. Novartis is working closely with payers to offer pay-over-time options up to five years and outcomes-based agreements up to five years, as well as providing a patient program to support affordability and access. *Zolgensma* is currently under regulatory review in Europe and in Japan.

Established Medicines

Galvus (vildagliptin) an oral DPP 4 inhibitor, and Eucreas, a single pill combination of vildagliptin and metformin

are indicated for the treatment of type 2 diabetes. The products were first approved in 2007. *Galvus* is currently available in more than 120 countries, including EU member states, Japan (as *Equa*), Latin America and Asia-Pacific. *Eucreas* is currently available in more than 120 countries. It was the first single-pill combination of a DPP-4 inhibitor and metformin approved in Japan (as *EquMet*) and Europe, and is marketed as *Galvus Met* in most non-EU countries. *Galvus* received approval in the EU for expanded use as a second-line monotherapy for type 2 diabetes patients who cannot take metformin. The EU also approved *Galvus* in combination with insulin, with or without metformin, for type 2 diabetes when diet, exercise and a stable dose of insulin do not result in glycemic control, and in triple combination with metformin and a sulfonylurea (SU) for type 2 diabetes when diet and exercise plus dual therapy with vildagliptin and metformin do not provide adequate glycemic control. In 2017, *Galvus* was approved as an add-on to insulin and an add-on to SU treatment.

Diovan (valsartan)

together with *Diovan HCT/Co-Diovan* (valsartan and hydrochlorothiazide), is an angiotensin II receptor blocker (ARB). *Diovan* is the only agent in its class approved to treat all of the following: patients with high blood pressure (including children six to 18 years old), high-risk heart attack survivors and patients with heart failure. First launched in 1996, *Diovan* is available in more than 120 countries. First launched in 1997, *Diovan HCT/Co-Diovan* is available in more than 115 countries.

Exforge (valsartan and amlodipine besylate)

is a single-pill combination of the ARB *Diovan* and the calcium channel blocker (CCB) amlodipine besylate. First approved for the treatment of high blood pressure in Switzerland in 2006, and in the US and EU in 2007, it is now available in more than 120 countries. *Exforge HCT* (valsartan, amlodipine besylate and hydrochlorothiazide) is a single pill combining three widely prescribed high blood pressure treatments: an ARB, a calcium channel blocker and a diuretic (hydrochlorothiazide). *Exforge HCT* was approved in the EU and the US in 2009, and is now available in more than 100 countries.

Neoral (cyclosporine, USP Modified)

is an immunosuppressant to prevent organ rejection following a kidney, liver, or heart transplant. *Neoral* is also approved for use in lung transplant in many countries outside of the US. This micro-emulsion formulation of cyclosporine is also indicated for treating certain autoimmune disorders such as psoriasis and rheumatoid arthritis. First launched in 1995, *Neoral* is marketed in approximately 100 countries.

Zortress/Certican (everolimus)

is an oral inhibitor of the mTOR pathway. *Zortress/Certican* is approved in countries including the US, EU member states and Japan for the prevention of organ rejection in adult patients at low to moderate immunological risk receiving an allogeneic kidney or liver transplant. Additionally, it is approved in EU member states and Japan for adult patients receiving a heart transplant. First approved in July 2003, *Zortress/Certican* is now available in more than 80 countries worldwide and is the only mTOR inhibitor approved for liver and heart transplants.

Key Development Products

ACZ885 (canakinumab)

was first approved as *Ilaris* in 2009 for cryopyrin-associated periodic syndromes. In 2017, data from CANTOS, a Phase III study evaluating quarterly injections of ACZ885 in people with a prior heart attack and inflammatory atherosclerosis, was presented at the European Society of Cardiology Congress and published simultaneously in The New England Journal of Medicine and The Lancet. A review of a blinded, pre-planned lung cancer safety analysis revealed a 77% reduction in lung cancer mortality and a 67% reduction in lung cancer cases in patients treated with 300 mg of ACZ885. As a result of these findings, Novartis initiated the CANOPY clinical program, which includes three Phase III studies of ACZ885, a selective IL-? inhibitor in lung cancer. Data from CANOPY primary analyses are expected to report out in 2021. We received a complete response letter from the FDA in October 2018 regarding our supplemental Biologics License Application for ACZ885 in cardiovascular risk reduction.

Cosentyx (secukinumab)

is a fully human monoclonal antibody that selectively neutralizes interleukin-17A (IL-17A). *Cosentyx* is approved in more than 90 countries, including the US, EU member states and Japan, for the treatment of moderate to severe plaque psoriasis. It is approved in more than 80 countries, including the US and EU member states, for the treatment of adults with ankylosing spondylitis and psoriatic arthritis. *Cosentyx* is in Phase III development in non-radiographic axial spondyloarthritis. We expect results from this trial in 2019. *Cosentyx* is also in a Phase III head-to-head clinical trial in psoriatic arthritis against Humira® (adalimumab), and a Phase III head-to-head clinical trial in ankylosing spondylitis against the Sandoz biosimilar *Hyrimoz* (adalimumab).

ECF843 (recombinant human lubricin)

is in development as a potential treatment to provide symptom relief for ocular surface disease including dry eye disease. A recent Phase II trial found that recombinant human Lubricin demonstrated greater improvement in signs and symptoms of disease compared to a marketed hyaluronic acid based artificial tear solution.

Entresto (sacubitril/valsartan)

is a first-in-class angiotensin receptor/neprilysin inhibitor approved and marketed for the treatment of chronic heart failure with reduced ejection fraction (HFrEF). Novartis is conducting multiple studies of *Entresto* as part of the FortiHFy clinical program. FortiHFy includes studies to provide reinforcing evidence in HFrEF, such as PIONEER-HF and TRANSITION, which both read out in 2018 and confirmed safety as well as superiority of *Entresto* versus enalapril, an angiotensin-converting enzyme inhibitor (ACE inhibitor), in the hospital setting in a wide range of HFrEF patients hemodynamically stabilized after an acute decompensated heart failure event. FortiHFy also includes studies to investigate *Entresto* use in novel indications and expanded patient populations. These include PARAGON-HF and PARALLAX-HF, Phase III trials of *Entresto* in patients with chronic heart failure with preserved ejection fraction (PARAGON-HF study closeout is in progress and results are expected in 2019, while PARALLAX-HF has also completed enrollment with results expected in 2020); PARADISE-MI, a Phase III trial for patients at high risk for heart failure after an acute myocardial infarction (enrollment is ongoing and results are expected in 2020); PARALLEL-HF, a Phase III trial in Japan for patients with HFrEF (study is complete and results are expected in 2019); and PANORAMA- HF, a Phase III trial for pediatric patients with heart failure (enrollment is ongoing and results are expected in 2021).

INC280 (capmatinib)

is an investigational, oral and selective MET inhibitor being evaluated as a potential treatment option for adults with locally advanced or metastatic non-small cell lung cancer that harbors the MET exon-14 skipping mutation. There are currently no approved targeted therapies for this aggressive form of NSLC, which includes about 3-4% of all NSCLC patients. In June 2019, Novartis research collaborators presented primary efficacy results from the GEOMETRY mono-1 clinical trial at the American Society of Clinical Oncology annual meeting. Overall response rate among patients receiving capmatinib was 68% for treatment-naive and 41% for previously treated patients. Median duration of response was also clinically meaningful irrespective of prior line of therapy. Discussions with global health authorities are underway. Both the FDA and Japan's Pharmaceuticals and Medical Devices Agency recognized capmatinib with Orphan Drug status. The FDA recently granted Breakthrough Therapy designation for capmatinib in patients with MET-mutated NSCLC on or after platinum-based chemotherapy. Early stage studies are ongoing investigating capmatinib in combination with other compounds. INC280 is licensed by Novartis from Incyte Corporation. Under the licensing agreement, Incyte granted Novartis exclusive worldwide development and commercialization rights for capmatinib.

KAF156 (ganaplacide)

belongs to a novel class of antimalarial compounds called imidazolopiperazines. It has the potential to clear malaria infection, including resistant strains, and to block the transmission of the malaria parasite. As demonstrated in a Phase IIa proof-of-concept trial, the compound is fast-acting and potent across multiple stages of the parasite's lifecycle, rapidly clearing both Plasmodium falciparum and Plasmodium vivax parasites. In August 2017, Novartis began a Phase IIb study to test multiple dosing combinations and dosing schedules of KAF156 and lumefantrine, including the feasibility of a single dose therapy in adults, adolescents and children.

Kisqali (ribociclib)

is a selective cyclin-dependent kinase inhibitor that inhibits two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). Novartis continues to assess *Kisqali* in the MONALEESA-2 and MONALEESA-3 trials in metastatic breast cancer as well as in the adjuvant setting in the NataLEE trial. These trials are evaluating *Kisqali* in multiple endocrine therapy combinations and treatment settings. *Kisqali* was developed by Novartis as part of a drug discovery collaboration with Astex Pharmaceuticals.

Kymriah (tisagenlecleucel)

is a CD19-directed genetically modified autologous chimeric antigen receptor T-cell (CAR-T) therapy that uses the patient’s own immune system to fight certain types of cancer. CARs are engineered proteins that enable a patient’s own T-cells to seek out specific target proteins present on a patient’s cancerous cells. When these cells are reintroduced into the patient’s blood, they demonstrate the potential to bind to the cancer cells and destroy them. *Kymriah* targets a protein called CD19, which is associated with a number of B-cell malignancies. Novartis is starting pivotal clinical studies of *Kymriah* in relapsed or refractory (r/r) follicular lymphoma, adult r/r acute lymphoblastic leukemia (ALL), first-line high-risk pediatric ALL and diffuse large B-cell lymphoma after first relapse. Novartis and the University of Pennsylvania’s Perelman School of Medicine, which developed *Kymriah*, have a global collaboration to research, develop and commercialize CAR-T therapies, including *Kymriah*, for the investigational treatment of cancers.

LJN452 (tropifexor)

is a potent, non-bile acid, farnesoid X receptor (FXR) agonist that is being developed for the treatment of nonalcoholic steatohepatitis (NASH). LJN452 has been shown to reduce steatosis, inflammation, and fibrosis in animal models, alongside a favorable safety profile in first in-human studies. This oral treatment is designed to break the cycle of fatty build-up in the liver and harness the body’s built-in mechanisms for coping with excess bile acid. Recruitment is underway for the first LJN452 clinical study with histological endpoints in NASH patients.

LNP023

is an investigational oral complement Factor B inhibitor which has the potential to be a first

disease modifying treatment option for several rare renal diseases. In first in-human studies LNP023 demonstrated target engagement alongside a favorable safety profile. Currently LNP023 is under development for IgA and Membranous Nephropathies, and C3 Glomerulopathy. A proof-of-concept study is also ongoing tor LNP023 in paroxysmal nocturnal hemoglobinuria.

177 Lu-PSMA-617

is an investigational radioligand therapy in development for metastatic castration-resistant prostate cancer (mCRPC). ^{177}Lu-PSMA-617 is designed to target the prostate-specific membrane antigen (PSMA), present in most patients with mCRPC, potentially offering a differentiated targeted treatment option. The 5-year survival rate for men with metastatic prostate cancer is approximately 30%. A Phase III study of ^{177}Lu-PSMA-617 is underway, with a readout anticipated in 2020.

OMB157 (ofatumumab)

is a fully human monoclonal antibody administered by subcutaneous injection in development for multiple sclerosis (MS). OMB157 works by binding to the CD20 molecule on the B-cell surface and inducing B-cell depletion. Positive Phase IIb results in MS patients were presented in 2014 and showed significant reduction in the number of new brain lesions in the first 24 weeks after OMB157 administration. Novartis initiated a Phase III program for OMB157 in relapsing MS in August 2016. The program is fully enrolled and is on track for completion in 2019. In addition, a registration study for Japan was initiated in March 2018.

PDR001 (spartalizumab)

is an investigational PD-1 antagonist that may restore the ability of immune cells to induce cell death and fight cancer. PDR001 is being evaluated in the ongoing COMBI-i study, a Phase III trial in combination with *Tafinlar* + *Mekinist* for metastatic BRAF V600+ melanoma, and in combination in other clinical trials across different tumor types. Early efficacy and safety results (in 36 patients) from the COMBI-i were presented in June 2019 at the American Society for Clinical Oncology annual meeting and further clinical trial updates are expected before the end of 2019.

Piqray (alpelisib, formerly BYL719)

is a kinase inhibitor approved by the FDA in combination with fulvestrant for the treatment of postmenopausal women and men with HR+/HER2-, PIK3CA-mutated, advanced or metastatic breast cancer, as detected by an FDA-approved test following progression on or after endocrine-based regimen. Novartis continues to assess patients in SOLAR-1 for secondary endpoints. Novartis is also conducting the Phase II open-label BYLieve trial evaluating *Piqray* plus fulvestrant or letrozole in patients with PIK3CA-mutated HR+/HER2- advanced breast cancer who have progressed on prior therapy. The study investigates *Piqray* in a broader patient population as compared with SOLAR-1, including two cohorts exclusively enrolling patients who have progressed on or after prior CDK4/6 inhibitor therapies. Discussions with health authorities worldwide are ongoing.

QAW039 (fevipiprant)

is a once-daily oral investigational compound that blocks the DP2 receptor, a principal regulator of the asthma inflammatory cascade. By targeting the DP2 pathway, QAW039 is expected to block the asthma inflammatory cascade at multiple points. In asthma, this should result in the reduction of eosinophil activation and migration; in the reduced release of pro-inflammatory cytokines IL-4, IL-5 and IL-13; and in the reduction of smooth muscle cell mass in the airways. Positive Phase II results showed improvement of lung function, reduction of sputum eosinophil levels, and improvement of asthma symptoms. Phase III studies are ongoing, and are assessing the effect of QAW039 on improvement of lung function and reduction of asthma attacks in moderate to severe patients with asthma that is not adequately controlled despite treatment with inhaled therapies. Phase III development started in 2015, with pivotal trial readouts expected in the second half of 2019.

QVM149 (indacaterol acetate, glycopyrronium bromide, mometasone furoate)

is an investigational fixed-dose combination of indacaterol acetate (an inhaled long-acting beta agonist), glycopyrronium bromide (an inhaled long-acting muscarinic receptor antagonist), and mometasone furoate (an inhaled corticosteroid), delivered once-daily via the dose-confirming *Breezhaler* device, a unit dose dry powder inhaler. It is in development as a maintenance treatment for inadequately controlled asthmatic patients. All three mono-components have previously been developed as individual drugs for either chronic obstructive pulmonary disease or asthma. Phase II results presented at ATS 2019 showed that QVM149 met the primary endpoint of improved lung function (peak FEV1) compared to salmeterol/fluticasone propionate after 21 days of treatment. QVM149 is currently undergoing Phase III clinical trials to support registration outside the US. In May 2019, the European Medicines Agency (EMA) accepted our marketing authorization application for regulatory review.

RTH258 (brolucizumab)

is a humanized, specifically engineered single-chain antibody fragment (scFv) advanced that acts as an anti-vascular endothelial growth factor (anti-VEGF) agent. RTH258 is currently in development for wet age-related macular degeneration (wet AMD) and diabetic macular edema. In wet AMD, RTH258 met its primary endpoint of non-inferiority to aflibercept in mean

change in best-corrected visual acuity in Phase III clinical trials, HAWK and HARRIER. Additionally, superiority was shown in three secondary endpoints that are considered key markers of wet AMD disease, central subfield retinal thickness (CST), retinal fluid (intraretinal and subretinal) and disease activity. A majority of patients were maintained on a 12-week treatment schedule immediately following the loading phase to Week 48, also assessed by secondary endpoints in the HAWK and HARRIER trials. Year Two data reaffirmed the Year One findings. We expect to make global regulatory filings for nAMD, starting in the US, the EU and Japan.

SAF312

is a potent, selective inhibitor of cation channel TRPV1. It achieved proof of concept in the treatment of corneal pain following PRK surgery and demonstrated a fast onset of action. Further clinical trials are planned for next year 2020.

SEG101 (crizanlizumab)

is an investigational humanized monoclonal antibody blocking P-selectin-mediated multi-cellular adhesion that is in late-stage development for the prevention of vaso-occlusive crises (VOCs), also known as pain crises, in patients with sickle cell disease (SCD). VOCs are unpredictable and extremely painful events that can lead to serious acute and chronic complications in patients with SCD. In July 2019, the US FDA granted Priority Review designation to crizanlizumab for its application to prevent VOCs in SCD.

TQJ230

is an investigational antisense oligonucleotide that has the potential to be the first medicine to treat high Lipoprotein(a) (Lp(a)). Lp(a) is an independent inherited CV risk factor and 20-30% of patients with established CV disease are believed to be at high risk due to elevated Lp(a). In a Phase IIb trial, TQJ230 demonstrated 80% Lp(a) reduction in patients with CV disease. Based on these results, a Phase III trial to assess the effect of TQJ230 on CV outcomes will be initiated in the first quarter of 2020.

UNR844

is in development as a potential topical treatment for presbyopia. UNR844 is believed to work through the reduction of disulfide bonds, returning the lens in the eye to an elastic state. Presbyopia is a common age-related loss of near-distance vision characterized by a progressive inability to focus on objects nearby, making everyday activities, such as reading, a challenge. In a Phase I/II masked, placebo-controlled proof-of-concept study, 50 patients were treated twice-daily for 90 days with topical UNR844, and 25 patients were treated with placebo. UNR844 showed a statistically significant difference to placebo in binocular distance-corrected near vision by day 8 and throughout the remainder of the treatment period. At day 90, 82% of participants treated with UNR844 had 20/40 binocular near vision (or 0.30 LogMAR) versus 48% in the placebo group. Near vision of 20/40 or better allows for the majority of near-vision tasks in most people. This improvement was sustained at 5 and 7 months after the final dosing with UNR844. UNR844 was acquired by Novartis through the

acquisition of Encore Vision, Inc., in January 2017.

Accordion:

Disclaimer:

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These materials contain forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995 that can generally be identified by words such as “potential,” “expected,” “will,” “planned,” “pipeline,” “outlook,” or similar expressions, or by express or implied discussions regarding potential new products, potential new indications for existing products, potential product launches, or regarding potential future revenues from any such products; or regarding the potential outcome, or financial or other impact on Novartis, of the proposed divestiture of certain portions of our Sandoz Division business in the US; or regarding the potential impact of the share buyback plan; or regarding potential future sales or earnings of the Group or any of its divisions or potential shareholder returns; or by discussions of strategy, plans, expectations or intentions. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. You should not place undue reliance on these statements. In particular, our expectations could be affected by, among other things: global trends toward healthcare cost containment, including ongoing government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; regulatory actions or delays or government regulation generally, including potential regulatory actions or delays with respect to the proposed transactions or the development of the products described in these materials; the potential that the strategic benefits, synergies or opportunities expected from the Alcon and Sandoz transactions may not be realized or may be more difficult or take longer to realize than expected; the inherent uncertainties involved in predicting shareholder returns; the uncertainties inherent in the research and development of new healthcare products, including clinical trial results and additional analysis of existing clinical data; our ability to obtain or maintain proprietary intellectual property protection, including the ultimate extent of the impact on Novartis of the loss of patent protection and exclusivity on key products that commenced in prior years and will continue this year; safety, quality or manufacturing issues; uncertainties regarding actual or potential legal proceedings, including, among others, product liability litigation, disputes and litigation with business partners or business collaborators, government investigations generally, litigation and investigations regarding sales and marketing practices, and intellectual property disputes; uncertainties involved in the development or adoption of potentially transformational technologies and business models; our performance on environmental, social and governance measures; general political, economic and trade conditions, including uncertainties regarding the effects of ongoing instability in various parts of the world; uncertainties regarding future global exchange rates; uncertainties regarding future demand for our products; uncertainties regarding potential significant breaches of data

security or data privacy, or disruptions of our information technology systems; and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in these materials as of this date and does not undertake any obligation to update any forward-looking statements as a result of new information, future events or otherwise.
