MS Portfolio

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Forward-looking statements

This presentation contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to: our strategy and plans; potential of, and expectations for, our commercial business and pipeline programs; capital allocation and investment strategy; clinical development programs, clinical trials, and data readouts and presentations; risks and uncertainties associated with drug development and commercialization; regulatory discussions, submissions, filings, and approvals and the timing thereof; the potential benefits, safety, and efficacy of our and our collaboration partners’ products and investigational therapies; the anticipated benefits and potential of investments, collaborations, and business development activities; and our future financial and operating results. These forward-looking statements may be accompanied by such words as “aim,” “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “plan,” “potential,” “possible,” “prospect,” “will,” “would,” and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including: our dependence on sales from our products; uncertainty of long-term success in developing, licensing, or acquiring other product candidates or additional indications for existing products; failure to compete effectively due to significant product competition in the markets for our products; failure to successfully execute or realize the anticipated benefits of our strategic and growth initiatives; difficulties in obtaining and maintaining adequate coverage, pricing, and reimbursement for our products; our dependence on collaborators, joint venture partners, and other third parties for the development, regulatory approval, and commercialization of products and other aspects of our business, which are outside of our full control; risks associated with current and potential future healthcare reforms; risks related to commercialization of biosimilars; failure to obtain, protect, and enforce our data, intellectual property, and other proprietary rights and the risks and uncertainties relating to intellectual property claims and challenges; the risk that positive results in a clinical trial may not be replicated in subsequent or confirmatory trials or success in early stage clinical trials may not be predictive of results in later stage or large scale clinical trials or trials in other potential indications; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events, restrictions on use with our products, or product liability claims; risks relating to the distribution and sale by third parties of counterfeit or unfit versions of our products; risks relating to the use of social media for our business; risks relating to technology failures or breaches; risks relating to management and key personnel changes, including attracting and retaining key personnel; failure to comply with legal and regulatory requirements; the risks of doing business internationally, including currency exchange rate fluctuations; risks relating to investment in our manufacturing capacity; problems with our manufacturing processes; fluctuations in our effective tax rate; the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations, and financial condition; fluctuations in our operating results; risks related to investment in properties; the market, interest, and credit risks associated with our investment portfolio; risks relating to share repurchase programs; risks relating to access to capital and credit markets; risks related to indebtedness; change in control provisions in certain of our collaboration agreements; environmental risks; and any other risks and uncertainties that are described in other reports we have filed with the U.S. Securities and Exchange Commission (SEC).

These statements are based on our current beliefs and expectations and speak only as of the date of this presentation. We do not undertake any obligation to publicly update any forward-looking statements.
For >40 years, Biogen has been a pioneer in neuroscience and developing transformative treatments for multiple sclerosis.
The Biogen MS pipeline demonstrates leadership in RMS while expanding our footprint in PMS and Neurorepair

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TRANSFORMATIVE THERAPIES FOR RMS
by developing agents with improved benefit risk profile

ADVANCE CARE IN PROGRESSIVE DISEASE
by targeting CNS-compartmentalized immune cells

IMPROVE DISABILITY AND RESTORE FUNCTION
by targeting remyelination and neurorepair

CNS = central nervous system; ID = identification; OP = optimization; R2D = research to development; IM = intra-muscular; LCM = lifecycle management; PMS = progressive multiple sclerosis; RMS = relapsing multiple sclerosis; SC = subcutaneous; IV = intravenous
Multiple Sclerosis – pathophysiology

Overview

**MS involves an immune-mediated process directed against the CNS**

- Aberrant inflammatory response triggered
- Immune system cells attack CNS myelin and nerve fibers
- Demyelination, nerve dysfunction, and axonal loss occurs
- Nerve impulses traveling to / from brain and spinal cord are distorted or interrupted
- Clinically characterized by episodes of acute neurological worsening (relapses) and progressive disability accumulation

CNS = central nervous system
Multiple Sclerosis – current unmet needs

Overview

The MS therapeutic landscape is ever evolving

No single agent can address all the unmet needs of MS treatment.

Current disease modifying therapies have variable and limited ability to slow the progression of disease. They differ in terms of how they are administered as well as their respective mode of action, efficacy and safety profiles; with more efficacious treatments tending to have a trade-off with safety profile.

Halting and reversing disability progression in MS remains elusive.

DMT = disease modifying therapy
Approaches to address the remaining unmet needs in MS

Current State

Clinical Development Pipeline

Relapsing MS DMTs with more favorable benefit-risk profiles and lower patient burden

Transform care in progressive MS; improve disability and restore functions

Capabilities

Advance the understanding of MS and improve patient outcomes

How Biogen Is Addressing Issue

Relapsing MS DMTs with more favorable benefit-risk profiles and lower patient burden

Target CNS compartmentalised inflammation, a potential key driver of progressive biology in MS; and develop remyelination/neuroreparative therapies

Enhance digital capabilities, with active integration into clinical trials. Advance Machine Learning/Artificial Intelligence to enable lesion characterisation, lesion development prediction and MS subtyping

DMT = disease modifying therapy
Biogen has a comprehensive BTK inhibitor program

Inflammation is a pathological driver at all stages of MS

Pathogenic B cells contribute to multiple sclerosis and BTK inhibitors have the potential to stop them from maturing

BTK = Bruton tyrosine kinase
Biogen has a comprehensive BTK inhibitor program with both peripheral and centrally acting agents.

BIIB091 is a reversible, highly selective, peripheral BTKi to treat acute inflammation. BIIB091 provides the unique opportunity to be studied as combinatory therapeutic option.

Orelabrutinib is a covalent, CNS penetrant BTKi with the potential of high efficacy providing the unique opportunity to address progressive biology by targeting CNS B cells, myeloid cells including microglia in addition to peripheral effects.

BTKi = BTK inhibitor; BCR = B cell receptor; FCR = Fc receptor; BBB = blood brain barrier
Orelabrutinib, our latest acquisition in MS, is a Phase 2 BTKi clinical stage asset, which accelerates our efforts in this class

Small molecule CNS-penetrant Bruton’s tyrosine kinase inhibitor (BTKi) for the potential treatment of MS

**License and collaboration agreement for small molecule CNS-penetrant BTKi**

- Orelabrutinib is a covalent BTKi developed in China for B-cell malignancies
- Orelabrutinib – Phase 2 ongoing in relapsing and remitting MS (RRMS)
- Developed by InnoCare Pharma, commercial-stage biopharmaceutical company

**Orelabrutinib is a clinically validated molecule**

- Orelabrutinib has received regulatory approval in China for several oncology indications
- Received FDA breakthrough designation June 2021 for relapsed/refractory mantle cell lymphoma
- Phase 2 data from other BTKi programs show potential benefit in RMS patients

Zhang et al. AACR 2020 Virtual Meeting/April 27, 2020
Beijing InnoCare Pharma Tech. Co. Ltd., Beijing, China

Potentially best-in-class BTKi, for both RMS and PMS, pending clinical trial assessment
Transformative therapies for RMS: potential best-in class anti-VLA4

- Well-established mechanism of action in RMS, building on our extensive experience with Tysabri
  - BIIB107 binds to a similar binding site in integrin α4 as Tysabri with decreased FcR effector function
- Reduced PK/PD variability due to stabilized hinge and higher affinity to integrin α4 as compared to Tysabri
- Optimized, fixed-interval dosing that is weight-based to personalize treatment
- SC and IV are currently being tested in Phase 1
- Opportunity to identify optimal dose and dosing interval that preserves Tysabri-like efficacy but enables PML risk reduction by leveraging Tysabri EID learnings to maximize safety benefits

BIIB107 (HP1/2) demonstrated dose dependent PK and a more sustained receptor occupancy (RO) than Tysabri after single IV dose in cynomolgus monkeys (Biogen, data on file)
Work to develop potentially first-in-class remyelination/neuroreparative therapies for MS to improve disability and reduce worsening

Target remyelination, repair and improve function for all MS subtypes

**Our Research Focus**
- Repair of Grey and White Matter Lesions
  - Neuronal cell death
  - Synaptic loss
  - Demyelination
  - Remyelination
  - Neuroprotection
  - Restore environment

**Our Development Focus**
- Learn from opicinumab data to optimize CDP and remyelination endpoints
- Identification of Patient populations amenable to repair
- Translate the learnings into future remyelination development plans including potentially BIIB061

**Invest in Capabilities and External Innovation**
- Research
  - Invest to understand molecular basis of MS progression via genetics, Omics and imaging
  - Model translatability
- Development
  - Optimized study design
  - Sensitive biomarkers for remyelination
- External Innovation
  - Identify new assets to enhance our pipeline
  - ML/AI prediction of remyelination
Biogen’s commitment to the MS community

Scientific expertise focused on bringing new and tailored options to MS patients

Committed to inform optimal MS management via collaborative approaches with external community

Biogen Scientific Leadership in MS is demonstrated through the current assets under clinical development geared toward addressing significant unmet needs, as well as the life cycle management activities for the approved RMS products in its portfolio.

Beyond treatment, Biogen is committed to personalizing medicine, generating robust evidence and continuing to deliver innovation that may change the way MS is managed. Through a variety of external collaboration agreements e.g. International Progressive MS Alliance (IPMSA), TheraPanacea, Genetech/Roche, MS PATHS, and through continued working with clinicians and researchers, Biogen aims to elevate the care of MS.
MS PATHS is a unique real world data collection tool

- Biobanking
- Imaging
- Enhanced Clinical Performance Outcome Measures/Application of Machine Learning Techniques

- Industry partnership to sequence MS PATHS
- Traits: Imaging, Clinical, Digital, PRO
- Biomarkers: sNfL, Lipids, Metabolites
- Disease severity & progression
- SNP & WGS

>7800 patients with a genetic sample

>15,000 Biobank Samples Collected with >52% of patients having at least 2 biobank data points

>22,000 MRI Assessments collected with 66% of patients having at least 2 MRI data points

>207,000 EMR files

MS PATHS Bolsters our efforts in real world predictive analytics and reverse translational research

EMR = electronic medical records; MRI = magnetic resonance imaging; PRO = patient reported outcome; sNfL = serum neurofilament light
Biogen continues to pioneer in neuroscience and developing transformative treatments for multiple sclerosis

There remains significant unmet medical need in the field of MS for treatments:
- with improved benefit / risk profiles and lower treatment burden
- that can halt disability progression
- that can restore neurological function

We remain steadfast in our vision to be the unrivaled and most valued leader in MS by transforming the care of people living with this debilitating disease at every step of their journey