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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.
Our Approach to Modalities
Biogen pursues the best modality for patients

Modalities – Design and Innovation
Small Molecules, Biologics, Oligonucleotides
Internal/External Innovation

Leveraging Synergies Across Modalities
Tissue-enhanced delivery of drug candidates

Providing Therapeutic Options to Patients
Multiple modalities for key targets
As a leader in neuroscience, Biogen pursues the best identified modality, a distinct approach that may potentially offer a competitive advantage.

The modality landscape to treat a wide range of diseases is evolving.

Key Considerations: Disease severity, available therapies, route of administration.

- **Sporadic Diseases**
  - Larger Patient Population
  - Small Molecules
  - Biologics
  - Protein Targets

- **Genetic Disorders**
  - Smaller Patient Population
  - Antisense Oligonucleotides
  - siRNA
  - Gene Therapy
  - Nucleic Acid Targets

siRNA = small interfering RNA
Biotherapeutics and Medicinal Sciences, together with key collaborators, delivers high-quality, differentiated drug candidates that may become future transformative medicines.

We enable potential new therapeutics through structural biology, chemical biology, assay science, and drug disposition and pharmacokinetics/pharmacodynamics (PK/PD) modeling studies.

- Small Molecules
- Oligonucleotides
- Therapeutic Proteins
- Gene Therapy

We are modality-'agnostic’
We are leveraging synergies across modalities
We are positioned to offer multiple treatment options to patients
Our preclinical portfolio reflects a multi-modality approach

Distribution represents modalities for preclinical programs across our disease areas

Refer to Junghae Suh’s presentation for a discussion on Gene Therapy
Small Molecules: Our property-based design has led to the successful invention of drug candidates that advance to the clinic.

Medicinal chemistry design practices result in favorable brain penetration, survival to the clinic, and low-dose projections.

CNS MPO: Central Nervous System Multi-Parameter Optimization; NOAEL = No Adverse Effect Level in Preclinical Safety Studies; TO = Target Occupancy
Small Molecules: Our property-based design drives novel CNS Positron Emission Tomography (PET) tracer discovery, increasing confidence in clinical dose selection

- 366 Compounds
  - CNS penetrant & permeable
  - 125 Compounds
    - Favorable chemical properties
    - 117 Compounds
      - Low non-specific binding
      - 111 Compounds
        - High potency
        - 8 Compounds

2 – 3 compounds were radiolabeled to identify a successful PET ligand.
Small Molecules: Expanding our target space and exploiting new modalities with collaborations

**Splice modulation with small molecules** provides an opportunity to closely mimic the pharmacology of oligonucleotides and promises to expand the list of genetic targets amenable to small molecule drug discovery.

**Protein degraders** are catalytic in nature and may allow for less frequent dosing based on target protein half-life; this is an attractive approach to protein degradation in neuroscience diseases.

![Graphic taken from C4T website](https://example.com/graphic)

SMA = Spinal Muscular Atrophy
Protein Degraders: Novel degrader achieves brain penetration and reduces target in the CNS after oral dosing

Degrader Properties

- DC50 = 6 nM
- Emax = 27%
- Total Brain/Plasma Ratio* = 0.7
- Oral Bioavailability* = 41%

DC50: Concentration that leads to 50% degradation; Emax: Maximum effect/Percentage of protein remaining; *Animal Species = rat
Biologics: Biogen has built an antibody discovery platform to generate multiple antibody options and help identify the best molecule for development of our programs.

- **Naïve library** (synthetically generated)
- **In vitro display platform**
- **In vivo derived library**

**Engineering**

- Rabbit
- Mouse
- Alpaca

**Deep interrogation of natural repertoires**

- **Antibodies**
- **Bispecifics**
- **Camelid VHHs**
- **Fusion Proteins**
- **Conjugates**
Biologics: BIIB059 is a home-grown antibody that has achieved proof of concept and has initiated Phase 3 in Lupus

- BIIB059 prevents the production of type-I interferons and other cytokines from plasmacytoid dendritic cells
- Selected from diverse panel of murine antibodies based on potency and developability
- Humanized antibody variable and constant domain sequences were engineered for optimal expression levels, stability, and potency

Fab = Fragment antigen binding

Crystal structure of BIIB059 Fab
Biologics: Strengthening our tissue-enhanced delivery efforts to increase exposure and potential efficacy of molecules in muscle and brain

Together with collaborators, we have an opportunity to exploit synergies across modalities such as enhanced delivery to tissues of interest for high-value targets.

**Antibody-Antisense Oligonucleotide (ASO) conjugate enhances delivery to muscle**

**Novel BBB shuttle antibody (Ab) for brain delivery**

Data generated using a Biogen proprietary antibody

TfR = Transferrin Receptor
Oligonucleotides: We continue to build our capabilities and pipeline in oligonucleotides with strong collaborations

Initial approvals for antisense oligonucleotide (ASO) and siRNA medicines have been primarily for genetic disorders such as spinal muscular atrophy.

Biogen is advancing ASOs in the clinic, aiming to broaden the impact of these modalities for sporadic indications (BIIB080 for Alzheimer’s disease).

Biogen is also progressing novel branched or divalent siRNA for Huntington’s disease.
Multiple modalities may enable Biogen to address patient needs by potentially providing future treatment options

Key areas can be de-risked through parallel approaches that offer patients complementary treatment and dosing options

- **Small molecules**
- **Recombinant proteins**
- **Antibodies**
- **Antisense oligonucleotides/siRNA**
- **Gene therapy**

Targets with >1 potential modality explored in clinic and/or preclinically:

- **A-beta**
- **Tau**
- **LRRK2**

**Neurodegeneration**

- **SMN**
- **SOD1**
- **C9orf72**

**Neuromuscular**

Multiple modalities can target different aspects of target biology; e.g., anti-Tau antibody vs. Tau antisense oligonucleotide or AAV-Tau

AAV = adeno-associated virus; LRRK2 = leucine rich repeat kinase 2; SMN = survival motor neuron; SOD1 = superoxide dismutase type 1
As a leader in neuroscience, Biogen has a unique approach to modalities.

We are truly modality-agnostic.

By driving a best modality approach, we have expanded target space in neuroscience.

By embracing multiple modalities, we are positioned to exploit synergies such as tissue-enhanced deliveries.

By embracing multiple modalities, we are positioned to offer multiple treatment options to patients.