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; 2021 financial guidance. 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.
Biomarkers are leading a transformation in neuroscience

<table>
<thead>
<tr>
<th>Diagnosis driven by constellation of clinical signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia</td>
</tr>
</tbody>
</table>

Molecular pathology and CSF analytes classify neurodegenerative diseases

<table>
<thead>
<tr>
<th>AD</th>
<th>PD-dementia</th>
<th>PSP</th>
<th>PD</th>
<th>MSA</th>
<th>DLB</th>
<th>FTLD</th>
<th>ALS</th>
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</thead>
<tbody>
<tr>
<td>β-amyloid</td>
<td>tau</td>
<td>α-Synuclein</td>
<td>TDP-43</td>
<td>SOD1</td>
<td></td>
<td></td>
<td></td>
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</table>

Molecular imaging can visualize molecular pathology

<table>
<thead>
<tr>
<th>β-amyloid</th>
<th>tau</th>
<th>α-Synuclein</th>
<th>TDP-43</th>
<th>SOD1</th>
</tr>
</thead>
</table>

CSF = Cerebrospinal fluid; AD = Alzheimer's disease; ALS = Amyotrophic lateral sclerosis; DLB = Dementia with Lewy bodies; FTLD = Fronto temporal dementia; MSA = multisystem atrophy; PD = Parkinson's disease; PSP = Progressive supranuclear palsy; SOD1 = superoxide dismutase 1; TDP-43 = TAR DNA binding protein 43; Hargreaves et al. Clin Pharm & Therapeutics 2015
New biomarker technologies may overcome challenges unique to the brain

Ultrasensitive Immunoassay

Novel Mass Spectrometry

Imaging

Multiplexed Proteomics

- Spatial resolution
- Temporal resolution
- Dosimetry

Protein Mixture

Affinity Enrichment

Lower Background Signal = Higher Sensitivity

Intensity

m/z

Peptide 1 ions
Using biomarkers to answer key questions may accelerate development milestones

- **Patient selection**
  - Who are the right patients? When to treat?
  - Patient selection based on expression of the target, specific pathophysiological features, and/or gene carrier status

- **Target engagement**
  - At what doses does the drug engage the target? For how long?
  - Define optimal dosing regimens for early efficacy studies or early termination

- **Pharmacodynamic response**
  - Does the drug modulate relevant biological pathways?
  - Confirm mechanism of action or downstream pathway modulation

- **Disease Pathophysiology**
  - Does the drug slow or reverse a defining pathology of the disease?
  - Provide biological evidence of the potential to alter disease progression

**A single biomarker can answer more than one question**
At Biogen, Biomarker strategies are developed for each program during Discovery

*Early investment ensures novel measurement tools are available in time for Phase 1*

Novel biofluid assays and imaging probes typically take at least two years to discover and develop for use in human drug trials. Some require 10+ years to establish sensitivity to disease severity and progression.

ELISA = enzyme-linked immunosorbent assay; PET = positron emission tomography
Examples of new biomarker measurements poised to accelerate Biogen’s pipeline
A seeding assay to detect α-synuclein aggregates in Parkinson’s

Current approach to Parkinson’s diagnosis

α-Synuclein Protein Misfolding Cyclic Amplification (PMCA) Assay

α-Synuclein PMCA reliably identifies Parkinson’s patients

Post-hoc analysis of Cimpanemab SPARK @Baseline with PMCA

α-syn = α-synuclein; DaTscan = dopamine transporter imaging; MSA = multiple system atrophy; PD = Parkinson’s disease; PMCA = Protein Misfolding Cyclic Amplification assay

Samples of CSF (40 μl) from patients with PD (PD), patients with MSA or healthy control individuals (HC) were subjected to α-syn-PMCA and the extent of aggregation was monitored by ThT fluorescence. Adapted from Shahnawaz et al Nature 2020.

**[18F]MK6240 Tau PET**

*A critical tool for accelerating drug development in Alzheimer’s disease*

**[18F]MK6240 human in vitro pharmacology**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>NFT selective block</th>
<th>Self-block</th>
<th>IHC (ground truth)</th>
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<tbody>
<tr>
<td>MK-6240</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>AV-1451</td>
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**[18F]MK6240 Primate in vivo pharmacology**

<table>
<thead>
<tr>
<th>[18F]MK-6240</th>
<th>[18F]MK-6240 + 1mg/kg MK6240</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
</tr>
</tbody>
</table>

**[18F]MK6240 human in vivo pharmacology**

- **SUVR Test/Retest**
- **SUVR time stability**

**AD**

<table>
<thead>
<tr>
<th>Test</th>
<th>Retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE 9</td>
<td>MMSE 22</td>
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<tr>
<td>3.2</td>
<td>3.2</td>
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</table>

**HV**

<table>
<thead>
<tr>
<th>Test</th>
<th>Retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE 9</td>
<td>MMSE 22</td>
</tr>
<tr>
<td>2.8</td>
<td>2.8</td>
</tr>
</tbody>
</table>

IHC = Immunohistochemistry; HV = healthy volunteer; MMSE = Mini Mental State Exam; NFT = neurofibrillary tangle; SUVR = standardized uptake value ratio; Hostetler et al., J Nucl Med 2016; Salinas et al., J Blood Flow & Metab 2020.
[¹⁸F]MK6240 Clinical characterization in Alzheimer’s disease

CTx = Cortex; MMSE = Mini Mental State Exam; Sur, Soc Nuc Med & Mol Imaging Meeting, 2017; Biogen internal data.
**[¹⁸F]MK6240 Tau PET**

*First evidence of tau pathology modification using PET imaging*

**EMERGE and ENGAGE:**

Aducanumab reduced tau pathophysiology as measured by [¹⁸F]MK6240 PET

![Bar charts showing adjusted mean change from baseline SUVR (SE) for Medial temporal composite, Temporal composite, and Frontal composite across Placebo (n=12), Low dose (n=14), and High dose (n=11) groups.](chart)

Pooled tau PET analysis population. *p<0.05; ***p<0.0001 compared with placebo (nominal). SE = standard error;
Higher cumulative dose of aducanumab was associated with a greater reduction in [18F]MK6240 tau PET.

Baseline and follow-up [18F]MK6240 tau PET images from representative patients in placebo and aducanumab 10mg/kg groups.

Higher cumulative dose of aducanumab was associated with a greater reduction in [18F]MK6240 tau PET.
Accelerating ALS development with blood tests for Neurofilament

*If you can’t measure it, you can’t use it*

<table>
<thead>
<tr>
<th>N = 33</th>
<th>ELISA</th>
<th>ECL-Assay</th>
<th>Simoa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (pg/mL)</td>
<td>78</td>
<td>15.6</td>
<td>0.62</td>
</tr>
<tr>
<td>% detected</td>
<td>45%</td>
<td>39%</td>
<td>100%</td>
</tr>
<tr>
<td>Serum pg/mL (range)</td>
<td>78 - 252</td>
<td>15.6 - 62.5</td>
<td>12.5 - 45.5</td>
</tr>
</tbody>
</table>

Plasma NfL is elevated in ALS

NfL = neurofilament light; ECL: Electrochemiluminescence; ALS = amyotrophic lateral sclerosis

Biogen internal data

Gaiottino et al, PLoS One 2013
Accelerating ALS development with blood tests for Neurofilament

Implementing a sensitive, standardized assay on a routine, globally available platform

Blood NfL implementation on Siemens Routine ImmunoAssay platforms

Relationship between ALS patient blood samples on Quanterix Simoa and Siemens Atellica

Assay Linearity

Relationship between ALS patient blood samples

Within lab CV

LLQ = 1.39 pg/ml

Biogen internal data

pNfL = plasma neurofilament; Biogen internal data
Accelerating ALS development with blood tests for Neurofilament

*From biological evidence of potential to slow progression, to pre-symptomatic patient selection*

Blood NfL from Phase 1/2 study of tofersen in SOD1-ALS generated using SIMOA and Siemens assays show comparable results

Elevations in NF observed prior to clinical evidence of ALS in participants with rapidly progressive SOD1

pNfL = plasma neurofilament; Biogen internal data
Blood-based biomarkers potentially on the horizon for Alzheimer’s

Patient selection

Pharmacodynamic response

Plasma pTau-217

Plasma pTau-231

Plasma pTau-181

Bateman et al, Nat Med 2020

Ashton et al, Acta Neurop 2021

Janelidze et al, Nat Med 2020

P-tau = phosphorylated tau; CU = cognitively unimpaired; MCI = mild cognitively impaired; PSP = progressive supranuclear palsy; CBD = cortico basal degeneration; bvFTD = behavioral variant frontotemporal dementia; VaD = vascular dementia; AUC = area under curve.
Neurofilament elevations precede symptoms thus enabling a pre-symptomatic trial in SOD1-ALS

BIIB080 The first clinical demonstration of an antisense-mediated suppression of CSF tau protein in patients with Alzheimer’s disease

Dose dependent decreases in PD measures after tofersen treatment in SOD1-ALS

FDA grants accelerated approval for ADUHELM™ as the first and only Alzheimer’s disease treatment to address a defining pathology of the disease

Using biomarkers to answer key questions may accelerate development milestones

Who are the right patients? When to treat?

At what doses does the drug engage the target? For how long?

Does the drug modulate relevant biological pathways?

Does the drug slow or reverse a defining pathology of the disease?