Biogen and Ionis Pharmaceuticals Expanded Strategic Collaboration

Antisense Oligonucleotide Drug Discovery Platform for Neuroscience

April 20, 2018

Forward-Looking Statements

This presentation contains forward-looking statements, including statements relating to: our strategy and plans; the potential benefits and results that may be achieved through Biogen's collaboration agreement with Ionis Pharmaceuticals Inc. (Ionis); risks and uncertainties associated with drug development and commercialization; the potential of Biogen's commercial business and pipeline programs, including SPINRAZA and potential novel antisense oligonucleotides (ASOs) drug candidates for a broad range of neurological disease areas, including Alzheimer's disease and dementia, neuromuscular diseases, movement disorders, ophthalmology, diseases of the inner ear, and neuropsychiatry; the anticipated completion and timing of the transaction; capital allocation and investment strategy; clinical trials and data readouts and presentations; the potential benefits, safety, and efficacy of SPINRAZA, BIIB080, and/or BIIB067; and uncertainty of success in commercialization of SPINRAZA, which may be impacted by, among other things, the level of preparedness of healthcare providers to treat patients, difficulties in obtaining or changes in the availability of reimbursement for SPINRAZA, the effectiveness of sales and marketing efforts, problems with the manufacturing process for SPINRAZA, the occurrence of adverse safety events, and/or unexpected concerns that may arise from additional data or analysis. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "will," 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 without limitation: risks that the transaction will be completed in a timely manner or at all; uncertainty as to whether the anticipated benefits and potential of Biogen's collaboration agreement with Ionis can be achieved; risks of unexpected costs or delays; uncertainty of success in the development and potential commercialization of novel ASO drug candidates for a broad range of neurological disease areas, including Alzheimer's disease and dementia, neuromuscular diseases, movement disorders, ophthalmology, diseases of the inner ear, and neuropsychiatry, which may be impacted by, among other things, the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of these drug candidates; Biogen and Ionis may encounter other unexpected hurdles which may be impacted by, among other things, the occurrence of adverse safety events, failure to obtain regulatory approvals in certain jurisdictions or failure to protect intellectual property and other proprietary rights; product liability claims; or third party collaboration risks. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission.

These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this presentation. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments, or otherwise.

Note regarding trademark: SPINRAZA® is a registered trademark of Biogen.

Agenda

Introduction	**Matt Calistri** VP, Investor Relations
Collaboration Overview & Scientific Rationale	**Michael Ehlers, M.D., Ph.D.** EVP, Research & Development
Deal Terms & Strategic Outlook	**Jeffrey Capello** EVP, Chief Financial Officer
Q&A	

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Collaboration Overview & Scientific Rationale

Michael Ehlers, M.D., Ph.D.
EVP, Research & Development

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Collaboration Highlights

1. We believe that **antisense oligonucleotide** therapeutics will provide **highly efficacious** treatment solutions for **numerous neurological diseases**, and this collaboration will position Biogen to be a clearly differentiated leader in this space

2. We believe this collaboration has the potential to create an **innovation engine** by uniting the long standing, **industry-leading expertise** and extensive intellectual property portfolio of Ionis in ASOs, with the considerable **neuroscience** translational and development capabilities of Biogen

3. We think ASOs are the single **most advanced genetically based approach** for targeting neurological diseases, which we believe could enable **accelerated development timelines**, give access to classically 'undruggable' targets, and **complement future gene therapy efforts**

4. This collaboration **will differentiate Biogen** by providing **exclusive rights to Ionis' ASO technology across a broad range of neuroscience**

5. Capital efficient deal structure that we believe leaves **substantial capacity** for **future business development** and **M&A activity,** as well as **share repurchases**

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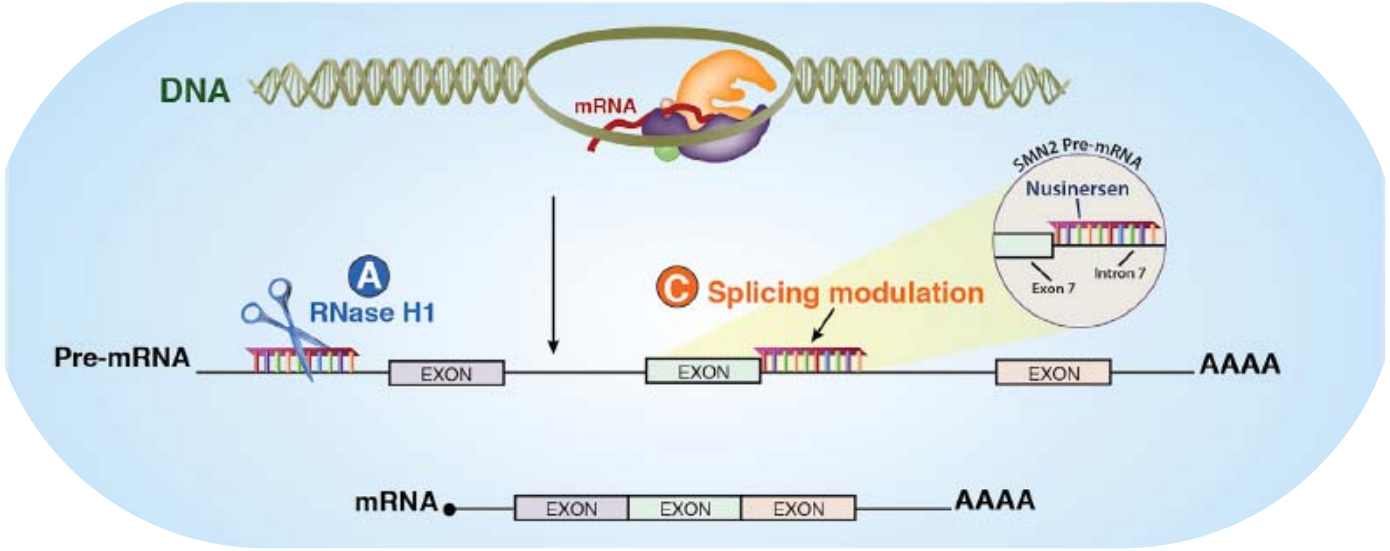
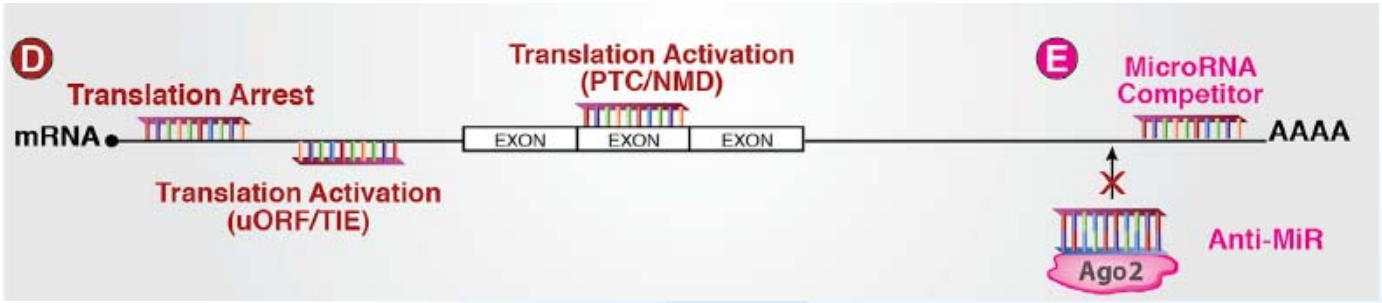
Expanding Therapeutic Options for ASOs May Enable Targeting of Multiple Neurological Diseases



Current ASO strategies – RNase H1 degradation and splicing

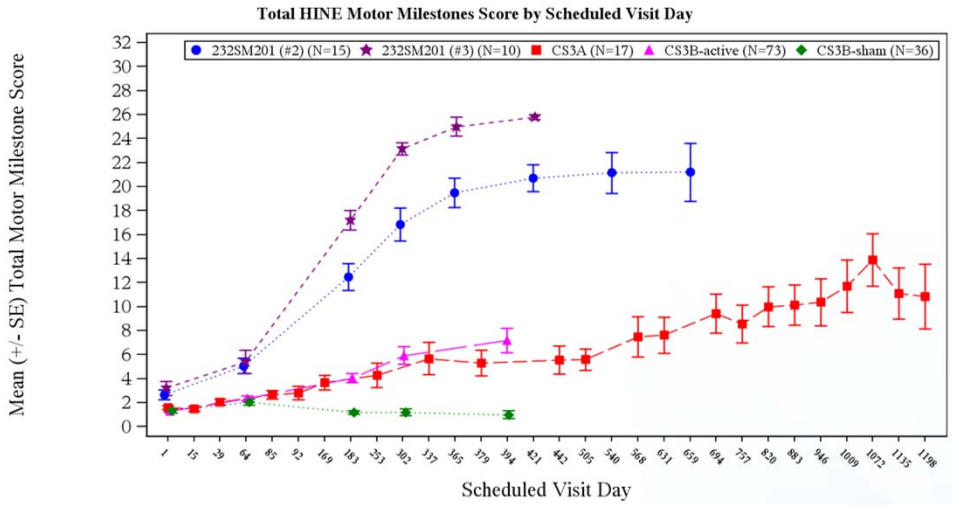


Emerging ASO strategies – modulation of RNA through new mechanisms

Crooke ST et al, Cell Reports, 2018

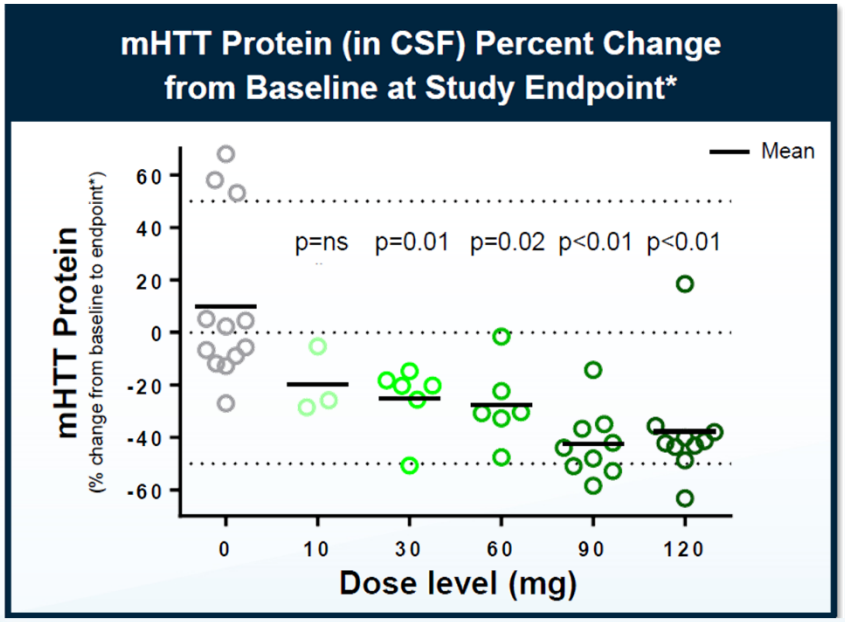
ASOs May Represent a Transformative Therapeutic Modality for Neurological Disease

SPINRAZA, approved for the treatment of spinal muscular atrophy



Darryl De Vito, Muscular Dystrophy Clinical Conference 2018

Phase 2 results for Ionis HTTRx programs support target engagement in Huntington's disease



Sarah Tabrizi, 13th Annual CHDI Conference; Licensed to Roche

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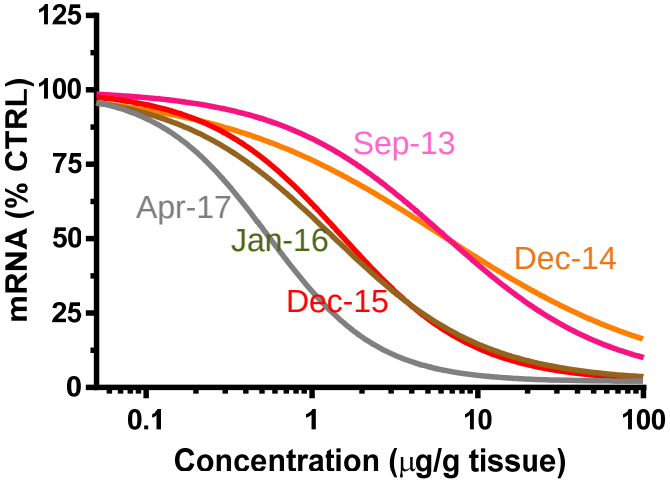
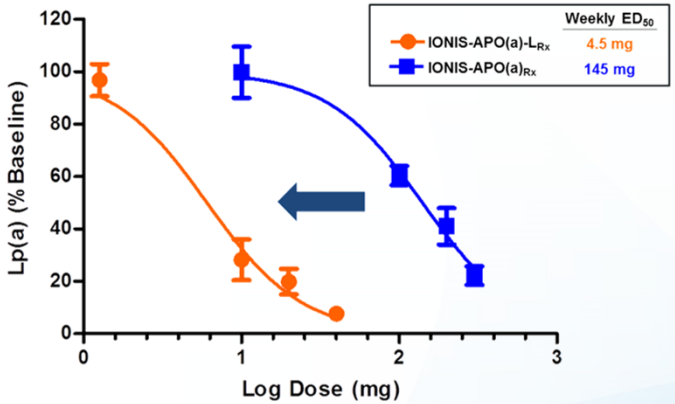
IONIS PHARMACEUTICALS

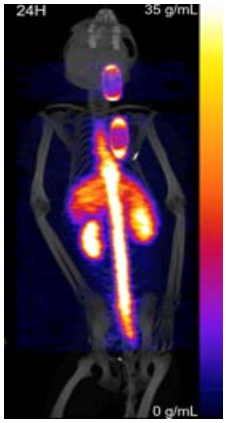
Continuous Improvement of ASO Technology



Improvement in RNase H ASO over Biogen Ionis collaboration[1]



Improvement in ASO dose response with advances in ASO chemistry[3]



New imaging to evaluate distribution across species[2]

Regimen	Non-LICA IONIS-APO(a)$_{Rx}$	LICA IONIS-APO(a)-L$_{Rx}$
Weekly Dose ED$_{50}$	145 mg (1.0-1.5 mL)	4.5 mg (0.05 mL)

Ligand conjugation of ASOs increases potency of ASOs in delivery to human liver[3]

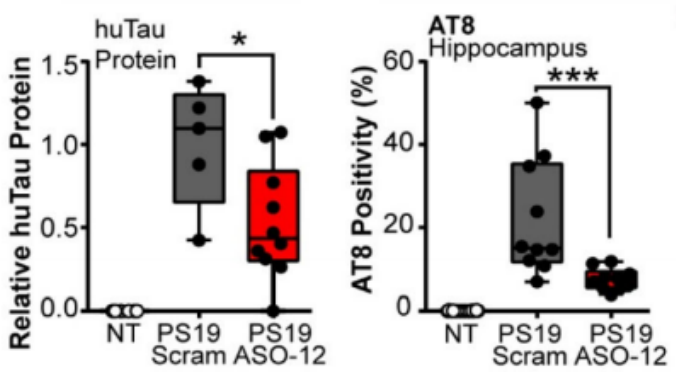
1. Ionis unpublished data; 2. Jenna M et al., American Academy of Neurology conference, 2016; 3. Viney NJ et al., Lancet 2016.

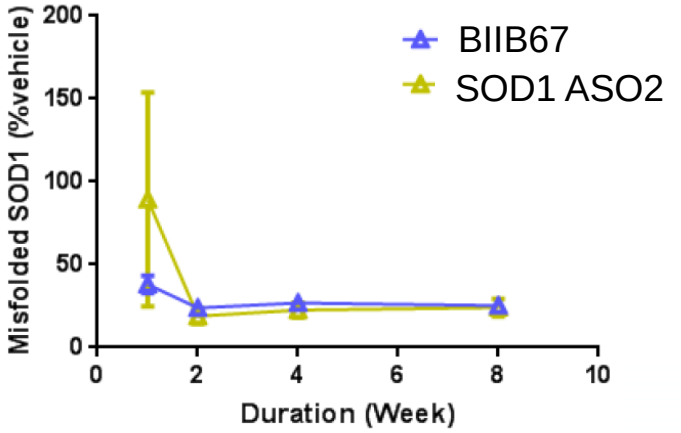
Tau and SOD1 ASO Program Preclinical Support

Tau (Target for Alzheimer's disease)

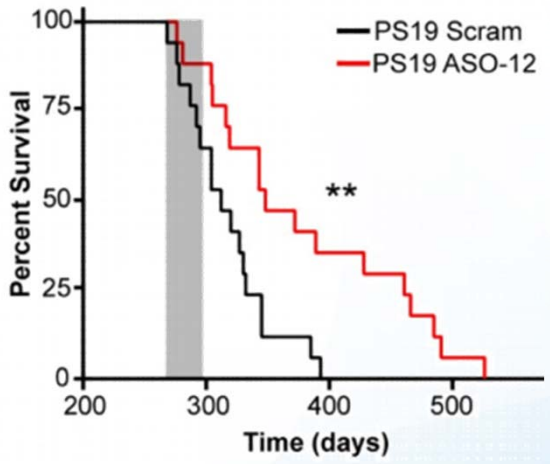
SOD1 (Target for SOD1 ALS)

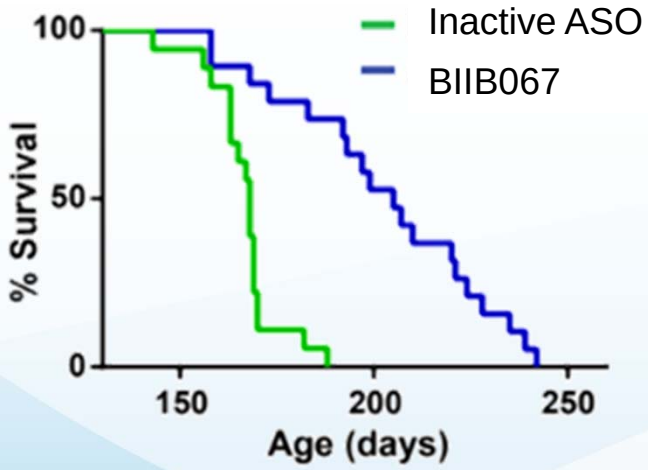
Toxic protein





Survival





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DeVos SL et al, Sci Transl Med, 2017

McCampbell et al, JCI, 2018 (Accepted manuscript)

ASOs Have Unique Benefits to Alternative Modalities

	ASOs	Small molecules	Antibodies	Gene Therapy	RNAi
Validated in neuroscience	✓✓	✓✓	✓✓	✓	
Broad CNS utility	✓✓✓	✓✓	✓	✓	Limited
Rapid path to IND	✓✓✓	✓	✓	✓✓	✓✓
Intracellular targeting	✓✓✓	✓✓✓	Limited	✓✓✓	✓✓✓
Infrequent delivery	✓✓	✓	✓	✓✓✓	✓✓✓
Ability to titrate dose	✓✓	✓✓✓	✓✓	Limited	✓✓

ASO Benefits

- Complement alternative therapeutic modalities
- Potential to address multiple diseases, and biological pathways in various ways (e.g., up- or down-regulation of RNA)
- Intrathecal drug delivery can achieve broad delivery to the brain, and has been associated with a favorable risk-benefit profile
- Continued innovation in next-generation ASOs and device-mediated delivery
- Robust IP position

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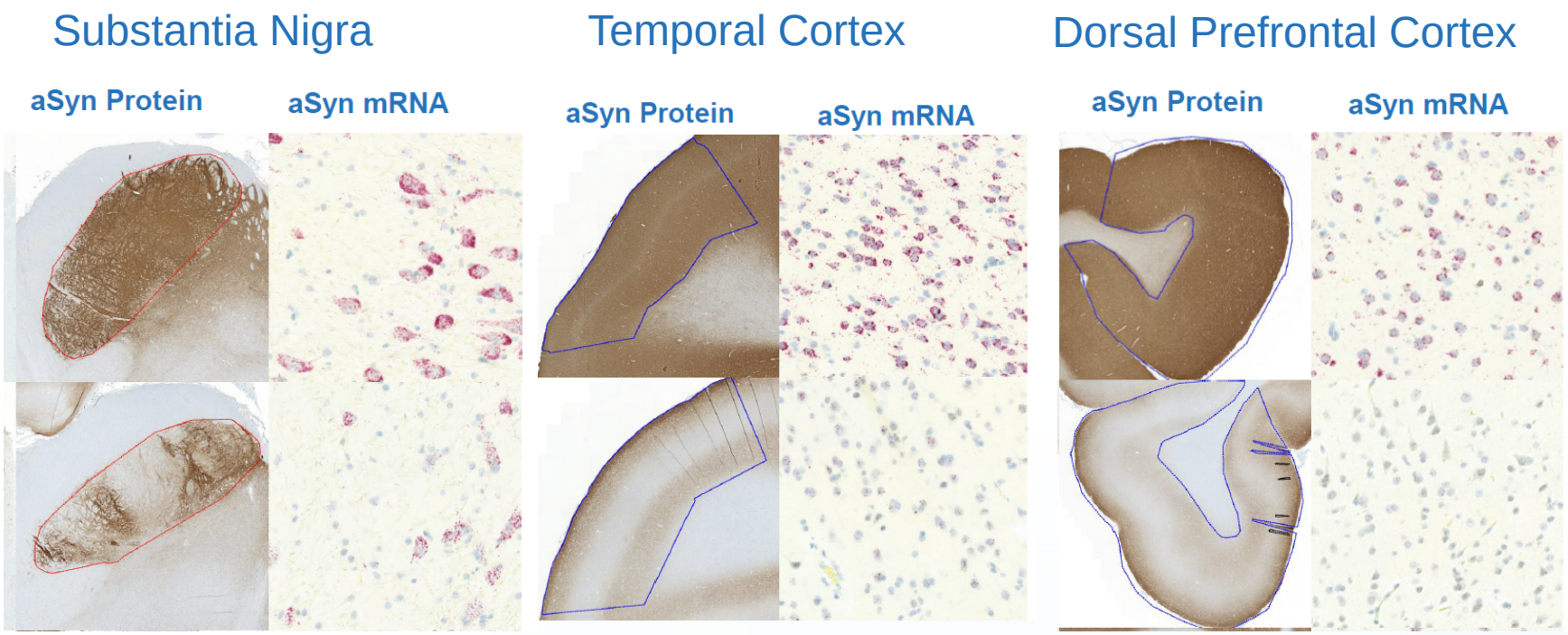
Intrathecal Delivery Results in Broad Tissue Distribution



Biogen unpublished data

Intrathecal bolus lowers alpha-synuclein mRNA and protein in target brain regions in Non-Human Primate

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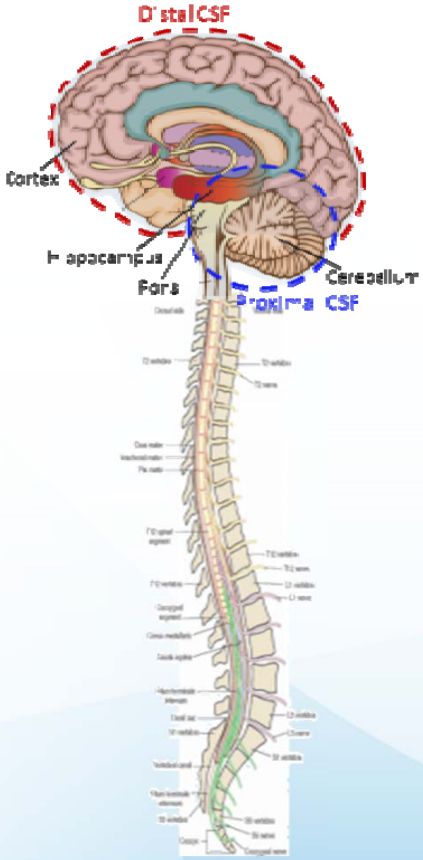
ASOs and Gene Therapy – Complementary CNS Treatment Modalities

Combination / sequential therapy, potential benefits:

- Additive activity at a cellular level
- Complementary distribution and transduction across the CNS
- Potential to augment activity with ASO, should AAV efficacy wane

Intrathecally delivered ASOs

- Well-tolerated
- Highly selective
- Able to both up- and down-regulate protein expression
- Not subject to immune surveillance
- Ability to titrate dose
- Readily manufactured



CNS targeted gene therapy

- Potential one-time treatment
- Remaining uncertainties:
  - Safety profile
  - Treatment of populations with anti-AAV serotype antibodies
  - Transduction across a variety of cell types
  - Manufacturing standards at commercial scale

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Numerous Potential Neurological Disease Targets

Disease	US Prevalence
Amyotrophic Lateral Sclerosis	30k
Angelman Syndrome	15k
Dravet Syndrome	10k
Fragile X	70k
Frontotemporal Dementia	50k
Parkinson's-GBA Mutation	100k
Progressive Supranuclear Palsy	18k
Rett Syndrome	10k
Spinal Muscular Atrophy	9k

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Source: Biogen internal estimates

Deal Terms & Strategic Outlook

Jeffrey Capello

EVP, Chief Financial Officer

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Efficient Use of Capital and Potential Value Creation

KEY TERMS	
Upfront Payment	$375M Upfront $500M Equity + $125M Cash Premium
Total Potential Pre-IND, development and regulatory milestones	Up to $125M or $270M, depending on the indication
Royalties	Tiered
Operational Responsibilities	Following opt-in, Biogen responsible for all clinical development, regulatory interactions and commercial activities
Duration	10 years

Note: Program specific milestone and royalty rates are dependent on program success and the estimated commercial opportunity size, as assessed during early development and reassessed following clinical study results.

- Biogen obtains exclusive access of leading ASO capability for broad range of neurological diseases
- We believe this collaboration could result in a number of breakthrough new medicines that will enter Biogen's clinical development pipeline over many years
- Favorable economics, with financial terms based on success
  - Tiered milestones and royalties, with largest milestones in later stage clinical development
- Estimate only one commercial product with success similar to SPINRAZA needed to generate positive deal value

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Capital Allocation Strategy

- Capital efficient deal structure that we believe leaves substantial capacity for future business development, M&A and share repurchases
- Disciplined approach with a focus on value creation
- Intend to strive for optimal capital structure and aim to have superior returns with the goal of maximizing long term value to shareholders

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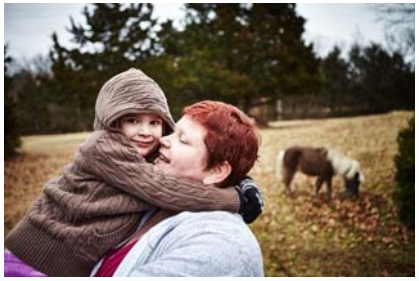
Questions & Answers







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