

where
science meets **humanity**[™]

Second Quarter 2022

Financial Results and Business Update



July 20, 2022

 **Biogen.**

Non-GAAP financial information

This presentation and the discussions during this conference call include certain financial measures that were not prepared in accordance with accounting principles generally accepted in the U.S. (GAAP), including adjusted net income, adjusted diluted earnings per share, revenue growth at constant currency, which excludes the impact of changes in foreign exchange rates and hedging gains or losses, and free cash flow, which is defined as net cash flow from operations less capital expenditures. Additional information regarding the GAAP and Non-GAAP financial measures and a reconciliation of the GAAP to Non-GAAP financial measures can be found on slides 54-58 of this presentation and in the Q2 2022 earnings release and related financial tables posted on the *Investors* section of Biogen.com. We believe that these and other Non-GAAP financial measures provide additional insight into the ongoing economics of our business and reflect how we manage our business internally, set operational goals, and form the basis of our management incentive programs. Non-GAAP financial measures are in addition to, not a substitute for, or superior to, measures of financial performance prepared in accordance with GAAP.

We do not provide guidance for GAAP reported financial measures (other than revenue) or a reconciliation of forward-looking Non-GAAP financial measures to the most directly comparable GAAP reported financial measures because we are unable to predict with reasonable certainty the financial impact of items such as the transaction, integration, and certain other costs related to acquisitions or large business development transactions; unusual gains and losses; potential future asset impairments; gains and losses from our equity security investments; and the ultimate outcome of pending significant litigation without unreasonable effort. These items are uncertain, depend on various factors, and could have a material impact on GAAP reported results for the guidance period. For the same reasons, we are unable to address the significance of the unavailable information, which could be material to future results.

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Forward-looking statements

This presentation and the discussions during this conference call contain 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; our future financial and operating results; 2022 financial guidance; plans relating to share repurchases. 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; risks that uncertainty as to whether the anticipated benefits of the transaction with Samsung Biologics can be achieved; uncertainty as to whether the anticipated benefits of the cost-reduction and productivity measures can be achieved; 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; the potential impact of the conflict in Ukraine; 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.

These statements are based on our current beliefs and expectations and speak only as of the date of this news release. We do not undertake any obligation to publicly update any forward-looking statements.

Q2 2022 earnings call agenda

Introduction

Michael Hencke

Head of Investor Relations

Overview

Michel Vounatsos

Chief Executive Officer

R&D Update

Priya Singhal, M.D., M.P.H.

Interim Head of Research & Development

Financial Update

Michael McDonnell

Chief Financial Officer

Overview

Michel Vounatsos
Chief Executive Officer



Key achievements in Alzheimer's disease and depression



Lecanemab BLA granted priority review under the accelerated approval pathway in the U.S.+

Expected FDA decision by January 6, 2023

Phase 3 Clarity AD study expected to read out Fall 2022

Positive Phase 3 data for zuranolone in postpartum depression

Phase 3 SKYLARK Study is now the second positive Phase 3 study of zuranolone in PPD

Single NDA filing in MDD and PPD expected to be complete by the end of 2022++

Progress on near-term operational priorities

R&D Prioritization

Accelerating zuranolone filing in PPD and terminating certain programs

Expense Management

On track to implement cost-reduction and productivity measures in order to align costs with revenue base

Global Growth Opportunities

Focusing on key emerging markets, such as China and certain markets in both Latin America and the Middle East

Renewed Biosimilar Growth

Launched BYOOVIZ, our first biosimilar in the U.S., referencing LUCENTIS®

Capital Allocation

*Continuing to pursue business development opportunities
Repurchased \$500M of Biogen stock*

Potential for renewed growth and value creation over time

✓ Achieved or Expected 2022 Milestone

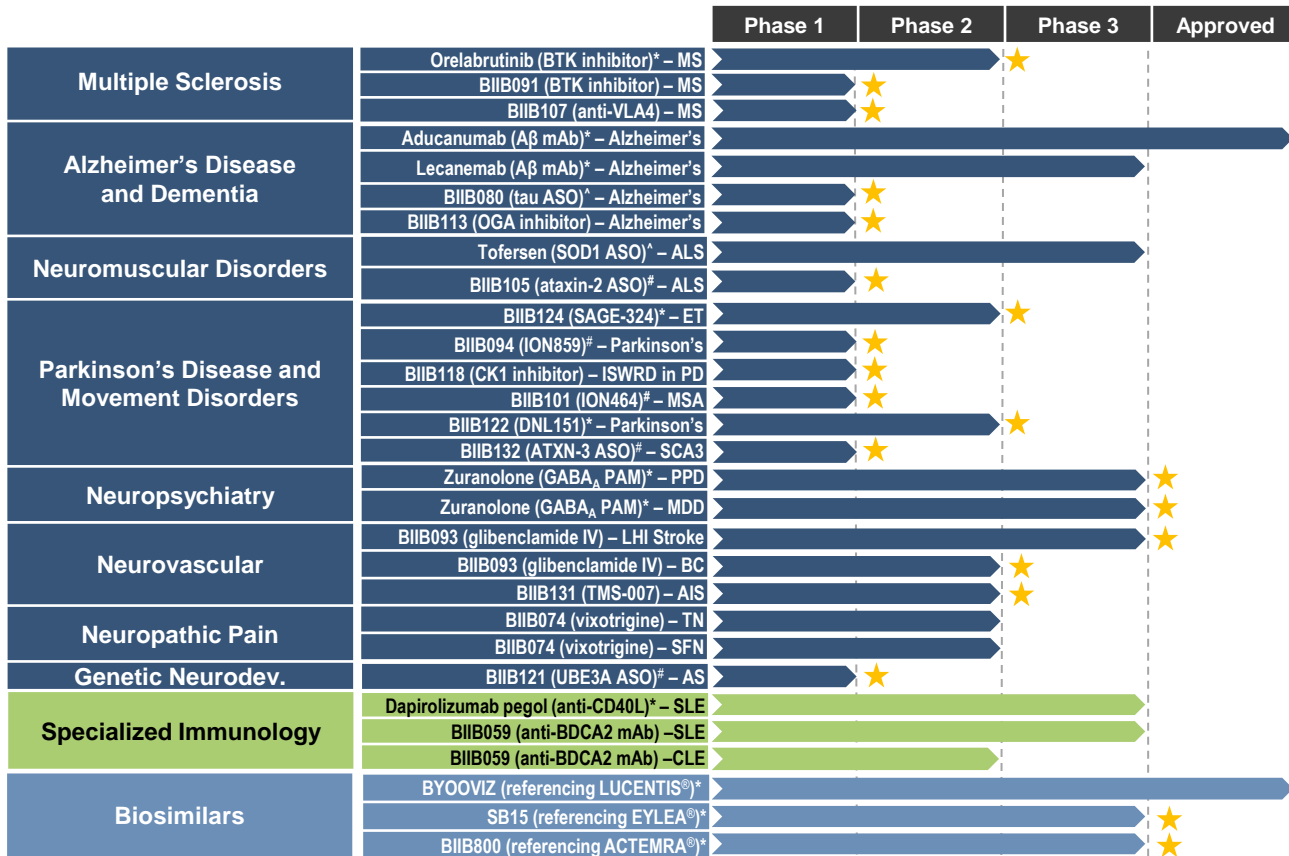
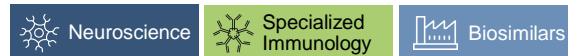


R&D Update

Priya Singhal, M.D., M.P.H.

Interim Head of Research & Development

Advancing a robust and diversified portfolio



29
Clinical programs today

10
Programs in Phase 3 or filed today

21
★ New clinical programs since 2017

> 30
Business development deals since 2017

* Collaboration program; # Option agreement; ^ Licensed from Ionis Pharmaceuticals, Inc.; MS = multiple sclerosis; ASO = antisense oligonucleotide; OGA = O-GlcNAcase; ALS = amyotrophic lateral sclerosis; SCA3 = spinocerebellar ataxia type 3; ET = essential tremor; ISWRD = irregular sleep wake rhythm disorder; PD = Parkinson's disease; MSA = Multiple System Atrophy; PPD = postpartum depression; MDD = major depressive disorder; LHI = large hemispheric infarction; BC = brain contusion; AIS = acute ischemic stroke; TN = trigeminal neuralgia; SFN = small fiber neuropathy; Genetic Neurodev. = genetic neurodevelopmental disorders; AS = Angelman syndrome; SLE = systemic lupus erythematosus; CLE = cutaneous lupus erythematosus

Pursuing new treatments for Alzheimer's disease

ALZHEIMER'S DISEASE

NEURO-PSYCHIATRY

NEURO-MUSCULAR

MOVEMENT DISORDERS

Lecanemab – Anti-amyloid monoclonal antibody

- **BLA accepted** by the FDA under the Accelerated Approval pathway and granted Priority Review – *Expected FDA decision by January 6, 2023*
- **Phase 3 Clarity AD Study** progressing with expected primary readout* in the Fall 2022

Primary Endpoint	CDR– Sum of boxes
Secondary Endpoints	Amyloid PET, ADAS-cog14, ADCOMS, ADCS-MCI-ADL
Stratified Randomization	ApoE4 carrier status, MCI due to AD/Mild AD, SoC combination group/non-SoC combination group, geographical region
Other Biomarkers (n)	PET (>350): tau CSF (>450): A β 1-42, A β 1-40, neurogranin, NfL, total tau, phospho tau Plasma (all participants): A β 1-42, A β 1-40, A β 42/40 ratio, NfL, phospho tau

- *Regulatory filings for traditional approval of lecanemab are planned for the U.S., E.U., and Japan by end of Q1 2023*

BIIB080 – Antisense oligonucleotide targeting tau

- **Phase 2 CELIA Study** in participants with Mild Cognitive Impairment due to AD and mild AD anticipated to start in 2022

Advancing a late-stage pipeline in Neuropsychiatry

ALZHEIMER'S
DISEASE

NEURO-
PSYCHIATRY

NEURO-
MUSCULAR

MOVEMENT
DISORDERS

Phase 3 SKYLARK Study of zuranolone in PPD met the primary and all key secondary endpoints

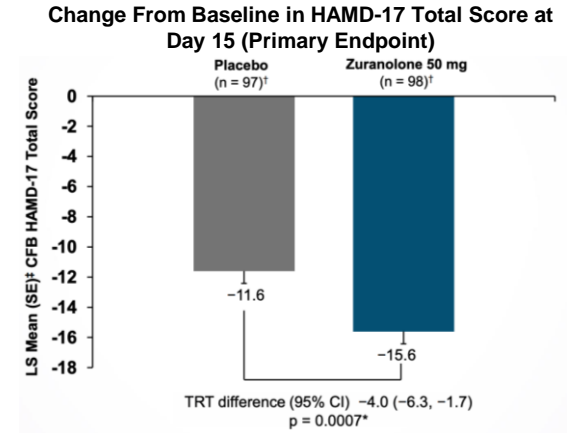
- Zuranolone 50 mg demonstrated a statistically significant improvement in depressive symptoms as early as Day 3 vs. placebo, which was sustained through Day 45
- Zuranolone was generally well tolerated with a safety profile consistent with the other trials in the LANDSCAPE (MDD) and NEST (PPD) programs to date

Sage and Biogen expect to complete a single NDA filing for zuranolone in MDD and PPD by end of 2022[^]

Zuranolone Human Abuse Liability Study results presented at CPDD

- 30 and 60 mg of zuranolone demonstrated lower abuse potential as compared with alprazolam 1.5 mg and 3 mg in recreational users of CNS depressants
- 90 mg zuranolone was comparable to alprazolam

The Phase 2 TALLY Study of BIIB104 in CIAS did not meet its primary or secondary efficacy endpoints; Biogen will discontinue the BIIB104 program in CIAS



Note: zuranolone is being developed in collaboration with Sage Therapeutics, Inc.; [^] Sage responsible for zuranolone regulatory filing
†Full analysis set was defined as all randomized participants who were administered zuranolone 50 mg or placebo with valid baseline and ≥ 1 post-baseline efficacy endpoint assessment. ‡LS mean and treatment difference along with CI and p values were calculated using MMRM. CFB = change from baseline; CI = confidence interval; CIAS = cognitive impairment associated with schizophrenia; CNS = central nervous system; CPDD = College on Problems of Drug Dependence; HAMD-17 = 17-item Hamilton Rating Scale for Depression; LS = least squares; MDD = major depressive disorder; NDA = new drug application; PPD = postpartum depression; MMRM = mixed model of repeated measures; SE = standard error; TRT = treatment
Sage data on file.

New data presented for tofersen in SOD1-ALS

ALZHEIMER'S
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NEURO-
PSYCHIATRY

NEURO-
MUSCULAR

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DISORDERS



Tofersen in SOD1-ALS

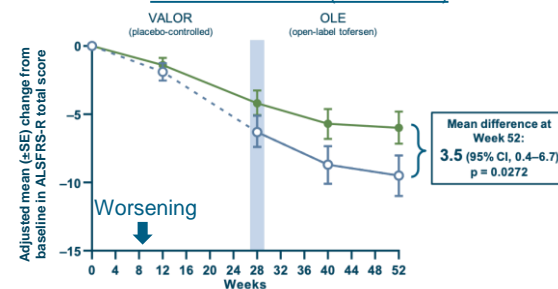
- While statistical significance was not achieved on the primary endpoint of ALSFRS-R at week 28 in VALOR, signs of reduced disease progression across multiple secondary and exploratory endpoints were observed
- Analyses of 12-month data from VALOR and its OLE show that that earlier initiation of tofersen compared to delayed initiation slowed declines in clinical function (ALSFRS-R), respiratory function (SVC), muscle strength (HHD), and quality of life (ALSAQ-5)
- The most common AEs in participants receiving tofersen in VALOR and the OLE study were headache, procedural pain, fall, back pain and pain in extremity. Serious neurologic events including myelitis, radiculitis, aseptic meningitis, and papilledema, were reported in 6.7 percent of participants receiving tofersen in VALOR and its OLE

Ongoing tofersen activities:

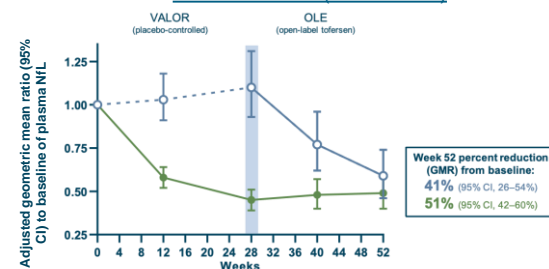
- Actively recruiting for ATLAS, the tofersen presymptomatic study
- Continuing to support the tofersen early access program
- Remain engaged with global regulators



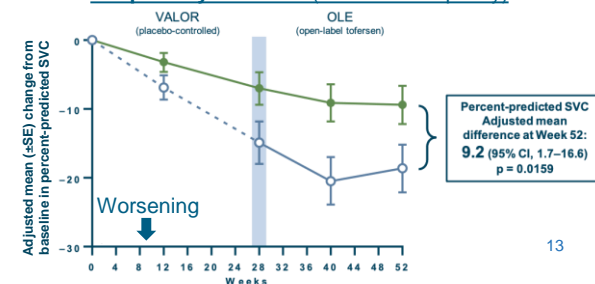
Clinical Function (ALSFRS-R)



Neurofilament (Plasma NfL)



Respiratory Function (Slow Vital Capacity)



New study initiated in Parkinson's disease

ALZHEIMER'S
DISEASE

NEURO-
PSYCHIATRY

NEURO-
MUSCULAR

MOVEMENT
DISORDERS

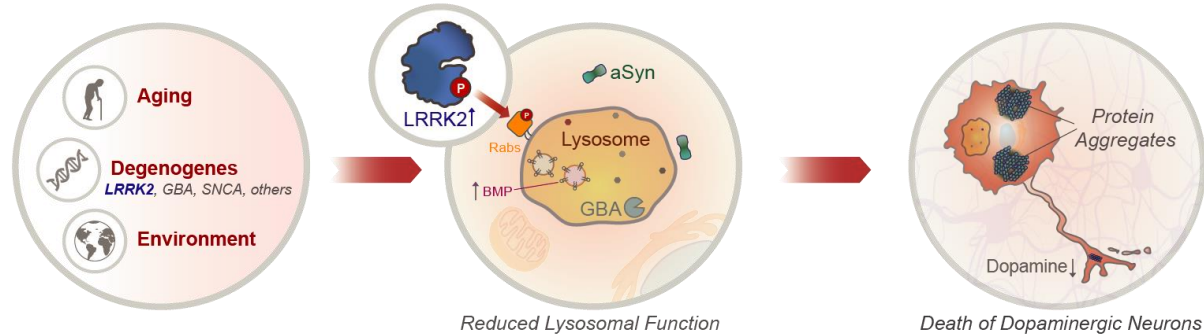


BIIB122 in Parkinson's disease

CELLULAR STRESS

LYSOSOMAL DYSFUNCTION

NEURONAL DEGENERATION



Phase 2b LUMA Study

- Patients **without** a pathogenic LRRK2 variant
- N = 640 patients (320 per arm)
- 225 mg oral once daily vs. placebo
- 48-week minimum treatment period
- Primary endpoint assessed using MDS-UPDRS
- **Initiated: May 2022**

Phase 3 LIGHTHOUSE Study

- Patients **with** a confirmed pathogenic LRRK2 variant
- N = 400 patients (200 per arm)
- 225 mg oral once daily vs. placebo
- 96-week minimum treatment period
- Primary endpoint assessed using MDS-UPDRS
- Initiation planned for 2022

Biogen continues to execute against 2022 R&D objectives

Regulatory Filings

- Lecanemab BLA in early Alzheimer's under the accelerated approval pathway accepted and granted priority review by FDA+ – Expected *PDUFA January 6, 2023*
- Zuranolone NDA filing in MDD and PPD to FDA (*Initiated in Q2; Expected to complete in H2 2022*)⁺⁺

Data Readouts

- Phase 3 CORAL study readout of zuranolone when co-initiated with a standard of care ADT
- ✗ Phase 1 readout of BIIB078 in C9orf72-associated ALS
 - *BIIB078 did not show clinical benefit; program discontinued*
- 12-month data of tofersen in *SOD1*-ALS from Phase 3 VALOR Study and its OLE presented at ENCALS
- Zuranolone Phase 3 SKYLARK Study in PPD – *Study met primary and all key secondary endpoints*
- ✗ BIIB104 Phase 2 TALLY Study in CIAS
 - *BIIB104 did not show clinical benefit; program discontinued*
- Lecanemab Phase 3 Clarity AD Study in Alzheimer's (*Fall*)

Initiation of New Programs and Clinical Studies

- Phase 1 study of BIIB113 (OGA small molecule inhibitor) in Alzheimer's disease
- Phase 1 study of BIIB132 (ATXN3 ASO) in spinocerebellar ataxia type 3
- Phase 3 ASCEND Study of SPINRAZA following Evrysdi® (risdiplam) treatment
- Phase 2b KINETIC 2 Study of BIIB124 / SAGE-324 (GABA_A PAM) in essential tremor
- Phase 2b LUMA Study of BIIB122 / DNL151 in Parkinson's disease without LRRK2 mutation
- Phase 3 LIGHTHOUSE Study of BIIB122 / DNL151 in Parkinson's disease with confirmed LRRK2 mutation
- Phase 2 CELIA Study of BIIB080 (tau ASO) in Alzheimer's disease
- Pivotal study of BIIB059 (anti-BDCA2 mAb) in cutaneous lupus erythematosus

● Completed ○ Anticipated

+ Eisai Co., Ltd responsible for lecanemab regulatory filing; ++ Sage Therapeutics, Inc. responsible for zuranolone filing

Note: lecanemab is being developed in collaboration with Eisai Co., Ltd; Zuranolone is being developed in collaboration with Sage Therapeutics, Inc.; BIIB122 is being developed with Denali Therapeutics
ADT = antidepressant therapy; ALS = amyotrophic lateral sclerosis; ASO = antisense oligonucleotide; BDCA2 = blood DC antigen 2; BLA = biologics license application; CIAS = cognitive impairment associated with schizophrenia; ENCALS = European Network to Cure ALS; GABA_A = γ-aminobutyric acid type A receptor; LRRK2 = Leucine-rich repeat kinase 2; mAb = monoclonal antibodies; MDD = major depressive disorder; NDA = new drug application; OGA = O-GlcNAcase; OLE = open label extension; PAM = positive allosteric modulator; PD = Parkinson's disease; PPD = postpartum depression

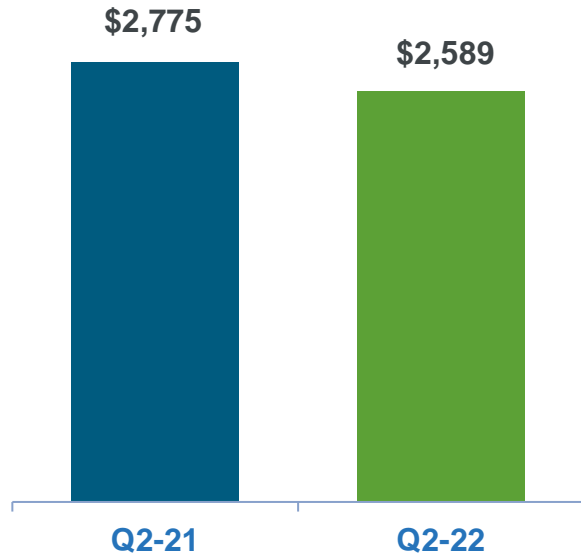
Financial Update

Michael McDonnell

Chief Financial Officer

Q2 2022 financial results

Total Revenue (\$M)

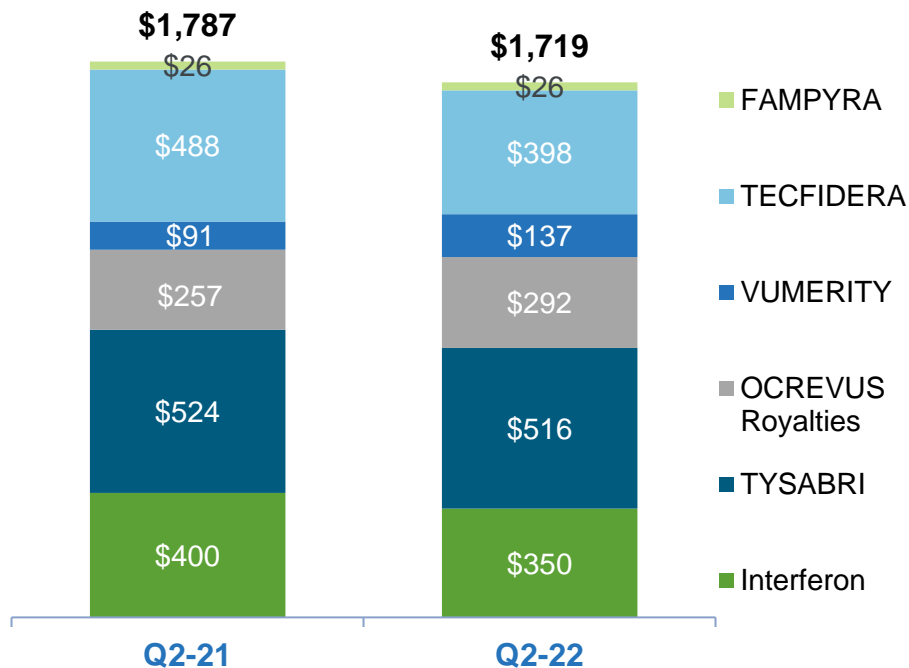


Non-GAAP Diluted EPS (\$)



Global multiple sclerosis revenue

MS Revenue (\$M)

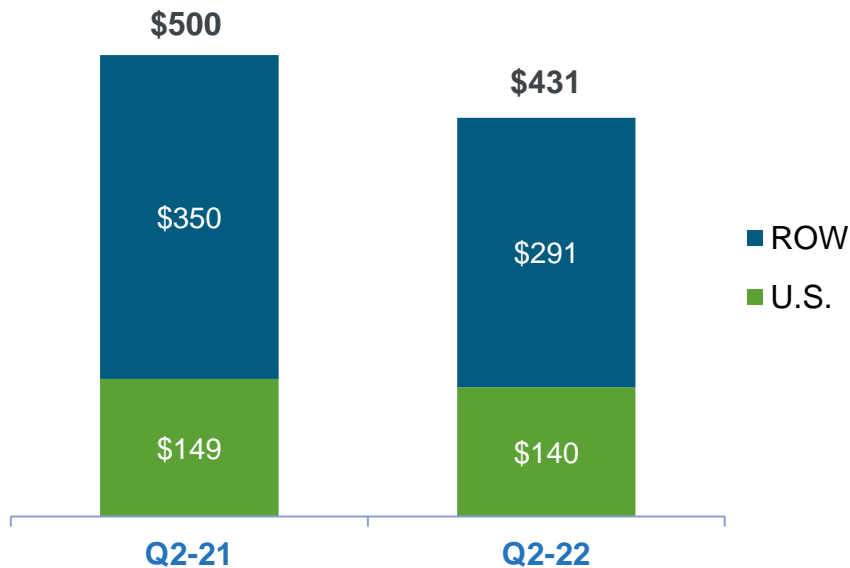


Highlights

- **Global MS revenue, including OCREVUS royalties**, declined 4% at actual currency and 3% at constant currency
- **TECFIDERA** revenue decreased 18% at actual currency and 17% at constant currency vs. prior year; impacted by the entrance of generics both in the U.S. and outside the U.S.
- **VUMERITY** revenue increased 51% at actual currency and 52% at constant currency vs. prior year
- **TYSABRI** revenue decreased 2% at actual currency and was flat at constant currency vs. prior year
 - Continued patient growth outside the U.S.

Global SPINRAZA revenue

SPINRAZA Revenue (\$M)

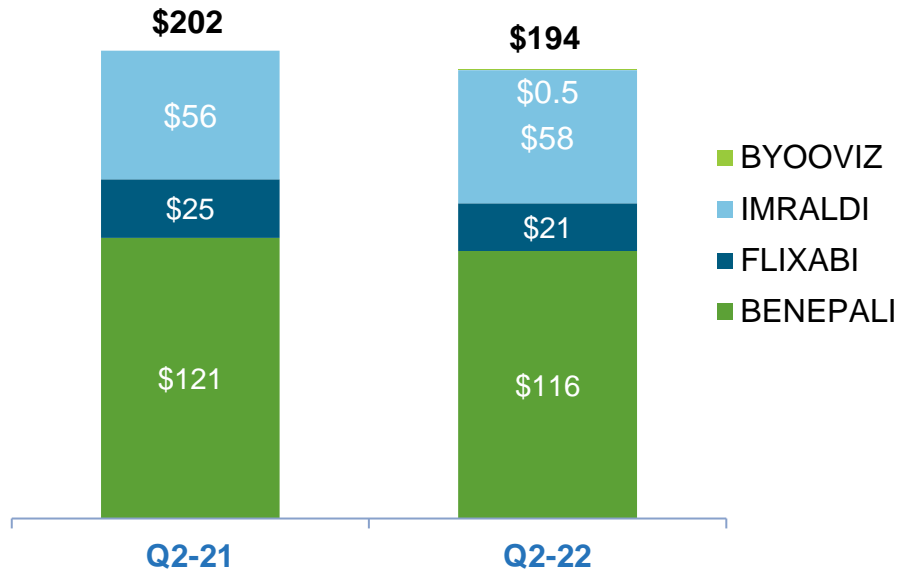


Highlights

- **Global SPINRAZA** revenue decreased 14% at actual currency and 11% at constant currency vs. prior year
 - **U.S. SPINRAZA** revenue decreased 6% vs. prior year
 - **ROW SPINRAZA** revenue decreased 17% vs. prior year; driven primarily by competition, along with timing of shipments in certain markets, pricing dynamics, and negative currency impacts
- **Global SPINRAZA** revenue decreased 9% versus the first quarter of 2022 at actual currency and 8% at constant currency; driven by competition and negative currency impacts outside the U.S. as well as some seasonality dynamics in the U.S.

Biosimilars revenue

Biosimilars Revenue (\$M)



Highlights

- **Biosimilars** revenue decreased 4% at actual currency and increased 3% at constant currency vs. prior year; volume increases more than offset by negative currency impacts and pricing pressure
- ~ **253,000** patients on Biogen biosimilar products at end of Q2 2022*
- **BYOOVIZ** (referencing LUCENTIS®) launched in the U.S. in June 2022

Q2 2022 revenue highlights

\$ in Millions	Q2 2022	Q2 2021	Δ Y/Y
Total Product Revenues*	\$2,055	\$2,236	(8%)
RITUXAN/GAZYVA Revenues	\$144	\$183	(21%)
OCREVUS Royalties	\$292	\$257	14%
Revenues from Anti-CD20 Therapeutic Programs	\$436	\$440	(1%)
Other Revenues	\$98	\$99	(1%)
Total Revenues*	\$2,589	\$2,775	(7%)

Q2 2022 financial results highlights

(\$ in Millions except EPS, Shares in Millions)	Q2 2022	Q2 2021*	Δ Y/Y
Revenue	\$2,589	\$2,775	(7%)
Cost of Sales	\$484	\$460	(5%)
Gross Profit	\$2,105	\$2,315	(9%)
% of revenue	81%	83%	
R&D Expense	\$529	\$585	10%
Non-GAAP SG&A Expense	\$570	\$635	10%
Collaboration Profit (Loss) Sharing	\$29	(\$15)	(294%)
Non-GAAP Amortization	\$7	\$0	NMF
Acquired In-Process Research and Development	\$0	\$18	100%
Non-GAAP Other (Income) Expense	\$79	\$58	(37%)
Non-GAAP Profit Before Taxes and JV Equity	\$890	\$1,034	(14%)
Non-GAAP Taxes	\$135	\$162	17%
Non-GAAP Taxes %	15.2%	15.7%	
Non-GAAP JV Equity Income (Loss)	\$13	\$50	(74%)
Non-GAAP Net Income	\$768	\$922	(17%)
Non-GAAP Net Income (Loss) Attributable to NonControlling Interests	\$1	\$84	(99%)
Non-GAAP Net Income Attributable to Biogen Inc.	\$767	\$838	(8%)
Weighted average diluted shares used in calculating diluted EPS	146	150	(3%)
Non-GAAP Diluted EPS	\$5.25	\$5.58	(6%)

Numbers may not foot or recalculate due to rounding. Percent changes represented as favorable/(unfavorable).

Our GAAP financial measures and a reconciliation of GAAP to Non-GAAP financial results are at the end of this presentation.

* Beginning in the first quarter of 2022 material payments paid on the acquisition of in-process research and development assets are no longer excluded in the determination of Non-GAAP net income. Prior period Non-GAAP results have been updated to reflect these changes.

Balance sheet and cash flow

Balance Sheet

(as of June 30, 2022)

\$5.9B Cash and marketable securities

\$7.3B Debt

\$1.4B Net debt

Note: Subsequent to June 30, 2022, the Company repaid its Senior Notes due September 2022, with an aggregate principal amount of \$1 billion.

Cash Flow

(Q2 2022)

\$737M Cash flow from operations

\$37M Capital expenditures

\$700M Free cash flow*

\$500M Share repurchases

* Free cash flow is defined as net cash flow from operations less capital expenditures.

Updating 2022 full year financial guidance

	Prior FY 2022 Guidance	Updated FY 2022 Guidance
Revenue	\$9.7 billion to \$10.0 billion	\$9.9 billion to \$10.1 billion
Non-GAAP Diluted EPS	\$14.25 to \$16.00	\$15.25 to \$16.75

Please see Biogen's Q2 2022 earnings release, available at the Investors section of Biogen's website at investors.biogen.com, for additional 2022 financial guidance assumptions.

Biogen may incur charges, realize gains or losses, or experience other events or circumstances in 2022 that could cause any of these assumptions to change and/or actual results to vary from this financial guidance.

Please see slide 2 of this presentation for additional information on our use of Non-GAAP measures, including forward-looking Non-GAAP financial measures.

Questions & Answers



Appendix



Continuing to advance our ESG priorities

Progress Highlights

ENVIRONMENT



- Signed 1st **Virtual Power Purchase Agreement (VPPA)**, covering **50%** of electricity use for U.S. operations with renewables
- Harvard T.H. Chan School of Public Health **meta-analysis on air pollution and dementia** presented at the American Academy of Neurology
- Realized **Science Based Targets initiative climate goals** from **18%** of top suppliers*

SOCIAL



- Introduced new benefit to **promote health access and equity** for all employees, with a focus on female health
- Celebrating **20 years of caring deeply** through the Biogen Foundation and Community Lab, the longest-running hands-on corporate science lab
- Announced **Community Lab 2.0**, a new goal to engage a total of **90,000** students in STEM education by 2025

GOVERNANCE



- Included **ESG in Corporate Scorecard** for 2nd year in a row
- Updated Biogen Anti-Slavery and Human Trafficking statement and **position on biodiversity**

Released ESG report



Enhanced disclosures on ESG issues, including global pay gap and employee wellbeing.

Provided update on progress to Health Climate, Healthy Lives™.

biogen.com/yearinreview

Recognition for ESG leadership



Disability Equality Index
Included on Disability:IN's list for Best Places to Work for Disability Inclusion for 5th year



LGBTQ+ Equality
Achieved 100% on HRC's Best Places to Work for LGBTQ+ Equality for 9th year



Best Corporate Citizens
Honored as one of 3BL's 100 Best Corporate Citizens

Lecanemab (A β mAb)



Neuroscience

PORTFOLIO

AD PIPELINE

- ❖ Aducanumab (ADUHELM) – A β mAb
- ❖ **Lecanemab (Ph3) – A β mAb**
- ❖ BILB080 (Ph1) – tau ASO

PROPOSED MECHANISM OF ACTION

- Lecanemab is humanized immunoglobulin G1 (IgG1) monoclonal antibody directed at A β
- Lecanemab selectively binds to soluble A β aggregate species with preferential activity for A β protofibrils over fibrils (>10x)

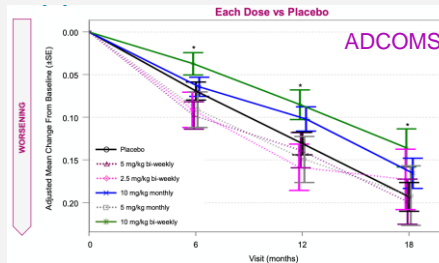
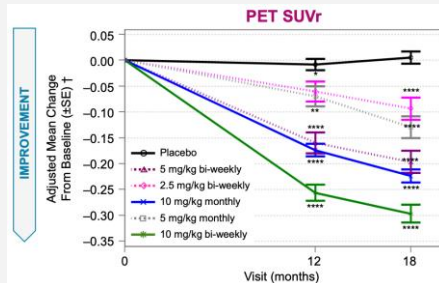
CLINICAL STUDY OVERVIEW

- Study 201 Phase 2b: is a global, placebo-controlled, double-blind, parallel-group, randomized trial with open-label extension
 - Core randomization phase (n=856) with primary endpoint ADCOMS at 12 Months and key secondary endpoints (amyloid PET, ADCOMS, CDR-SB, ADAS-cog, and fluid biomarkers) at 18 months
 - GAP period of 9-59 months (average 24 months) off treatment from end of core phase and initiation of OLE
 - OLE for up to 60 months (ongoing) with 10 mg/kg IV biweekly treatment
- Clarity AD Phase 3: A Phase 3 Placebo-Controlled, Double-Blind, Parallel-Group, 18-Month Study Evaluating Lecanemab (BAN2401) in Early Alzheimer's Disease (n=1766)
 - Primary endpoint CDR-SB at 18 months; Enrollment complete, follow-up ongoing
 - **Phase 3 readout anticipated in Fall 2022** with potential to be the first anti-amyloid antibody with traditional approval in Alzheimer's disease

Current Status:

- AHEAD 3-45 Phase III study in preclinical AD ongoing (n=1400)
- Breakthrough therapy designation in the U.S.
- **Lecanemab filing granted priority review in the U.S. with a PDUFA of January 6, 2023**

PHASE 2 CLINICAL DATA¹



- (Swanson, 2018) Dose dependent reduction in amyloid PET values (Florbetapir tracer)
- At 18 months, 10-mg/kg biweekly lecanemab reduced brain amyloid (-0.306 SUVR units)
- Lecanemab significantly reduced amyloid PET values across all doses and converted subjects from amyloid positive to negative across most doses based on visual read
- >80% amyloid negative by visual read for 10 mg/kg IV biweekly at 18 months
- Dose and time dependent reduction in decline on ADCOMS; starting at 6 months of lecanemab treatment showing a drug-placebo difference in favor of active treatment by 30% at 18 months in the 10 mg/kg biweekly cohort
- The rate of amyloid-related imaging abnormalities-edema/effusion (ARIA-E), an adverse event associated with amyloid directed therapies, for the 10 mg/kg biweekly dosing was 9.9%.

¹ Swanson et al., AAIC 2018

Note: lecanemab is being developed in collaboration with Eisai Co., Ltd

BIIB080 (tau ASO)



Neuroscience

PORTFOLIO

AD PIPELINE

- ❖ Aducanumab (ADUHELM) – A β mAb
- ❖ Lecanemab (Ph3) – A β mAb
- ❖ BIIB080 (Ph2) – tau ASO

PROPOSED MECHANISM OF ACTION

BIIB080 is a tau mRNA-directed ASO that reduces de novo production of all 6 human splice isoforms of tau, thereby reducing all forms of tau including aggregates, as demonstrated in preclinical animal studies,¹ and other toxic species, and is expected to slow disease progression in Alzheimer's Disease and other tauopathies

CLINICAL STUDY OVERVIEW

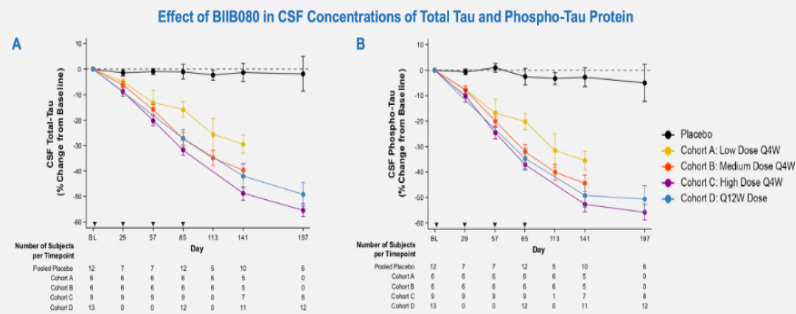
- First in Human Phase 1b Study [NCT03186989] is a two-part study evaluating the safety, tolerability, pharmacokinetics, and target engagement of BIIB080 in patients with mild Alzheimer's disease (with consistent CSF biomarkers). Part 1: a randomized double-blind, placebo controlled multiple ascending dose period, followed by Part 2: the open-label, long-term extension period.
- The placebo-controlled 36-week MAD Part 1 is complete; the open-label Part 2 is complete and data analysis is currently in progress.
- For Part 1, four ascending dose cohorts were enrolled sequentially and randomized 3:1 to intrathecal bolus administrations of BIIB080 or placebo every four weeks (first 3 cohorts) or every 12 weeks (last cohort) during the 13-week Treatment Period, followed by a 23-week Post-Treatment Period. The primary endpoint was safety and tolerability. The secondary endpoint was BIIB080 pharmacokinetics in cerebrospinal fluid (CSF). The prespecified key exploratory outcome was CSF total tau (t-tau) protein concentration.
- 46 mild AD participants enrolled in the trial with 34 randomized to BIIB080 and 12 randomized to placebo.

Current Status:

- Phase 2 CELIA Study in participants with Mild Cognitive Impairment due to AD and mild AD anticipated to start in 2022 [NCT05399888]

PHASE 1b CLINICAL DATA

- BIIB080 was generally well tolerated in mild AD participants. All Adverse Events (AEs) were considered mild (Grade 1) or moderate (Grade 2). No patients discontinued the study due to an AE.
- Total tau in the CSF continued to decline 16 weeks post-last dose in participants treated with BIIB080 in the high dose four-week and 12-week dose groups, showing ~50% mean reduction from baseline.
- The responses of CSF total tau and phospho-tau are very similar
- Based on Phase 1b safety and pharmacokinetic data, BIIB080 will be evaluated in Phase 2 for Alzheimer's disease



Note: BIIB080 is licensed from Ionis Pharmaceuticals Inc.

¹ DeVos SL, et al. *Sci. Transl. Med.* 2017

AD = Alzheimer's disease; AE = adverse event; ASO – antisense oligonucleotide; CSF = cerebrospinal fluid

Tofersen (SOD1-ALS ASO)



Neuroscience

PORTFOLIO

ALS PIPELINE

- ❖ Genetic ALS:
 - Tofersen (Ph3) – SOD1 ASO
- ❖ Broad ALS:
 - BIIB105 (Ph1) – Ataxin2 ASO

PROPOSED MECHANISM OF ACTION

- Mutations in the SOD1 gene lead to accumulation of toxic SOD1 protein
- Tofersen mediates RNase H-dependent degradation of SOD1 mRNA to reduce synthesis of SOD1 protein

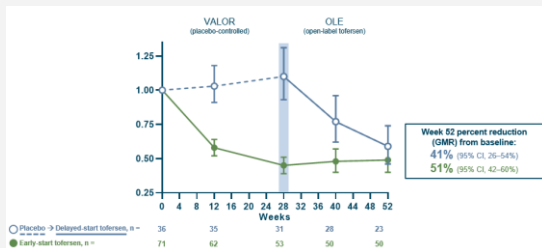
CLINICAL STUDY OVERVIEW

- 6-month, placebo-controlled, Phase 3 VALOR study in symptomatic SOD1-ALS read out in October 2021 [[NCT02623699](#)]; statistical significance not achieved on primary endpoint of change in ALSFRS-R score; robust reductions in total CSF SOD1 (an indirect marker of target engagement) and plasma NfL (a marker of axonal injury and neurodegeneration) observed with tofersen treatment; trends favoring tofersen observed across measures of function, strength, and quality of life
- Combined data from VALOR and a new cut of its ongoing open-label-extension (OLE) study [[NCT03070119](#)] study debuted at ENCALS illustrating effects of early (in VALOR) vs. delayed (in the OLE) initiation of tofersen
- ATLAS, initiated in June 2021; was designed to evaluate if initiation of tofersen in pre-symptomatic SOD1 mutation carriers with elevated plasma NfL levels can delay onset of clinical symptoms or signs of ALS [[NCT04856982](#)]
- Remain engaged with regulators on potential next steps for tofersen

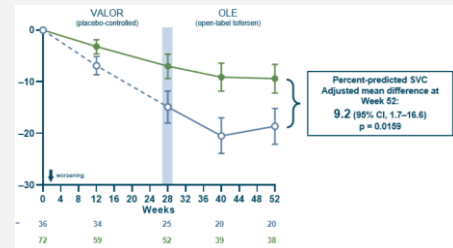
Integrated data from VALOR and its OLE

- Reductions in total CSF SOD1 and plasma NfL over 52 weeks
- At 52-weeks, the early-start tofersen group consistently experienced less decline in clinical function (ALSFRS-R), respiratory function (SVC), strength (HHD), and quality of life (ALSAQ-5, EQ-5D-5L) as compared to the delayed-start group
- The median time to death or PV could not be estimated because the majority of participants survived without PV. However, early data suggest a lower risk of death or PV in the early-start group
- The most common adverse events (AEs) in participants receiving tofersen were headache, procedural pain, fall, back pain and pain in extremity. Serious neurologic events including myelitis, aseptic meningitis, and papilledema were reported in 7 (6.7%) of patients

LS geometric mean ratio to baseline of plasma NfL



Adjusted mean (±SE) change in % predicted SVC



Note: Tofersen is licensed from Ionis Pharmaceuticals

ALSFRS-R = revised ALS Functional Rating Scale; CI = confidence interval; ENCALS = European Network to Cure ALS; OLE = open label extension; SAE = serious adverse event; SOD1 = superoxide dismutase 1

Miller et al., ENCALS 2021

Zuranolone (GABA_A PAM) – Major Depressive Disorder



Neuroscience

PORTFOLIO

NEUROPSYCHIATRY PIPELINE

- ❖ Zuranolone (Ph3) – MDD
- ❖ Zuranolone (Ph3) – PPD

PROPOSED MECHANISM OF ACTION

- Zuranolone is an oral positive allosteric modulator of both synaptic and extrasynaptic GABA_A receptors with a novel MOA
- Zuranolone is thought to upregulate GABA_A receptor expression and enhance inhibitory GABAergic signaling, and is hypothesized to rapidly restore network balance in brain areas dysregulated in depression

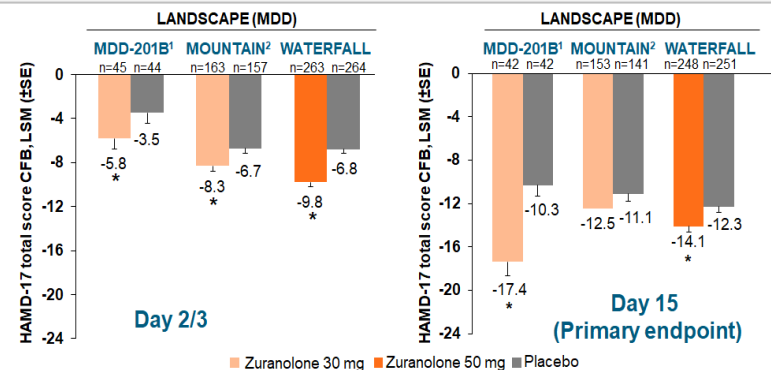
CLINICAL STUDY OVERVIEW

- The LANDSCAPE Program includes 1 Phase 2 study and 4 Phase 3 studies of zuranolone in patients with MDD
- MDD-201B: (102 patients) A Phase 2, double-blind, placebo-controlled study evaluating the safety, tolerability, PK and efficacy of zuranolone 30 mg in the treatment of adults with moderate to severe MDD. Study met its primary endpoint. [[NCT03000530](#)]
- MDD-301A (MOUNTAIN): (581 patients) A Phase 3, double-blind, placebo-controlled study evaluating the efficacy of zuranolone 30 mg and 20 mg in the treatment of adults with MDD. Study missed the primary endpoint at Day 15 but resulted in improvements at every earlier timepoint (Days 3, 8 and 12) and provides supportive information. [[NCT03672175](#)]
- MDD-301B (WATERFALL): (543 patients) A Phase 3, double-blind, placebo-controlled study evaluating the efficacy of zuranolone 50 mg in the treatment of adults with MDD. Study met its primary endpoint. [[NCT04442490](#)]
- MDD-305 (CORAL): (440 patients) A Phase 3 double-blind, placebo-controlled study comparing the efficacy and safety of zuranolone 50 mg co-initiated with an antidepressant versus placebo co-initiated with an antidepressant in adults with MDD. Study met its primary endpoint. [[NCT04476030](#)]

Current Status:

- **Ongoing:** MDD-303 (SHORELINE): (target 1550 patients) a Phase 3 open-label study evaluating repeat treatments of zuranolone (up to 50 mg) over the course of one year in adults with MDD. In Q4-2021, an interim readout of a cohort of 199 patients receiving 50 mg showed no new safety findings. [[NCT03864614](#)]
- **NDA joint filing in MDD and PPD expected to complete in 2022**

CLINICAL DATA



The clinical trials above differ in sample size, patient population, entry criteria, study sites as well as other design elements. No direct comparison can be made across these clinical trials based on the graph above. MDD-201B, MOUNTAIN, and WATERFALL enrolled patients with MDD. Studies with Day 3 data: MOUNTAIN, WATERFALL; Study with Day 2 data: MDD-201B.

¹p<0.05 vs placebo. p values for Day 2/3 LSM treatment difference are not adjusted for multiplicity and for WATERFALL is nominal. CFB = change from baseline; HAMD-17 = 17-Item Hamilton Rating Scale for Depression total score; LSM = least squares mean; MDD = major depressive disorder; n = number of patients at that visit.

1. Gunduz-Bruce H et al. *N Engl J Med*. 2019;381(10):903-911. 2. Mittal A, et al. Poster presented at the American Academy of Neurology Annual Meeting, Toronto, Canada, April 25-May 1, 2020.

Zuranolone was generally well tolerated in clinical studies to date. The most common treatment-emergent adverse events observed with zuranolone across the program were somnolence, dizziness, headache, and sedation. Among patients with MDD treated with zuranolone <5% discontinued treatment due to AEs

Note: zuranolone is being developed in collaboration with Sage Therapeutics, Inc.

CIAS = cognitive impairment associated with schizophrenia; GABA_A = γ-Aminobutyric acid type A receptor; MDD = major depressive disorder; PAM = positive allosteric modulator;

PPD = postpartum depression; AE = adverse event



Zuranolone (GABA_A PAM) – Postpartum Depression



Neuroscience

PORTFOLIO

NEUROPSYCHIATRY PIPELINE

- ❖ Zuranolone (Ph3) – MDD
- ❖ Zuranolone (Ph3) – PPD

PROPOSED MECHANISM OF ACTION

- Zuranolone is an oral positive allosteric modulator of both synaptic and extrasynaptic GABA_A receptors with a novel MOA
- Zuranolone is thought to upregulate GABA_A receptor expression and enhance inhibitory GABAergic signaling, and is hypothesized to rapidly restore network balance in brain areas dysregulated in depression

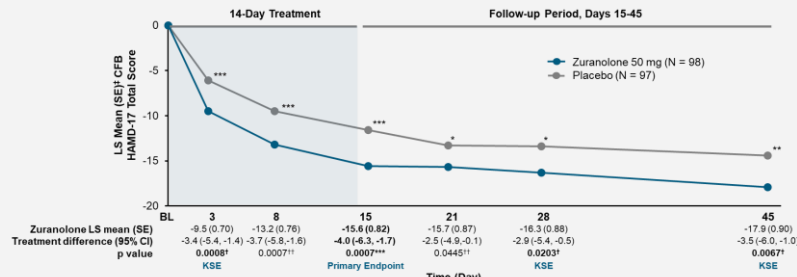
CLINICAL STUDY OVERVIEW

- The NEST Program includes two Phase 3 studies of zuranolone in patients with PPD.
- PPD-201B (ROBIN): (151 patients) A Phase 3 double-blind, placebo-controlled study evaluating the efficacy, safety and pharmacokinetics of zuranolone 30 mg in adult females diagnosed with severe PPD. Study met its primary endpoint. [[NCT02978326](#)]
- PPD-301 (SKYLARK): (200 patients) A Phase 3 double-blind, placebo-controlled study evaluating the efficacy and safety of zuranolone 50 mg in adult females diagnosed with severe PPD. Study met its primary endpoint and all key secondary endpoints. [[NCT04442503](#)]
- The efficacy and safety results for the zuranolone 50 mg SKYLARK Study were generally consistent with results from the zuranolone 30 mg ROBIN study.

Current Status:

- **NDA joint filing in MDD and PPD expected to complete in 2022**

PHASE 3 SKYLARK Study Data



[†]Statistically significant (per fixed hierarchical testing for key secondary endpoints [CFB HAMD-17 total score at Days 3, 28, and 45]); ^{††}additional timepoints [Days 8 and 21] were not adjusted for multiplicity); ^{†††}LS mean and treatment difference along with CI and p values were calculated using MMRM. *p<0.05; **p<0.01, ***p<0.001. BL = baseline; CFB = change from baseline; CI = confidence interval; HAMD-17 = 17-item Hamilton Rating Scale for Depression; KSE = key secondary endpoint; LS = least squares; MMRM = Mixed Model of Repeated Measures; SE = standard error; TRT = treatment.

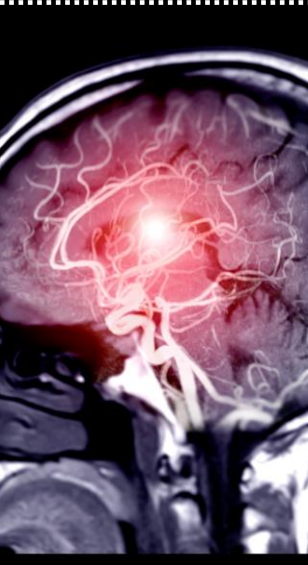
Adult patients with PPD who received treatment with zuranolone 50 mg had statistically significant improvement in depressive symptoms compared to placebo as assessed by CFB in HAMD-17 total score at the primary endpoint of Day 15. Statistically significant improvements in depressive symptoms were observed as early as Day 3, and were observed to be maintained out to Day 45.

In SKYLARK Study, zuranolone was generally well tolerated with a safety profile consistent with other LANDSCAPE and NEST clinical trials. The most common treatment-emergent adverse events observed with zuranolone in SKYLARK included somnolence, dizziness, sedation, and headache. <5% of participants treated with zuranolone in SKYLARK discontinued treatment due to AEs.

BIIB093 (IV glibenclamide)



Neuroscience



PORTFOLIO

NEUROVASCULAR PIPELINE

- ❖ BIIB093 (Ph3) – Large Hemispheric Infarction (LHI)
- ❖ BIIB131 (Ph2) – Acute Ischemic Stroke (AIS)
- ❖ BIIB093 (Ph2) – Brain Contusion (BCN)

PROPOSED MECHANISM OF ACTION

- BIIB093 inhibits the SUR1-TRPM4 non-selective cation channel, which is upregulated in the CNS during ischemia, and aims to reduce cerebral edema

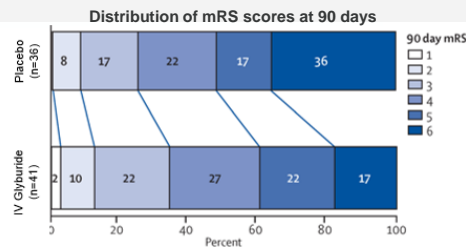
PHASE 3 CLINICAL STUDY OVERVIEW

- A first of its kind, randomized, double-blind, placebo-controlled, parallel-group, global, Phase 3 study to evaluate BIIB093's safety and efficacy in LHI patients
- Study population: Acute ischemic stroke patients aged 18 to ≤ 85 years (N=768 of which n=80 are aged 70-85) at risk of severe cerebral edema due to LHI
- BIIB093 or placebo administered as intravenous (IV) infusion over 72 hours with started within 10 hours of last known normal
- Primary endpoint is 90 Day mRS

Current Status:

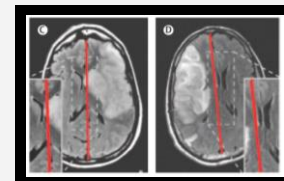
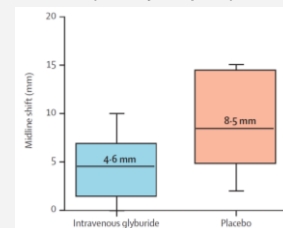
- Phase 3 CHARM study ongoing [[NCT02864953](https://clinicaltrials.gov/ct2/show/study/NCT02864953)]

PHASE 2 CLINICAL DATA



- Primary endpoint: mRS score of 0–4 at 90 days without decompressive craniectomy; OR = 1.91 did not meet statistical significance.
- 31 subjects (70.5%) in the BIIB093 group and 28 subjects (71.8%) in the placebo group experienced SAEs. 4 SAEs of hypoglycemia (all asymptomatic) occurred in the BIIB093 group vs. 0 in the placebo group - all resolved on the same day with glucose supplementation and/or reduction in study drug dose.
- Mortality at 90 days was 17% and 36% for BIIB093 and placebo groups, respectively

Reduction in Midline Shift- at 72-96 hours (Tertiary Endpoint)



BIIB131 (formerly TMS-007)



Neuroscience

PORTFOLIO

NEUROVASCULAR PIPELINE

- ❖ BIIB093 (Ph3) – Large Hemispheric Infarction (LHI)
- ❖ BIIB093 (Ph2) – Brain Contusion (BCN)

❖ **BIIB131 (Ph2) – Acute Ischemic Stroke (AIS)**

PROPOSED MECHANISM OF ACTION

- BIIB131 is a novel thrombolytic small molecule with putative dual clot-dissolving and anti-inflammatory properties, by enhancing plasminogen-fibrin binding and soluble epoxide hydrolase inhibition

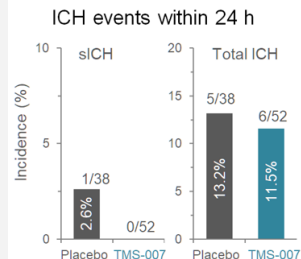
CLINICAL STUDY OVERVIEW

- Phase 2a, randomized, double-blind, placebo-controlled, dose escalation study to evaluate the safety, efficacy, PK, PD, and mechanisms of action of BIIB131 [[JapicCTI-183842](#)]
- Study population: Acute Ischemic Stroke adult patients (N=90) within 12 hours of symptom onset and <88 years old
- BIIB131 or placebo was administered as a single IV infusion over 30 minutes; dose cohorts of 1, 3 and 6mg/kg with maximum dose of 360mg
- The primary endpoint was the incidence of symptomatic intracranial hemorrhage with NIHSS deterioration of ≥4-point at 24 hours

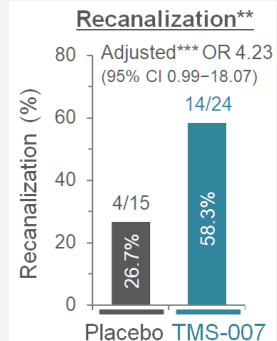
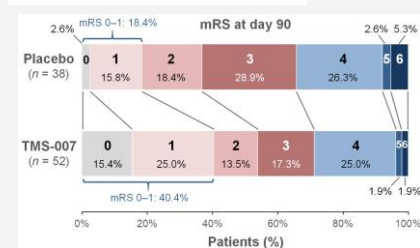
Current Status:

- Ph 2a study completed; further clinical studies to confirm safety and efficacy up to 24 hours of symptom onset are under development

PHASE 2a* CLINICAL DATA



sICH with worsening of NIHSS ≥4 points: zero (0%) in BIIB131 groups and one (2.6%) in the placebo group



**Recanalization of AUL score of 2-3 for the subset of patients that had visible occlusion on MRA at baseline
 ***Calculated from the logistic regression with covariates (treatment and participant subgroup) adjustment

* Study conducted by TMS Co., LTD
 mRS = modified Rankin Scale; sICH = symptomatic intracranial hemorrhage; NIHSS = National Institutes of Health Stroke Scale; OR = odds ratio

BIIB124/SAGE 324 (GABA_A PAM) - Essential Tremor



Neuroscience

PORTFOLIO

PARKINSON'S DISEASE AND MOVEMENT DISORDERS PIPELINE

- ❖ BIIB124 (Ph2b) – Essential Tremor (ET)
- ❖ BIIB118 (Ph1) – Irregular Sleep Wake Rhythm Disorder in Parkinson's
- ❖ BIIB122 (Ph2b) – Parkinson's disease
- ❖ BIIB101 (Ph1) – Multiple System Atrophy
- ❖ BIIB094 (Ph1) – Parkinson's disease
- ❖ BIIB132 (Ph1) – Spinocerebellar Ataxia Type 3

PROPOSED MECHANISM OF ACTION

- BIIB124 is an oral neuroactive steroid GABA_A receptor positive allosteric modulator (PAM)
- GABA_A PAMs have the potential to enhance inhibitory activity of the GABAergic system, the major inhibitory neurotransmission system in the brain
- Because deficits in inhibitory signaling may play a role in the pathophysiology of ET, GABA_A PAMs may have utility in treating ET

CLINICAL STUDY OVERVIEW

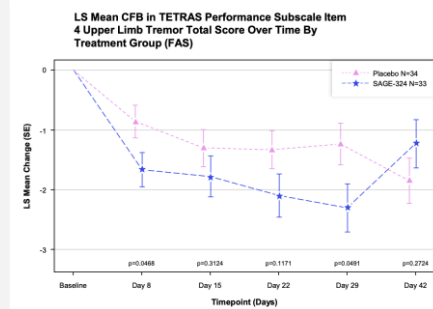
- Phase 2a, randomized, double-blind, placebo-controlled study was conducted to evaluate the efficacy, safety, and tolerability of BIIB124 [NCT04305275]
- The inclusion criteria were 18-80 years with ET diagnosis: isolated action tremor bilateral upper limb at least 3 years duration, with or without tremors in other locations and absence of other neurological signs, and willing to discontinue ET medications
- BIIB124 60 mg or placebo was administered orally in the morning for 28 days (n=69)
- The primary efficacy endpoint was change from baseline compared to placebo in the TETRAS Performance Subscale Item 4 upper limb tremor score on Day 29

Current Status:

- Ph 2b dose finding study is recruiting [NCT05173012]

PHASE 2a CLINICAL DATA

BIIB124 showed a statistically significant reduction from baseline in Upper Limb Tremor Score as measured by Item 4 of TETRAS Performance Subscale on Day 29 compared to placebo



The most common TEAEs that occurred in $\geq 10\%$ of patients in the BIIB124 treatment group and at a rate at least twice as high as that of patients in the placebo group were: somnolence 68%; dizziness 38%; balance disorder 15%; diplopia 12%; dysarthria 12%; and gait disturbance 12%

BIIB122/DNL151 (LRRK2i) - Parkinson's disease



Neuroscience

PORTFOLIO

PARKINSON'S DISEASE AND MOVEMENT DISORDERS PIPELINE

- ❖ BIIB124 (Ph2b) – Essential Tremor (ET)
- ❖ BIIB101 (Ph1) – Multiple System Atrophy
- ❖ **BIIB122 (Ph2b) – Parkinson's disease**
- ❖ BIIB132 (Ph1) – Spinocerebellar Ataxia Type 3
- ❖ BIIB094 (Ph1) – Parkinson's disease

PROPOSED MECHANISM OF ACTION

- BIIB122 is a selective, central nervous system-penetrant, small molecule inhibitor of leucine-rich repeat kinase 2 (LRRK2)
- LRRK2 activity is increased in Parkinson's disease and negatively regulates lysosomal function; LRRK2 inhibition rescues lysosomal function and normalizes protein processing
- LRRK2 inhibitors may have therapeutic potential to treat Parkinson's Disease with or without a LRRK2 mutation

CLINICAL STUDY OVERVIEW

- Two randomized, double-blind, placebo-controlled studies were conducted to evaluate the safety, tolerability, and pharmacokinetics of BIIB122 in Ph1 with 186 healthy volunteers [NCT04557800] and Ph1b with 36 PD participants [NCT04056689]
- BIIB122 doses were given in single and multiple doses of 10-400mg QD or BID for up to 14 or 28 days in Ph1; multiple doses of 80, 130, or 300mg QD for up to 28 days in Ph1b
- Key safety outcomes: adverse events, pulmonary function tests, safety labs, ECGs and vital signs
- Key pharmacodynamic outcomes: peripheral kinase inhibition (pS935), direct LRRK2 substrate (pRAB10) and downstream lysosomal function (BMP)

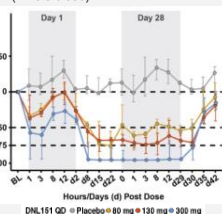
Current Status:

- Ph 2b LUMA Study in people with Parkinson's disease without a confirmed pathogenic LRRK2 mutation [NCT05348785] - **Achieved FPI May 2022**
- Phase 3 LIGHTHOUSE Study in people with Parkinson's disease with a confirmed pathogenic LRRK2 mutation [NCT05418673]– **Planned for 2022**
- LUMA and LIGHTHOUSE studies will utilize 225 mg oral once daily BIIB121 administration

PHASE 1b CLINICAL DATA

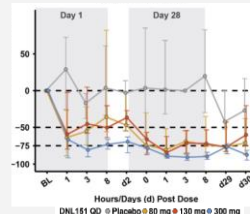
Target Engagement

Reduction of pS935 LRRK2 (Whole blood)



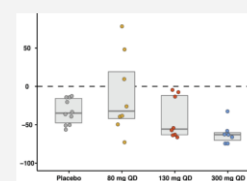
Pathway Engagement

Reduction of pRAB10 (PBMCs)



Lysosomal Function

Reduction of BMP (Urine)



- BIIB122 was generally well tolerated in healthy volunteers and PD participants
- BIIB122 demonstrated a dose-dependent reduction of pS935, with $\geq 50\%$ pS935 reduction at doses ≥ 70 mg daily and $\geq 80\%$ reduction at doses ≥ 225 mg daily
- Reduction in pRAB10 (with $\geq 70\%$ reduction in pRAB10 at doses ≥ 225 mg daily) and reduction in urine BMP at 130 and 300mg doses were observed in Ph1b

Note: BIIB122 / DNL151 is being developed in collaboration with Denali Therapeutics, Inc.
pS935= phosphorylated serine 935 LRRK2; pRAB10= phosphorylated threonine 73; BMP= bis(monoacylglycerol)phosphate

BIIB135 Orelabrutinib (BTKi) – Multiple Sclerosis



Neuroscience

PORTFOLIO

MS PIPELINE

- ❖ Orelabrutinib BIIB135 (Ph2)
- ❖ BIIB091 (Ph1)
- ❖ BIIB107 (Ph1)

PROPOSED MECHANISM OF ACTION

- Orelabrutinib is a covalent, irreversible, small molecule, CNS-penetrant Bruton's tyrosine kinase inhibitor (BTKi) with high kinase selectivity. Orelabrutinib has the potential to be a best-in-class BTK inhibitor for relapsing and progressive forms of MS.

CLINICAL STUDY OVERVIEW

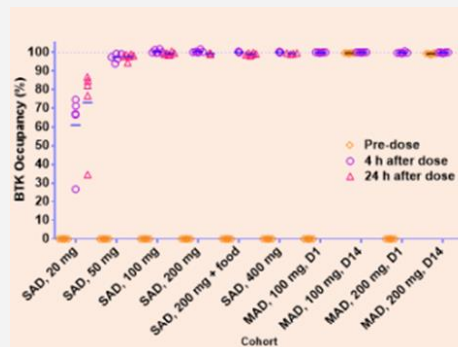
- Study ICP-CL-00112 Phase 2 in relapsing and remitting MS: is a global, placebo-controlled, double-blind, randomized trial with open-label extension
- Core randomization phase (n=160) with primary endpoint of cumulative number of new gadolinium-enhancing (GdE) T1 magnetic resonance (MRI) brain lesions versus placebo over 12 weeks of treatment.
- Key secondary endpoints: Incidence of treatment-emergent adverse events and annualized relapse rate
- The OLE part is an open-label, single treatment arm study to enroll patients who have completed the Week 24 visit in the Core Part for continued treatment and collect additional long-term safety and efficacy data. All patients will receive the low dose of Orelabrutinib from the Core part of the study.

Current Status:

Recruitment of the phase 2 study is ongoing with FPI having been achieved July 16, 2021

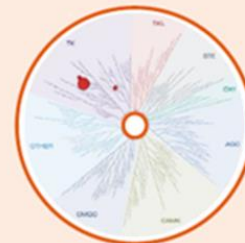
Orelabrutinib has received regulatory approval in China for several oncology indications; and received FDA breakthrough designation June 2021 for relapsed/refractory mantle cell lymphoma.

PHASE 1 CLINICAL DATA¹



- Favorable PK/PD profile in healthy volunteers
- Near 100% occupancy for 24hrs at > 50mg
- No decrease in BTK occupancy between 4 and 24hrs post-dosing

Orelabrutinib



- At 1 μ M against 456 kinases in a KINOMEScan, orelabrutinib shows significant inhibition of only BTK by >90% and demonstrates no significant inhibition of other kinases

BIIB059 (Anti-BDCA2 mAb) – Systemic Lupus Erythematosus



PORTFOLIO

LUPUS PIPELINE

- ❖ Dapirolizumab Pegol (Ph3) – Systemic Lupus Erythematosus
- ❖ **BIIB059 (Ph3) – Systemic Lupus Erythematosus**
- ❖ BIIB059 (Ph2) – Cutaneous Lupus Erythematosus

PROPOSED MECHANISM OF ACTION

- BIIB059 is a humanized monoclonal antibody that binds to BDCA2, a protein uniquely expressed on plasmacytoid dendritic cells (pDCs), thereby inhibiting the production of inflammatory mediators such as Type-I interferons (IFN-I).
- As elevated levels of IFN-I have been observed in people with SLE and CLE, inhibiting pDC production of IFN-I as well as other cytokines and chemokines may have the potential to decrease inflammation and reduce tissue damage.
- BIIB059, which selectively targets pDC production of IFN-I via BDCA2, is not expected to affect the IFN-I response to viral infection mediated by other immune cells.

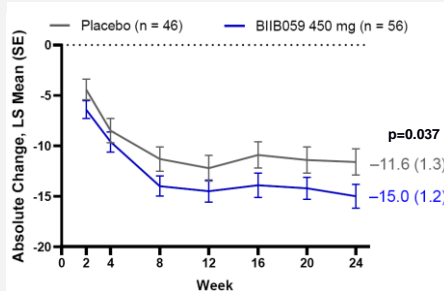
CLINICAL STUDY OVERVIEW

- Ph2 LILAC study met its primary endpoints, demonstrating a statistically significant reduction of disease activity in patients with SLE and CLE.
- Global Phase 3 TOPAZ-1 and TOPAZ-2 studies will evaluate the efficacy and safety of BIIB059, as compared to placebo, in active systemic lupus erythematosus (SLE).
- BIIB059 enrollment targets are set to reflect the prevalence of SLE in black / African American and Hispanic communities with the aim to achieve appropriate representation in the TOPAZ-1 and -2 studies.

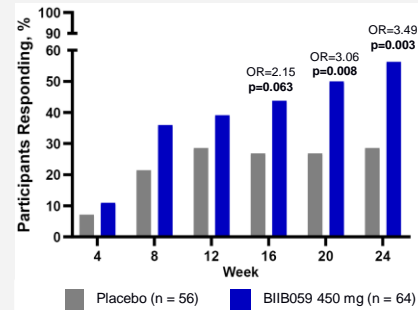
Current Status:

- TOPAZ-1 achieved FPI in June 2021; TOPAZ-2 achieved FPI in August 2021 [[NCT04895241](https://clinicaltrials.gov/ct2/show/study/NCT04895241) [NCT04961567](https://clinicaltrials.gov/ct2/show/study/NCT04961567)]

PHASE 2: CHANGE IN TOTAL ACTIVE JOINT COUNT AT WEEK 24 (Primary Endpoint)



PHASE 2: SLE RESPONDER INDEX-4 RESPONSE RATE AT WEEK 24



Furie et al., ACR 2020

- Rates of adverse events in LILAC part A were similar in placebo (67.9%) and BIIB059 (59.2%) treatment groups
- AEs in the Infections and Infestations System Organ Class occurred in 39.3% and 35.5% of participants receiving placebo and BIIB059, respectively



BIIB059 (Anti-BDCA2 mAb) – Cutaneous Lupus Erythematosus



Specialized
Immunology

PORTFOLIO

LUPUS PIPELINE

- ❖ Dapirolizumab Pegol (Ph3) – Systemic Lupus Erythematosus
- ❖ BIIB059 (Ph3) – Systemic Lupus Erythematosus
- ❖ **BIIB059 (Ph2) – Cutaneous Lupus Erythematosus**

PROPOSED MECHANISM OF ACTION

- BIIB059 is a humanized monoclonal antibody that binds to BDCA2, a protein uniquely expressed on plasmacytoid dendritic cells (pDCs), thereby inhibiting the production of inflammatory mediators such as Type-I interferons (IFN-I).
- As elevated levels of IFN-I have been observed in people with SLE and CLE, inhibiting pDC production of IFN-I as well as other cytokines and chemokines may have the potential to decrease inflammation and reduce tissue damage.
- BIIB059, which selectively targets pDC production of IFN-I via BDCA2, is not expected to affect the IFN-I response to viral infection mediated by other immune cells.

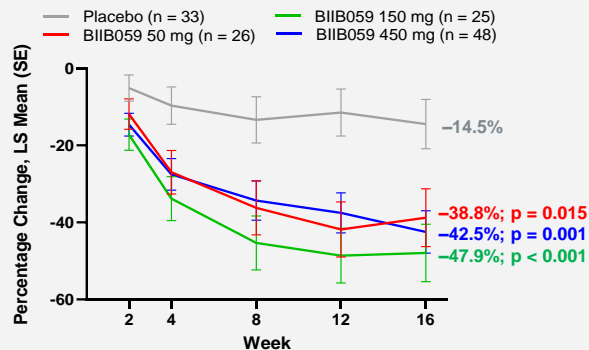
CLINICAL STUDY OVERVIEW

- Ph2 LILAC study met its primary endpoints, demonstrating a statistically significant reduction of disease activity in patients with SLE and CLE.
 - BIIB059 demonstrated a dose response on the percent change from baseline in the Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity (CLASI-A) score at week 16 in people with CLE.
- Safety and tolerability data further support the continued development of BIIB059
 - Rates of adverse events in LILAC part B were similar in the placebo (66.7%) and pooled BIIB059 (71.7%) treatment groups
 - AEs in the Infections and Infestations System Organ Class occurred in 30.3% and 34.3% of participants receiving placebo and BIIB059, respectively

Current Status:

- Currently planned pivotal study start in CLE in 2022.

PHASE 2: CHANGES IN CLASI-A SCORES FROM BASELINE TO WEEK 16



Werth et al., ACR 2020

Dapirolizumab Pegol (anti-CD40L)



Specialized
Immunology

PORTFOLIO

LUPUS PIPELINE

- ❖ Dapirolizumab Pegol (Ph3) – Systemic Lupus Erythematosus
- ❖ BIIB059 (Ph3) – Systemic Lupus Erythematosus
- ❖ BIIB059 (Ph2) – Cutaneous Lupus Erythematosus

PROPOSED MECHANISM OF ACTION

- Dapirolizumab pegol (DZP) is a polyethylene glycol (PEG)-conjugated anti-CD40L Fab' fragment, lacking a functional Fc domain
- The inhibition of CD40-CD40L interactions suppresses inflammation by reducing B cell, T-cell and APC activation, the production of pathogenic autoantibodies, and inflammatory events that can lead to organ damage accrual^{1,2}

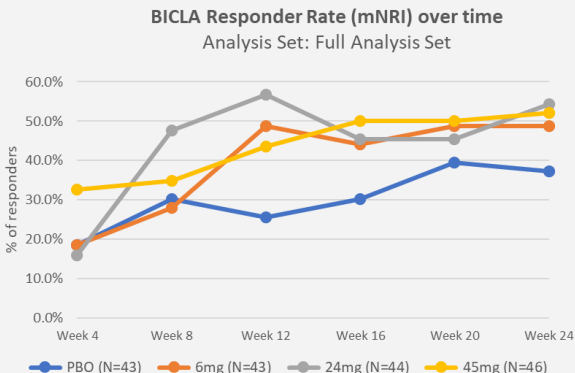
CLINICAL STUDY OVERVIEW

- Ph3 double-blind, multi-center, randomized, placebo-controlled, parallel group, global study, to evaluate the efficacy and safety of DZP in patients (N=450) with moderately to severely active SLE despite standard of care treatment. ([NCT04294667](#))
- Primary endpoint is achievement of BICLA response at Week 48.
- In the Ph2 SLE study³, although the primary endpoint (on dose response) was not met, DZP exhibited improvements across multiple clinical and immunological measures of disease activity after 24-weeks compared with placebo
 - TEAEs and serious TEAEs were generally balanced across treatment groups during the 24-week double-blind period; more upper respiratory tract infections were observed with DZP compared with placebo (e.g. nasopharyngitis 10.2% vs 4.4% and pharyngitis 8.0% vs 2.2% of patients for DZP and placebo, respectively).
- UCB/Biogen are reinforcing their commitment to the inclusion of under-represented groups in our clinical trials. Enrollment targets have been set to reflect the prevalence of SLE in Black / African American and Hispanic communities.

Current Status:

- Ph3 ongoing; first patient dosed August 2020

BICLA RESULTS FROM PHASE 2 STUDY³



¹ Ramanujam et al. Autoimmun Rev. 2020; 19(11): 102668. ² Karnell et al. Adv Drug Deliv Rev. 2019; 141: 92-103. ³ Furie et al. EULAR 2019. Furie et al. Rheumatology 2021; 60: 5397 – 5407.

Note: Dapirolizumab is being developed in collaboration with UCB; SLE = systemic lupus erythematosus; TEAE = treatment emergent adverse events; BICLA = BILAG-based composite lupus assessment



Inspired by patients.
Driven by science.



Biogen. 40

Biogen Digital Health Portfolio



PORTFOLIO FOCUS

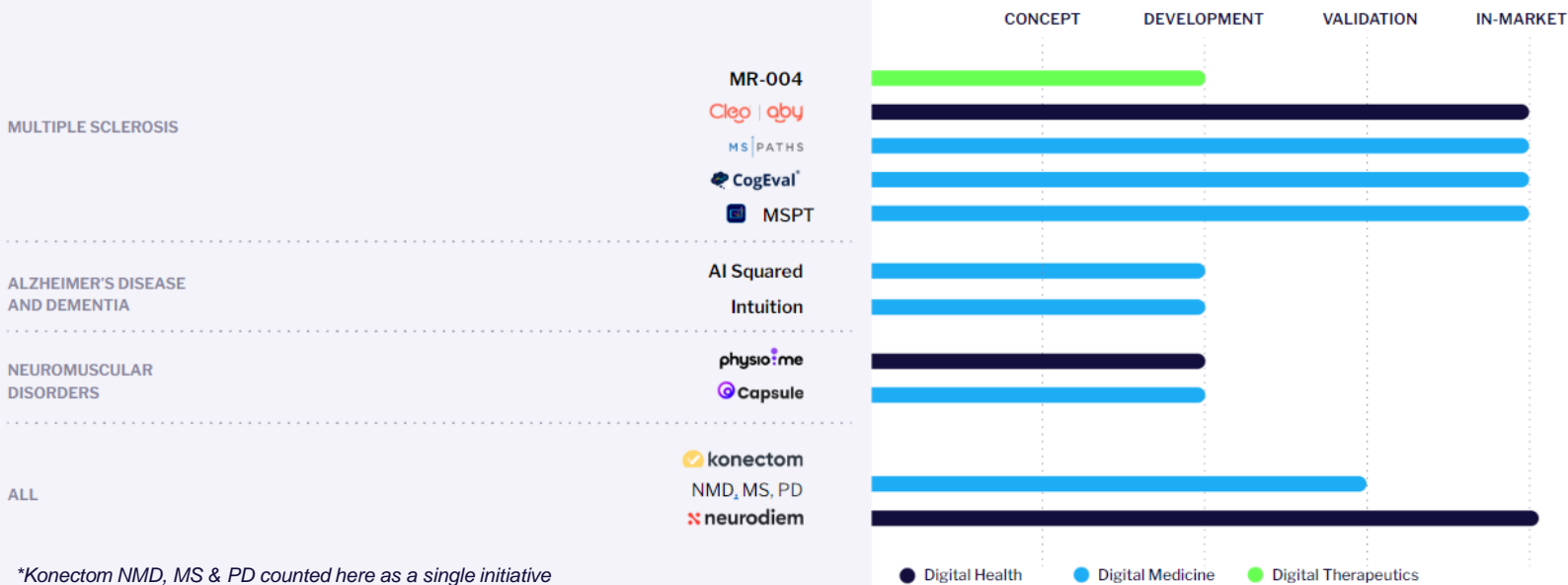
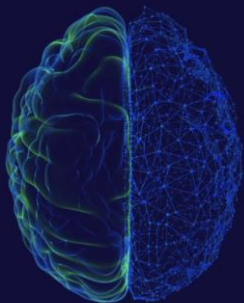
- ❖ Digital Biomarkers
- ❖ Personalized Medicine
- ❖ Patient Pathway Improvement
- ❖ Digital Therapeutics

- 11 disclosed initiatives focused across clinical development and real-world settings
- 5 initiatives in market with 6 initiatives in development or validation stages across disease areas*

VALUE CREATION OBJECTIVES

- Potentially improve efficiency of clinical development
- Evidence and companion technologies that may enhance risk/benefit profile of Biogen therapies
- Aim to expand market opportunities (screening, diagnosis, adherence, compliance)
- Potential adjacent source of revenue (prescription digital therapeutics, software as a service – imaging, digital biomarkers etc.)

Digital Health



*Konectom NMD, MS & PD counted here as a single initiative

Biogen Digital Health



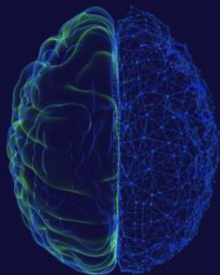
Digital Health

PORTFOLIO FOCUS

- ❖ Digital Biomarkers
- ❖ Personalized Medicine
- ❖ Patient Pathway Improvement
- ❖ Digital Therapeutics

Disease Area: Multiple Sclerosis

Initiative	Stage	Focus	Description
MR-004 - DTx	Development	MS Patients walking & independence	Biogen entered into a license agreement with MedRhythms to develop and commercialize MR-004, an investigational prescription digital therapeutic for the potential treatment of gait deficits in multiple sclerosis. The investigational prescription digital therapeutic uses a combination of sensors, software, and music based on Rhythmic Auditory Stimulation (RAS).
Cleo/Aby – <i>Digital Companion</i>	In-Market	Patient Pathway Improvement	Cleo (Aby in North America) is a digital care companion app to help people live with Multiple Sclerosis. It provides information, tips, symptoms tracking, reminders, tailored programs for self-care such as nutrition, mindfulness, and a nurse chat.
MS PATHS – <i>Research Network</i>	In-Market	Digital Biomarkers/ Personalized Medicine	Uses advanced technologies to generate & collect standardized patient data during routine office visits potentially resulting in a large, high definition and diverse real-world MS cohort.
CogEval – <i>Cognitive Assessment</i>	In-Market	Digital Biomarkers/ Personalized Medicine	CogEval is an iPad-based assessment designed to evaluate cognitive function in-clinic for patients with multiple sclerosis.
MS Performance Test – <i>Digital Biomarkers</i>	In-Market	Digital Biomarkers/ Personalized Medicine	In-clinic assessment tool that aims to objectively quantify the major motor, visual, and cognitive systems, as well as quality of life and disease history for patients with MS. HCPs can access patient results at the point of care.



Biogen Digital Health



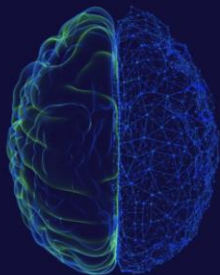
Digital Health

PORTFOLIO FOCUS

- ❖ Digital Biomarkers
- ❖ Personalized Medicine
- ❖ Patient Pathway Improvement
- ❖ Digital Therapeutics

Disease Area: Alzheimer's Disease and Dementia

Initiative	Stage	Focus	Description
AI^2 ARIA Identification – <i>Imaging AI</i>	Development	Personalized Medicine	AI-squared may be integrated in radiologist workflow/PACS and aims to provide validated, automated MRI assessment report of quantification, severity status and location of ARIA-H and ARIA-E events.
Intuition – Digital Biomarkers	Development	Digital Biomarkers	[INTUITION Study] : Virtual, observational study leveraging the Apple Watch, iPhone, and CANTAB battery to potentially discover digital biomarkers for MCI screening and potentially track cognitive changes in adults.



Biogen Digital Health



Digital Health

PORTFOLIO FOCUS

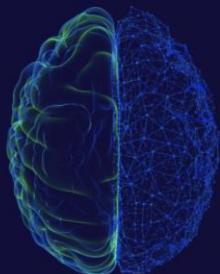
- ❖ Digital Biomarkers
- ❖ Personalized Medicine
- ❖ Patient Pathway Improvement
- ❖ Digital Therapeutics

Disease Area: Neuromuscular Disorders

Initiative	Stage	Focus	Description
Physio.me – <i>Digital Companion</i>	Development	Patient Pathway Improvement Personalized Medicine	Digital physiotherapy companion that offers to perform at-home, tailored, secure exercise so NMD patients can potentially achieve their goals, measure progress and share progress with their care team.
Capsule – <i>VR solution</i>	Development	Patient Pathway Improvement	Evidence-based medical device that combines immersion through virtual reality technology and medical hypnosis to potentially alleviate anxiety related to intrathecal injection procedures.

Disease Area: All

Initiative	Stage	Focus	Description
Konectom (MS, NMD, PD) – <i>Digital Biomarkers</i>	Validation	Digital Biomarkers/ Personalized Medicine	Smartphone-based digital measurement platform that aims to assess key neurological functions such as cognition, fine and gross motor control, walk, quality of life and mobility in clinical studies, in-clinic or remotely.
Neurodiem – <i>Digital Portal</i>	In-Market	Patient Pathway Improvement	Independent information & education portal for HCPs specialized in the care of patients with neurological diseases. Allows HCPs to access scientifically-validated, independent content to help them remain at the forefront of their practice and deliver the best care to their patients.



BYOOVIZ™ (referencing LUCENTIS®)



Biosimilars

Reference Molecule

BIOSIMILARS PIPELINE

- ❖ BYOOVIZ™ [SB11] – referencing LUCENTIS®
- ❖ Launch commenced USA June 2022
- ❖ Approvals secured by EMA, MHRA in 2H 2021, CA Q1 2022

ORIGINATOR MARKET L12M Revenue (US/ROW), \$M:

❖ Lucentis: \$1,385M US / \$2,135M ROW¹

MECHANISM OF ACTION

BYOOVIZ™ binds with high affinity to vascular endothelial growth factor (VEGF)-A isoforms (e.g. VEGF110, VEGF121 and VEGF165), thereby preventing binding of VEGF-A to its receptors VEGFR-1 and VEGFR-2. Binding of VEGF-A to its receptors leads to endothelial cell proliferation and neovascularisation, as well as vascular leakage, all of which are thought to contribute to the progression of the neovascular form of age-related macular degeneration, pathologic myopia and CNV secondary to pathologic myopia or to visual impairment caused by either diabetic macular oedema or macular oedema secondary to retinal vein occlusion in adults.

CLINICAL STUDY OVERVIEW

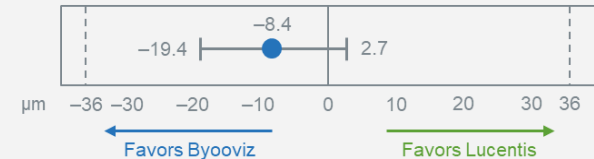
- A randomized, double-masked, parallel-group, phase III study conducted in 75 centers in 9 countries globally from March 2018 to December 2019
- Patients with nAMD were randomized (1:1) to receive either SB11 (n=351) or ranibizumab (Lucentis®) (n=354)
- Primary endpoints were:
 - Change from baseline in BCVA at Week 8 in the FAS (for US FDA)
 - Change from baseline in CST at Week 4 in the PPS-CST (for EMA)
- Secondary endpoints included change from baseline in BCVA, CST, CRLT, CNV size, proportion of subjects with active CNV leakage up to week 52, in addition to safety (ocular and non-ocular adverse events), immunogenicity and pharmacokinetics.
- Primary endpoint was met with 95% CI of LS mean difference contained within pre-defined equivalence margin. The secondary endpoint also supported similarity in efficacy.
- The safety, PK, and immunogenicity profiles were comparable between treatment groups. Observed treatment-emergent adverse events (TEAEs) were consistent with ranibizumab's safety profile, with "intraocular pressure increased" as the only ocular TEAE occurring in ≥5% of participants for both treatment groups. The most common non-ocular TEAEs were nasopharyngitis and hypertension. The most frequently reported AEs of special interest were increased intraocular pressure (SB11, 1 [0.3%]; ranibizumab, 6 [1.7%]) and iridocyclitis (SB11, 3 [0.9%]).

CLINICAL DATA OVERVIEW²

Difference of mean change in BCVA at Week 8



Difference of mean change in CST at week 4



nAMD = neovascular age-related macular degeneration; BCVA = best corrected visual acuity; FAS = full analysis set; CST = central subfield thickness; PPS-CST = per-protocol set -CST; CNV = choroidal neovascularization; CRLT = central retinal lesion thickness; CI = confidence interval.
Note: Biosimilar indications may vary by product or region;

¹SB11 refers to the Samsung Bioepis product candidate name
Source: ¹Evaluate pharma Q1 2022; ²Se Joon Woo et al.
JAMA Ophthalmol 2021;139:68–76



SB15 (referencing EYLEA®)



Biosimilars

Reference Molecule

BIOSIMILARS PIPELINE

❖ SB15ⁱ (Ph3) – referencing EYLEA®

ORIGINATOR MARKET L12M Revenue (US/ROW), \$M:

❖ Eylea® \$5,963 M US / \$4,158M ROW¹

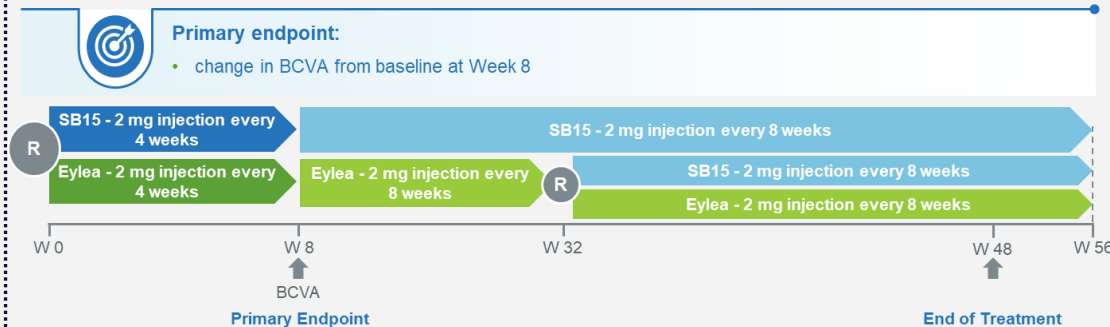
MECHANISM OF ACTION

Vascular endothelial growth factor-A (VEGF-A) and placental growth factor (PlGF) are members of the VEGF family of angiogenic factors that can act as potent mitogenic, chemotactic, and vascular permeability factors for endothelial cells. VEGF acts via two receptor tyrosine kinases; VEGFR-1 and VEGFR-2, present on the surface of endothelial cells. PlGF binds only to VEGFR-1, which is also present on the surface of leucocytes. Excessive activation of these receptors by VEGF-A can result in pathological neovascularisation and excessive vascular permeability. PlGF can synergize with VEGF-A in these processes, and is also known to promote leucocyte infiltration and vascular inflammation. Aflibercept acts as a soluble decoy receptor that binds VEGF-A and PlGF with higher affinity than their natural receptors, and thereby can inhibit the binding and activation of these cognate VEGF receptorsⁱⁱ

CLINICAL STUDY OVERVIEW

- Randomized, double-masked, parallel group, phase-III study trial conducted in 57 centers across 10 countries. Study start July 2020; completed Q1 2022
- Patients (n=449) with nAMD randomized (1:1) to receive either SB15 or aflibercept (Eylea)
- Primary-endpoints:
 - Change from baseline BCVA to BCVA at Week 8
- Secondary endpoints include efficacy, safety, immunogenicity and pharmacokinetics up to week 56.

CLINICAL DATA OVERVIEW



Data readout for SB15 expected not before Q4 2022

BCVA = best corrected visual acuity. Note: Biosimilar indications may vary by product or region.

ⁱSB15 refers to the Samsung Bioepis product candidate name; ⁱⁱ Eylea SmPC. Source: ¹Evaluate pharma Q1 2022; R indicates Randomized



BIIB800 (referencing ACTEMRA®)



Biosimilars

Reference Molecule

BIOSIMILARS PIPELINE

❖ BIIB800 [BAT1806]¹ Ph3 completed

MECHANISM OF ACTION

- IL-6 receptor signaling activates intracellular JAK MAPK and JAK-STAT3 signaling pathways involved in several inflammatory diseases, including Rheumatoid Arthritis.
- Tocilizumab binds to membrane-bound and soluble IL-6 receptor (IL-6R) thereby preventing IL-6 from binding to IL-6R, inhibiting IL-6 signaling.

CLINICAL STUDY OVERVIEW

- Phase I²: A randomized, double-blind, three-arm (RoActemra® (EU) (n=42), Actemra® (US) (n=42), BIIB800 [BAT1806] n=45)), parallel-group study of single 4 mg/kg dose administered i.v. to healthy volunteers followed for 57 days for PK, immunogenicity and safety
- Phase III³: A multicentre, randomized, double-blind, parallel-group, active-control study to compare efficacy, safety, immunogenicity, and PK of BIIB800 [BAT1806] with RoActemra® in 621 subjects with moderate to severe Rheumatoid Arthritis (RA) inadequately controlled by MTX; study comprised a ≤ 28-day screening period, a 48-week randomized treatment period, and a 4-week safety follow-up
- Biogen believes that BIIB800 [BAT1806] demonstrated equivalence in efficacy and pharmacokinetics and has a comparable safety and immunogenicity profile to the reference product⁴
- Phase III primary results poster was a narrated presentation during the EULAR Congress 2022; abstract published in ARD BMJ⁵

ORIGINATOR MARKET L12M Revenue (US/ROW), \$M:

❖ Actemra \$1,999M US / \$2,192M ROW¹

CLINICAL DATA

A Phase 3, Randomised, Double-Blind, Active-Controlled Clinical Trial to Compare BAT1806/BIIB800, a Proposed Tocilizumab Biosimilar, with a Tocilizumab Reference Product in Subjects with Moderate to Severe Rheumatoid Arthritis with an Inadequate Response to Methotrexate Therapy

Xiang, H., Chen, Y., Zhang, H., et al. (2022). A Phase 3, Randomised, Double-Blind, Active-Controlled Clinical Trial to Compare BAT1806/BIIB800, a Proposed Tocilizumab Biosimilar, with a Tocilizumab Reference Product in Subjects with Moderate to Severe Rheumatoid Arthritis with an Inadequate Response to Methotrexate Therapy. *Frontiers in Pharmacology*, 13, 895222. doi:10.3389/fphar.2022.895222

Introduction

Objectives

Methods

Results

Conclusions

POS0287

EULAR 13-14 June 2022 | Copenhagen, Denmark

Note: Biosimilar indications may vary by product or region. ¹BAT1806 refers to the Bio-Thera Solutions product candidate name. Source: ¹Evaluate Pharma Q1 2022; ²Zhang H et al. Front Pharmacol. 2021;11:609522. doi: 10.3389/fphar.2020.609522; ³ www.clinicaltrialsregister.eu/ctr-search/trial/2018-002202-31/BG.

⁴ <https://investors.biogen.com/news-releases/news-release-details/biogen-and-bio-thera-announce-positive-results-phase-3-study>

⁵ https://ard.bmj.com/content/81/Suppl_1/388.2



BIIB801 (referencing CIMZIA®)



Biosimilars



Reference Molecule

BIOSIMILARS PIPELINE

- ❖ BIIB801 [Pre-Clinical]

ORIGINATOR MARKET L12M Revenue (US/ROW), \$M:

- ❖ Cimzia \$1,399M US / \$779M ROW¹

MECHANISM OF ACTION

Certolizumab-pegol is a novel Fc-free, PEGylated, anti-TNF α monoclonal antibody, which binds and neutralizes soluble and transmembrane TNF α . This blocks the interaction between TNF α and TNF α receptors type 1 and 2 (TNFR1 and TNFR2), thereby neutralizing the NF- κ B transduction pathway. Lacking an Fc region, certolizumab pegol does not induce apoptosis nor cause antibody-dependent cell-mediated cytotoxicity, while the PEG molecule provides advantages for half-life, solubility, stability and immunogenicity.

INDICATIONS OVERVIEW^{2, 3}

CIMZIA is a tumor necrosis factor (TNF) blocker indicated for:

- Reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy⁴
- Treatment of adults with moderately to severely active rheumatoid arthritis
- Treatment of adult patients with active psoriatic arthritis
- Treatment of adults with active ankylosing spondylitis⁴
- Treatment of adults with axial spondyloarthritis⁵
- Treatment of adults with plaque psoriasis⁵

CLINICAL STUDY OVERVIEW

- Preclinical development work ongoing
- Mapping of the Clinical Development Plan is in progress

COMMERCIAL AGREEMENT OVERVIEW

- Biogen will be the Marketing Authorization Holder
- Unlimited duration of agreement
- Global scope

Note: Biosimilar indications may vary by product or region. Source: ¹ Evaluate pharma 2021; ² FDA database; ³ EMA database; ⁴ FDA only; ⁵ EMA only

Lecanemab collaboration accounting

Collaboration Economics

- Both companies share collaboration profits and losses equally

Revenue

- Eisai will record 100% of product revenue
- After regulatory approval, Biogen's 50% share of profits and losses will be reflected as a component of Other Revenue

Royalties

- Eisai will pay BioArctic AB royalties in the high single-digits
- Biogen's 50% share these royalties will be reflected as a net reduction of Other Revenue

SG&A Expense

- Prior to regulatory approval: The net reimbursement to Eisai will be recorded as an expense within SG&A
- After regulatory approval: The net reimbursement to Eisai will be recorded as a net reduction of Other Revenue

R&D Expense

- Biogen's share of expenditures are recorded within R&D expense, both before and after regulatory approval

Accounting for the manufacturing and sale of lecanemab inventory to Eisai:

Biogen

- Biogen will manufacture the lecanemab drug substance in its Solothurn, Switzerland facility
- As product is manufactured, Biogen will capitalize as inventory until sold to Eisai

Inventory

Biogen will recognize contract manufacturing revenue and contract manufacturing cost of goods sold at a minimal gross margin

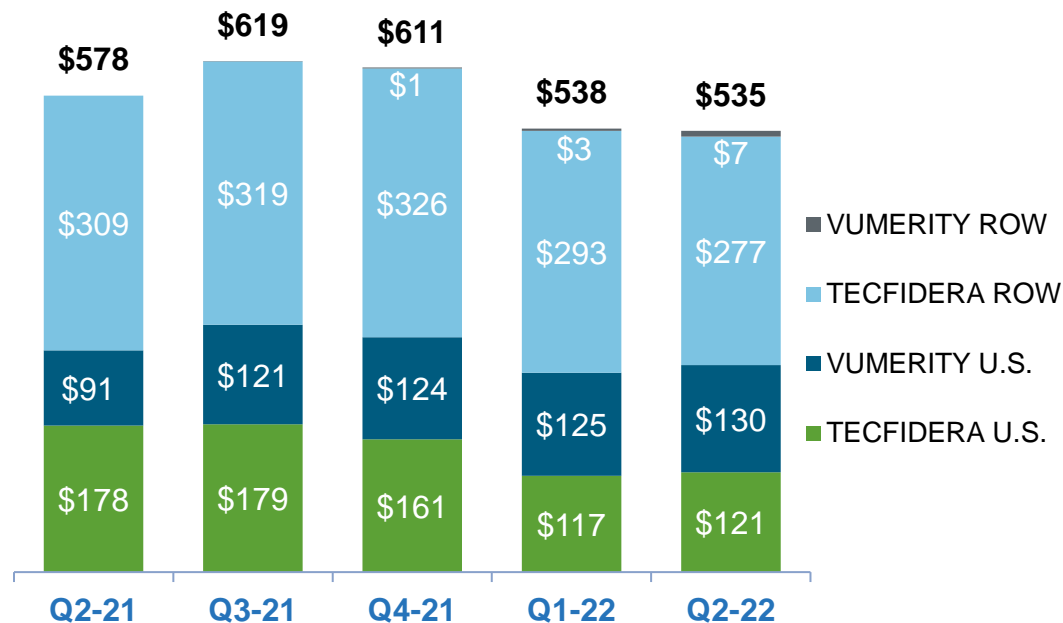
Eisai

- As Eisai sells lecanemab inventory to customers, Biogen will record its 50% share of cost of goods sold, which will be reflected as a reduction of Other Revenue

Global fumarate revenue



Fumarate Revenue (\$M)



Q2 2022 Highlights

Revenue vs. Q2 2021 and Q1 2022

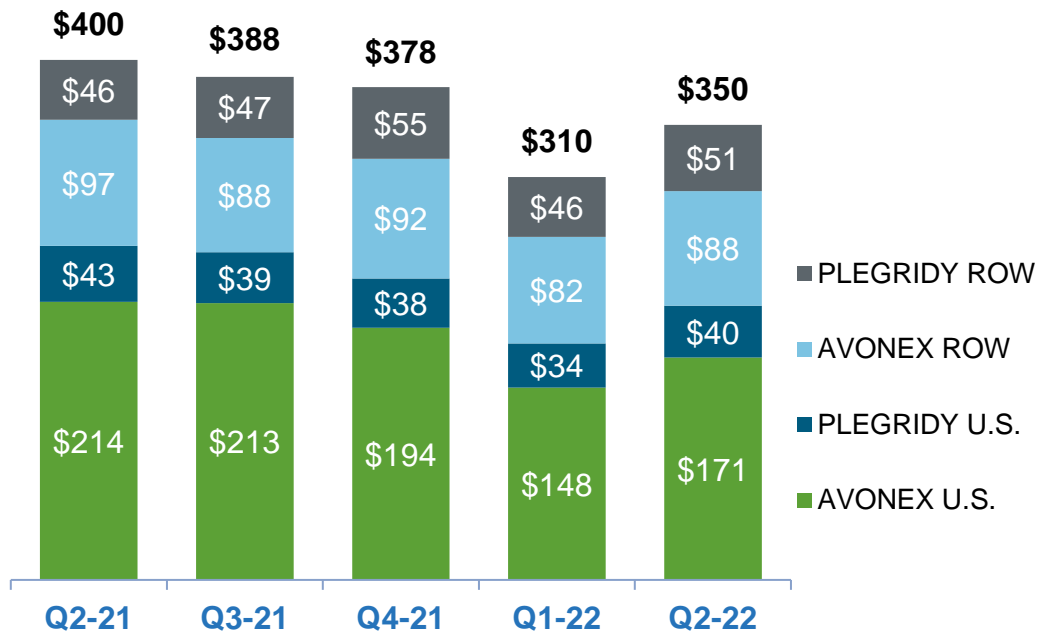
	<u>ΔY/Y</u>		<u>ΔQ/Q</u>
WW	- 8%	and	- 1%
ROW	- 8%	and	- 4%
U.S.	- 7%	and	+ 3%

- U.S. Tecfidera increased versus the first quarter of 2022 primarily due to channel dynamics

Global interferon revenue



Interferon Revenue (\$M)



Numbers may not foot or recalculate due to rounding.

Q2 2022 Highlights

Revenue vs. Q2 2021 and Q1 2022

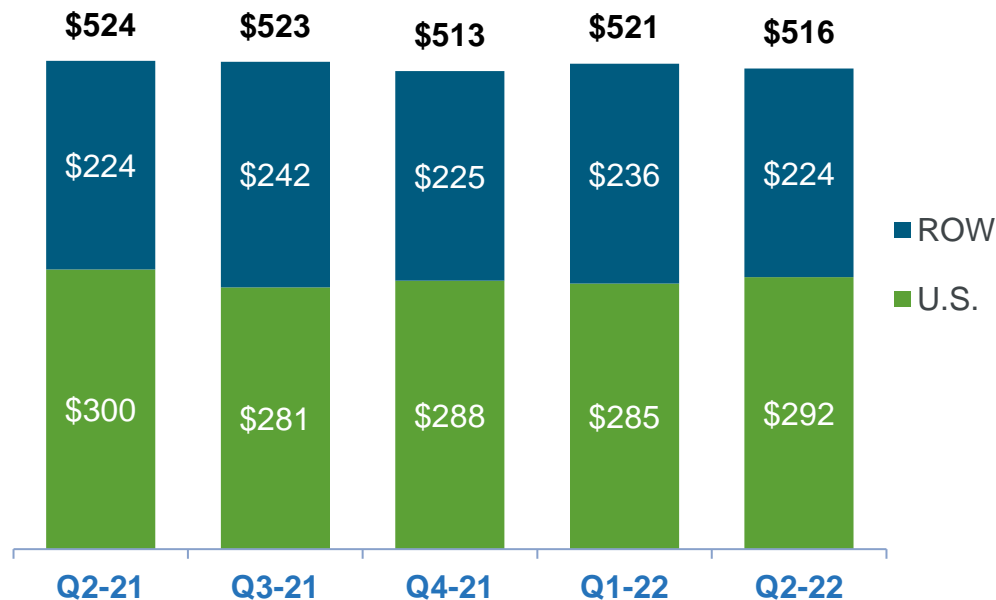
	<u>ΔY/Y</u>	and	<u>ΔQ/Q</u>
WW	- 13%		+ 13%
ROW	- 3%		+ 9%
U.S.	- 18%		+ 16%

- Global interferon revenue increased 13% at actual currency and 14% at constant currency versus the first quarter of 2022 primarily due to seasonality and channel dynamics in the U.S.

Global TYSABRI revenue



TYSABRI Revenue (\$M)



Numbers may not foot or recalculate due to rounding.

Q2 2022 Highlights

Revenue vs. Q2 2021 and Q1 2022

	<u>ΔY/Y</u>		<u>ΔQ/Q</u>
WW	- 2%	and	- 1%
ROW	- 0%	and	- 5%
U.S.	- 3%	and	+ 3%

Consolidated Statement of Income

(unaudited, in millions, except per share amounts)

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2022	2021	2022	2021
Revenue:				
Product, net	\$ 2,054.9	\$ 2,236.0	\$ 4,121.2	\$ 4,447.7
Revenue from anti-CD20 therapeutic programs	436.3	440.0	835.7	829.0
Other	97.9	99.0	164.0	192.3
Total revenue	2,589.1	2,775.0	5,120.9	5,469.0
Cost and expense:				
Cost of sales, excluding amortization and impairment of acquired intangible assets	484.0	459.7	1,237.9	937.8
Research and development	528.6	585.1	1,080.3	1,099.3
Selling, general and administrative	572.6	637.3	1,207.5	1,232.3
Amortization and impairment of acquired intangible assets	67.5	604.1	134.4	702.2
Collaboration profit (loss) sharing	29.4	(15.2)	(87.9)	53.3
(Gain) loss on fair value remeasurement of contingent consideration	(4.5)	0.3	(11.6)	(33.5)
Acquired in-process research and development	—	18.0	—	18.0
Restructuring charges	70.6	—	108.7	—
Other (income) expense, net	(428.6)	(96.4)	(165.3)	410.5
Total cost and expense	1,319.6	2,192.9	3,504.0	4,419.9
Income before income tax expense and equity in loss of investee, net of tax	1,269.5	582.1	1,616.9	1,049.1
Income tax (benefit) expense	216.7	(409.1)	342.3	(364.9)
Equity in (income) loss of investee, net of tax	(5.9)	(34.3)	(2.6)	(16.1)
Net income	1,058.7	1,025.5	1,277.2	1,430.1
Net income (loss) attributable to noncontrolling interests, net of tax	0.7	577.0	(84.6)	571.4
Net income attributable to Biogen Inc.	\$ 1,058.0	\$ 448.5	\$ 1,361.8	\$ 858.7
Net income per share:				
Basic earnings per share attributable to Biogen Inc.	\$ 7.25	\$ 3.00	\$ 9.30	\$ 5.70
Diluted earnings per share attributable to Biogen Inc.	\$ 7.24	\$ 2.99	\$ 9.27	\$ 5.68
Weighted-average shares used in calculating:				
Basic earnings per share attributable to Biogen Inc.	145.9	149.7	146.5	150.8
Diluted earnings per share attributable to Biogen Inc.	146.2	150.1	146.8	151.2

GAAP to Non-GAAP Reconciliation

Operating Expense, Other (Income) Expense, net and Income Tax
(unaudited, in millions, except per share amounts)

(In millions, except per share amounts)	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2022 ⁽¹⁾	2021 ^(1,2)	2022 ⁽¹⁾	2021 ^(1,2)
Selling, General and Administrative Expense:				
Total selling, general and administrative, GAAP	\$ 572.6	\$ 637.3	\$ 1,207.5	\$ 1,232.3
Less: other	2.2	2.0	2.0	2.2
Total selling, general and administrative, Non-GAAP	\$ 570.4	\$ 635.3	\$ 1,205.5	\$ 1,230.1
Amortization and Impairment of Acquired Intangible Assets:				
Total amortization and impairment of acquired intangible assets, GAAP	\$ 67.5	\$ 604.1	\$ 134.4	\$ 702.2
Less: impairment charges ^A	—	541.6	—	585.9
Less: amortization of acquired intangible assets	60.2	62.5	119.5	116.3
Total amortization and impairment of acquired intangible assets, Non-GAAP	\$ 7.3	\$ —	\$ 14.9	\$ —
(Gain) Loss on Fair Value Remeasurement of Contingent Consideration:				
Total (gain) loss on fair value remeasurement of contingent consideration, GAAP	\$ (4.5)	\$ 0.3	\$ (11.6)	\$ (33.5)
Less: (gain) loss on fair value remeasurement of contingent consideration	(4.5)	0.3	(11.6)	(33.5)
Total (gain) loss on fair value remeasurement of contingent consideration, Non-GAAP	\$ —	\$ —	\$ —	\$ —
Other (Income) Expense, net:				
Total other (income) expense, net, GAAP	\$ (428.6)	\$ (96.4)	\$ (165.3)	\$ 410.5
Less: (gain) loss on equity security investments	77.2	(154.3)	267.9	281.8
Less: (gain) on sale of equity interest in Samsung Bioepis ^B	(1,505.3)	—	(1,505.3)	—
Less: litigation settlement agreed to in principle ^C	900.0	—	900.0	—
Less: other	\$ 20.0	\$ —	\$ 20.0	\$ 9.5
Total other (income) expense, net, Non-GAAP	\$ 79.5	\$ 57.9	\$ 152.1	\$ 119.2
Income Tax (Benefit) Expense:				
Total income tax (benefit) expense, GAAP	\$ 216.7	\$ (409.1)	\$ 342.3	\$ (364.9)
Less: Neurimmune step-up tax basis ^D	—	(492.0)	83.9	(492.0)
Less: international reorganization & income tax effect related to Non-GAAP reconciling items	81.5	(79.6)	25.6	(188.7)
Total income tax expense, Non-GAAP	\$ 135.2	\$ 162.5	\$ 232.8	\$ 315.8
Effective Tax Rate:				
Total effective tax rate, GAAP	17.1 %	(70.3)%	21.2 %	(34.8)%
Less: Neurimmune step-up tax basis ^D	—	(84.5)	5.2	(46.9)
Less: impact of GAAP to Non-GAAP adjustments	1.9	(1.5)	0.7	(3.6)
Total effective tax rate, Non-GAAP	15.2 %	15.7 %	15.3 %	15.7 %

Use of Non-GAAP Financial Measures

We supplement our GAAP consolidated financial statements and GAAP financial measures with other financial measures, such as adjusted net income, adjusted diluted earnings per share, revenue growth at constant currency, which excludes the impact of changes in foreign exchange rates and hedging gains or losses, and free cash flow, which is defined as net flow from operations less capital expenditures. We believe that these and other Non-GAAP financial measures provide additional insight into the ongoing economics of our business and reflect how we manage our business internally, set operational goals and form the basis of our management incentive programs. Non-GAAP financial measures are in addition to, not a substitute for, or superior to, measures of financial performance prepared in accordance with GAAP.

Our “Non-GAAP net income attributable to Biogen Inc.” and “Non-GAAP earnings per share - Diluted” financial measures exclude the following items from “GAAP net income attributable to Biogen Inc.” and “GAAP earnings per share - Diluted”:

1. Acquisitions and divestitures

We exclude transaction, integration and certain other costs related to the acquisition and divestiture of businesses and items associated with the initial consolidation or deconsolidation of variable interest entities. These adjustments include, but are not limited to, the amortization and impairment of intangible assets, charges or credits from the fair value remeasurement of our contingent consideration obligations and losses on assets and liabilities held for sale.

2. Restructuring, business transformation and other cost saving initiatives

We exclude costs associated with our execution of certain strategies and initiatives to streamline operations, achieve targeted cost reductions, rationalize manufacturing facilities or refocus research and development activities. These costs may include employee separation costs, retention bonuses, facility closing and exit costs, asset impairment charges or additional depreciation when the expected useful life of certain assets have been shortened due to changes in anticipated usage and other costs or credits that management believes do not have a direct correlation to our ongoing or future business operations.

3. (Gain) loss on equity security investments

We exclude unrealized and realized gains and losses and discounts or premiums on our equity security investments as we do not believe that these components of income or expense have a direct correlation to our ongoing or future business operations.

4. Other items

We evaluate other items of income and expense on an individual basis and consider both the quantitative and qualitative aspects of the item, including (i) its size and nature, (ii) whether or not it relates to our ongoing business operations and (iii) whether or not we expect it to occur as part of our normal business on a regular basis. We also include an adjustment to reflect the related tax effect of all reconciling items within our reconciliation of our GAAP to Non-GAAP net income attributable to Biogen Inc. and earnings per share - diluted.

GAAP to Non-GAAP Reconciliation

Equity (Income)/Loss of Investee, Noncontrolling Interests, Net Income & Diluted EPS
(unaudited, in millions, except per share amounts)

(In millions, except per share amounts)	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2022 ⁽¹⁾	2021 ^(1,2)	2022 ⁽¹⁾	2021 ^(1,2)
Equity in (Income) Loss of Investee, Net of Tax:				
Total equity in (income) loss of investee, GAAP	\$ (5.9)	\$ (34.3)	\$ (2.6)	\$ (16.1)
Less: amortization of equity in (income) loss of investee	7.1	16.0	14.4	23.2
Total equity in (income) loss of investee, Non-GAAP	\$ (13.0)	\$ (50.3)	\$ (17.0)	\$ (39.3)
Net Income (Loss) Attributable to Noncontrolling Interests, Net of Tax:				
Total net income (loss) attributable to noncontrolling interests, GAAP	\$ 0.7	\$ 577.0	\$ (84.6)	\$ 571.4
Less: Neurimmune step-up tax basis ^D	—	492.0	(83.9)	492.0
Less: other	—	0.9	(1.5)	(4.4)
Total net income (loss) attributable to noncontrolling interests, Non-GAAP	\$ 0.7	\$ 84.1	\$ 0.8	\$ 83.8
Net Income Attributable to Biogen Inc.:				
Total net income attributable to Biogen Inc., GAAP	\$ 1,058.0	\$ 448.5	\$ 1,361.8	\$ 858.7
Plus: impairment charges ^A	—	541.6	—	585.9
Plus: amortization of acquired intangible assets	60.2	62.5	119.5	116.3
Plus: restructuring charges	70.6	—	108.7	—
Plus: (gain) loss on fair value remeasurement of contingent consideration	(4.5)	0.3	(11.6)	(33.5)
Plus: (gain) loss on equity security investments	77.2	(154.3)	267.9	281.8
Plus: noncontrolling interests, amortization of equity in (income) loss of investee & other	7.1	16.9	12.9	18.8
Plus: premium paid on debt exchange or early debt redemption	—	—	—	—
Plus: gain on sale of equity interest in Samsung Bioepis ^B	(1,505.3)	—	(1,505.3)	—
Plus: litigation settlement agreed to in principle ^C	900.0	—	900.0	—
Plus: international reorganization & income tax effect related to Non-GAAP reconciling items	81.5	(79.6)	25.6	(188.7)
Plus: other	22.2	2.1	22.1	11.7
Total net income attributable to Biogen Inc., Non-GAAP	\$ 767.0	\$ 838.0	\$ 1,301.6	\$ 1,651.0
Diluted Earnings Per Share				
Total diluted earnings per share, GAAP	\$ 7.24	\$ 2.99	\$ 9.27	\$ 5.68
(Less) Plus: adjustments to GAAP net income attributable to Biogen Inc. (as detailed above)	(1.99)	2.59	(0.41)	5.24
Total diluted earnings per share, Non-GAAP	\$ 5.25	\$ 5.58	\$ 8.86	\$ 10.92

⁽¹⁾ Beginning in the second quarter of 2021 material upfront payments and premiums paid on the acquisition of common stock associated with significant collaboration and licensing arrangements along with the related transaction costs incurred are no longer excluded from Non-GAAP research and development expense and selling, general and administrative expense. Beginning in the first quarter of 2022 material payments paid on the acquisition of in-process research and development assets are no longer excluded in the determination of Non-GAAP net income. Prior period Non-GAAP results have been updated to reflect these changes.

⁽²⁾ Beginning in the third quarter of 2021 amortization expense recorded in intangible assets that arose from collaboration and licensing arrangements is no longer excluded from our Non-GAAP results on a prospective basis. Non-GAAP financial results prior to the third quarter of 2021 have not been updated to reflect this change.

GAAP to Non-GAAP Reconciliation

Constant Currency & Free Cash Flow
(unaudited, in millions)

Revenue growth at constant currency vs. 2021

Percentage changes in revenue growth at constant currency are presented excluding the impact of changes in foreign currency exchange rates and hedging gains or losses. The current period's foreign currency revenue values are converted into U.S. dollars using the average exchange rates from the prior period.

	For the Three Months Ended June 30, 2022 vs. Comparable Period in 2021	For the Six Months Ended June 30, 2022 vs. Comparable Period in 2021
Total Revenue		
Revenue change, as reported	(6.7)%	(6.4)%
Less: impact of foreign currency translation and hedging gains / losses	(1.7)	(1.6)
Revenue change at constant currency	(5.0)%	(4.8)%
Total MS Revenue (including OCREVUS royalties)		
Revenue change, as reported	(3.8)%	(3.3)%
Less: impact of foreign currency translation and hedging gains / losses	(1.1)	(0.9)
Revenue change at constant currency	(2.7)%	(2.4)%
Total TECFIDERA Revenue		
Revenue change, as reported	(18.4)%	(16.5)%
Less: impact of foreign currency translation and hedging gains / losses	(1.9)	(1.1)
Revenue change at constant currency	(16.5)%	(15.4)%
Total VUMERITY Revenue		
Revenue change, as reported	50.6 %	60.9 %
Less: impact of foreign currency translation and hedging gains / losses	(0.9)	(0.6)
Revenue change at constant currency	51.5 %	61.5 %
Total TYSABRI Revenue		
Revenue change, as reported	(1.5)%	0.9 %
Less: impact of foreign currency translation and hedging gains / losses	(1.2)	(1.0)
Revenue change at constant currency	(0.3)%	1.9 %
Total INTERFERON Revenue		
Revenue change, as reported	(12.5)%	(17.6)%
Less: impact of foreign currency translation and hedging gains / losses	(1.2)	(1.0)
Revenue change at constant currency	(11.3)%	(16.6)%
Total SPINRAZA Revenue		
Revenue change, as reported	(13.8)%	(11.4)%
Less: impact of foreign currency translation and hedging gains / losses	(2.7)	(2.8)
Revenue change at constant currency	(11.1)%	(8.6)%
Total Biosimilars Revenue		
Revenue change, as reported	(4.0)%	(4.6)%
Less: impact of foreign currency translation and hedging gains / losses	(6.5)	(5.6)
Revenue change at constant currency	2.5 %	1.0 %

Revenue growth at constant currency vs. Q1 2022

	For the Three Months Ended June 30, 2022 vs. Three Months Ended March 31, 2022
Total INTERFERON Revenue	
Revenue change, as reported	13.2 %
Less: impact of foreign currency translation and hedging gains / losses	(1.0)
Revenue change at constant currency	14.2 %
Total SPINRAZA Revenue	
Revenue change, as reported	(8.8)%
Less: impact of foreign currency translation and hedging gains / losses	(0.4)
Revenue change at constant currency	(8.4)%

Free cash flow

We define free cash flow as net cash provided by (used in) operating activities in the period less capital expenditures made in the period. The following table reconciles net cash provided by (used in) operating activities, a GAAP measure, to free cash flow, a Non-GAAP measure.

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2022	2021	2022	2021
Cash Flow:				
Net cash provided by (used in) operating activities	\$ 736.5	\$ 1,227.3	\$ 898.3	\$ 1,996.3
Net cash provided by (used in) investing activities	693.5	(152.7)	45.5	(217.4)
Net cash provided by (used in) financing activities	(471.5)	(564.5)	(488.0)	(1,349.5)
Net increase (decrease) in cash and cash equivalents	<u>\$ 958.5</u>	<u>\$ 510.1</u>	<u>\$ 455.8</u>	<u>\$ 429.4</u>
Net cash provided by (used in) operating activities	\$ 736.5	\$ 1,227.3	\$ 898.3	\$ 1,996.3
Less: Purchases of property, plant and equipment	36.9	71.9	94.8	164.5
Free cash flow	\$ 699.6	\$ 1,155.4	\$ 803.5	\$ 1,831.8

Notes to GAAP to Non-GAAP Reconciliation

Operating Expense & Net Income Attributable to Biogen Inc.

^A Amortization and impairment of acquired intangible assets for the three and six months ended June 30, 2022, compared to the same periods in 2021, decreased primarily due to \$585.9 million of impairment charges recorded during 2021.

For the three and six months ended June 30, 2022, we had no impairment charges. For the three months ended June 30, 2021, amortization and impairment of acquired intangible assets reflects a \$350.0 million impairment charge related to BIIB111 (timrepigene emparvovec) for the potential treatment of choroideremia and a \$191.6 million impairment charge related to BIIB112 (cotoretigene toliparvovec) for the potential treatment of X-linked retinitis pigmentosa.

For the six months ended June 30, 2021, amortization and impairment of acquired intangible assets also reflects a \$44.3 million impairment charge related to vixotrigine (BIIB074) for the potential treatment of trigeminal neuralgia (TGN).

During the second quarter of 2021 we announced that our Phase 3 STAR study of BIIB111 did not meet its primary or key secondary endpoints. We reassessed the fair value of the program based on the results of this study and recognized an impairment charge of \$350.0 million during the second quarter of 2021, which resulted in a reduction of the IPR&D intangible asset from \$365.0 million to \$15.0 million.

During the second quarter of 2021 we announced that our Phase 2/3 XIRIUS study of BIIB112 did not meet its primary endpoint; however, positive trends were observed across several clinically relevant prespecified secondary endpoints. We reassessed the fair value of the program based on the results of this study and recognized an impairment charge of \$191.6 million during the second quarter of 2021, which resulted in a reduction of the IPR&D intangible asset from \$220.0 million to \$28.4 million.

^B In April 2022 we completed the sale of our 49.9% equity interest in Samsung Bioepis to Samsung BioLogics. Under the terms of this transaction, we received approximately \$1.0 billion in cash at closing and expect to receive approximately \$1.3 billion to be deferred over two payments of approximately \$812.5 million due at the first anniversary and approximately \$437.5 million due at the second anniversary of the closing of the transaction. For the three and six months ended June 30, 2022, we recognized a pre-tax gain of approximately \$1.5 billion related to the transaction, which was recorded in other (income) expense, net in our condensed consolidated statements of income.

Notes to GAAP to Non-GAAP Reconciliation

Operating Expense & Net Income Attributable to Biogen Inc.

^c For the three months ended June 30, 2022, we recorded \$900.0 million related to an agreement in principle to resolve previously disclosed qui tam litigation relating to conduct prior to 2015. This agreement in principle does not include any admission of liability and is subject to the negotiation of final settlement agreements and documents.

^d For the three and six months ended June 30, 2022, compared to the same periods in 2021, the increases in our GAAP effective tax rate was primarily due to a deferred tax expense related to a valuation allowance, as discussed below, and the non-cash tax effects of changes in the value of our equity investments. The tax effects of this change in value of our equity investments were recorded discretely, since changes in value of equity investments cannot be forecasted.

During the second quarter of 2021 we recorded a net deferred tax asset in Switzerland of approximately \$490.0 million on Neurimmune SubOne AG's (Neurimmune) tax basis in ADUHELM, the realization of which is dependent on future sales of ADUHELM. During the fourth quarter of 2021, due to reduced future expected revenue associated with ADUHELM, we recorded a valuation allowance of approximately \$390.0 million.

During the first quarter of 2022, upon issuance of the final NCD related to ADUHELM, we recorded an additional valuation allowance of approximately \$85.0 million to reduce the net value of this deferred tax asset to zero. These adjustments to our deferred tax assets and their valuation allowances are each recorded with an equal and offsetting amount assigned to net income (loss) attributable to noncontrolling interests, net of tax in our condensed consolidated statements of income, resulting in a zero net impact to net income attributable to Biogen Inc.