

where
science meets **humanity**[™]

Third Quarter 2022

Financial Results and Business Update



October 25, 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 57-61 of this presentation and in the Q3 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; 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; 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; 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 technology failures or breaches; problems with our manufacturing processes; risks relating to management and personnel changes, including attracting and retaining 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; 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; fluctuations in our effective tax rate; 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.

Q3 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



Significant achievement in Alzheimer's disease

Lecanemab Phase 3 Clarity AD study met the primary and all key secondary endpoints in early Alzheimer's disease

- *Highly statistically significant change on CDR-SB vs. placebo, with efficacy as early as 6-months and a treatment effect that expanded over the 18-month study period on an absolute basis*
- *Slowing of clinical decline on all key secondary endpoints assessing multiple domains of Alzheimer's disease*
- *Incidence of ARIA (ARIA-E and/or ARIA-H) was 21.3% for lecanemab vs. 9.3% for placebo*
- ***Lecanemab has the potential to be the first globally approved treatment to slow the progression of Alzheimer's disease***

Biogen is continuing to advance a diversified portfolio of programs in Alzheimer's disease including B1IB080



Note: lecanemab is being developed with Eisai Co., Ltd
ARIA = amyloid-related imaging abnormalities; CDR-SB = clinical dementia rating scale – sum of boxes



Near-term opportunities in depression and ALS

Profile of zuranolone demonstrated in clinical trials highlights potential to be a meaningful new treatment in depression

- *Novel hypothesized mechanism of action*
- *Observed rapid onset of efficacy in as little as 3 days*
- *Consistent safety and tolerability results across studies with no incidence of sexual dysfunction or weight gain reported to date*
- ***U.S. regulatory filing for zuranolone in MDD and PPD expected to complete in H2 2022****

Tofersen has the potential to be the first genetically targeted therapy in SOD1-ALS, a rare genetic form of ALS

- *Regulatory filing for tofersen in SOD1-ALS accepted by the FDA under the accelerated approval pathway and granted priority review*
- ***U.S. FDA PDUFA date of April 25, 2023***

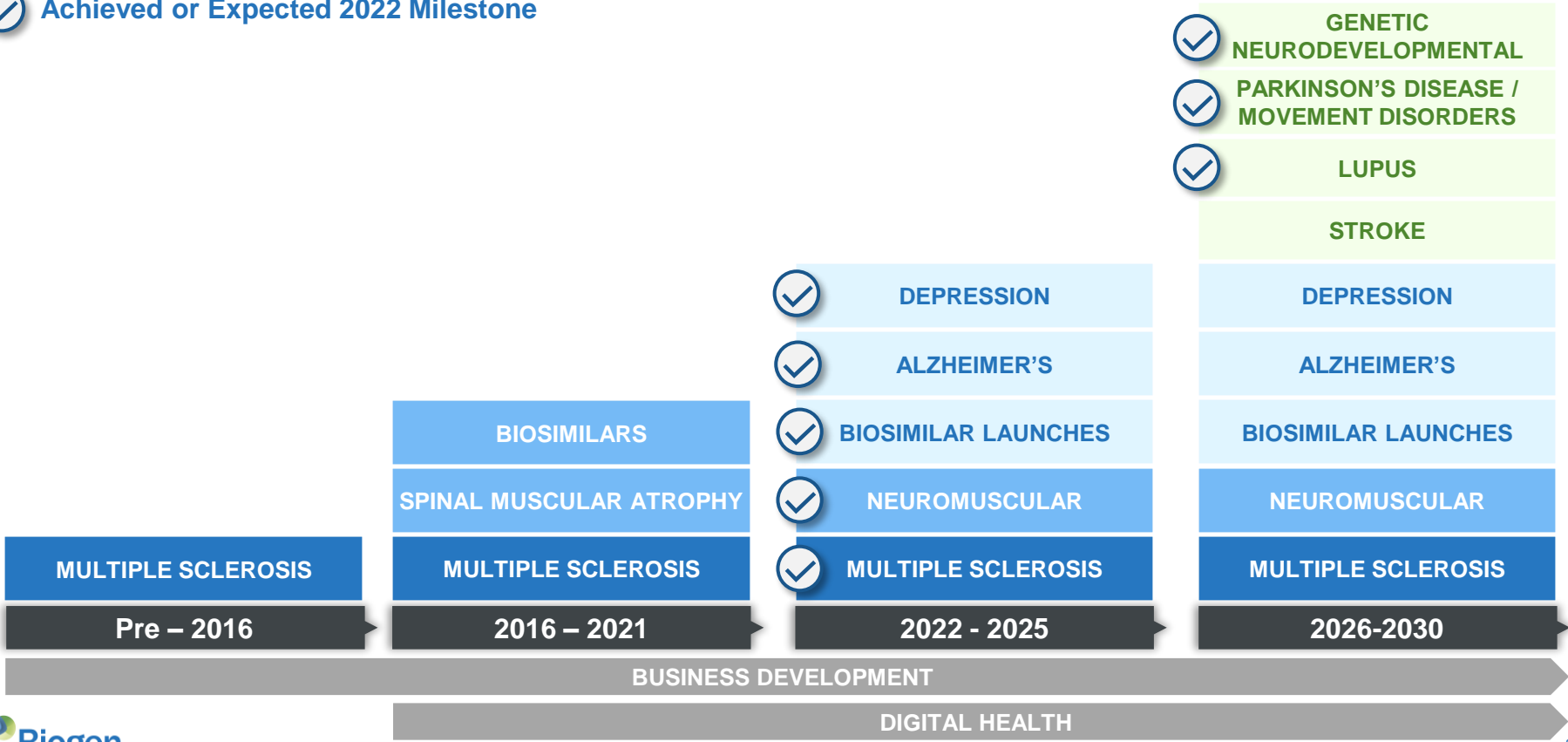


Note: zuranolone is being developed in collaboration with Sage Therapeutics, Inc; tofersen is licensed from Ionis Pharmaceuticals, Inc.; * Sage Therapeutics, Inc responsible for zuranolone U.S. regulatory filing
ALS = amyotrophic lateral sclerosis; MDD = major depressive disorder; PPD = postpartum depression; SOD1 = superoxide dismutase type 1



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

Lecanemab slows clinical decline in early Alzheimer's disease

ALZHEIMER'S DISEASE

NEURO-PSYCHIATRY

NEURO-MUSCULAR

MOVEMENT DISORDERS

SPECIALIZED IMMUNOLOGY

Phase 3 Clarity AD Study met primary endpoint and all key secondary endpoints

Lecanemab treatment resulted in a highly statistically significant slowing of clinical decline as measured by CDR-SB vs. placebo as early as 6 months and across all time points

- Highly statistically significant reduction in clinical decline at 18-months and all time points vs. placebo
- Treatment effect expanded over the 18-month study period on an absolute basis

All key secondary endpoints met with highly statistically significant results vs. placebo

- Change from baseline at 18-months vs. placebo as measured by amyloid PET, ADAS-Cog14, ADCOMS, and ADCS-MCI-ADL

Observed ARIA rate of 21.3% (inclusive of ARIA-E and ARIA-H)

Regulatory filing accepted by FDA under
ACCELERATED APPROVAL PATHWAY

PDUFA date of **January 6, 2023**

Regulatory filings for **TRADITIONAL APPROVAL**
in early AD planned for U.S., E.U., and Japan

Expected by **End of Q1 2023**

Advancing a comprehensive development program for lecanemab

AHEAD 3-45 Trial in preclinical
Alzheimer's disease

Development of maintenance
dosing regimen

Development of subcutaneous
formulation

Biogen is advancing an industry leading Alzheimer's portfolio

Program	Target	Modality	Preclinical	Phase 1	Phase 2	Phase 3	Approved
Aducanumab (ADUHELM®)*	Amyloid-β	mAb					
Lecanemab*	Amyloid-β	mAb					
BIIB080#	Tau	ASO					
BIIB113	OGA	Small molecule					
ATV-Amyloid-β##	Amyloid-β	mAb					
Undisclosed assets	Amyloid-β	mAb					
Undisclosed asset	Genetically Validated Targets	Small molecule					



New data further support the potential treatment benefit of zuranolone in depression

ALZHEIMER'S
DISEASE

NEURO-
PSYCHIATRY

NEURO-
MUSCULAR

MOVEMENT
DISORDERS

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IMMUNOLOGY

New zuranolone data presented in both MDD and PPD

New analysis from the ongoing, longitudinal SHORELINE Study in MDD presented at Psych Congress

- New analysis from the ongoing, longitudinal SHORELINE study assessing median time to first repeat zuranolone treatment course for patients responding to initial 14-day treatment course

Initial 14-day treatment course

30 mg zuranolone

135 Days (Median)

◆ First retreatment

50 mg zuranolone

249 Days (Median)

◆ First retreatment

New data from the positive Phase 3 SKYLARK study evaluating 50 mg zuranolone in PPD presented at European Congress of Neuropsychopharmacology

- Additional secondary endpoint data showed a higher proportion of patients in the zuranolone arm achieved a HAMD-17 response vs. placebo at Days 3, 8, 15, 21, and 28 ($p < 0.05$ at all time points) and HAMD-17 remission from Day 3 through Day 45 (Day 45 $p < 0.05$)

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

Continuing to advance tofersen in SOD1-ALS

ALZHEIMER'S
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NEURO-
PSYCHIATRY

NEURO-
MUSCULAR

MOVEMENT
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SPECIALIZED
IMMUNOLOGY

Regulatory filing for tofersen in SOD1-ALS, a rare genetic form of ALS, accepted by the FDA under the accelerated approval pathway

- Filing granted priority review
- **FDA PDUFA date of April 25, 2023**

Pivotal tofersen data published in *The New England Journal of Medicine*

- Analyses of 12-month data and beyond from VALOR and its OLE show that earlier initiation of tofersen compared to delayed initiation slowed declines in clinical function, respiratory function, muscle strength, and quality of life
- 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 Study, the tofersen presymptomatic study
- Continuing to support the tofersen early access program
- Engaging with global regulators



Note: tofersen is licensed from Ionis Pharmaceuticals, Inc.
AE = adverse event; ALS = amyotrophic lateral sclerosis; OLE = open label extension; SOD1 = superoxide dismutase type 1; SVC = slow vital capacity
Analysis of tofersen 12-month data from VALOR and OLE presented at ENCAL, 2022 and available on Biogen's website at www.investors.biogen.com

Phase 3 LIGHTHOUSE Study initiated in Parkinson's disease

ALZHEIMER'S
DISEASE

NEURO-
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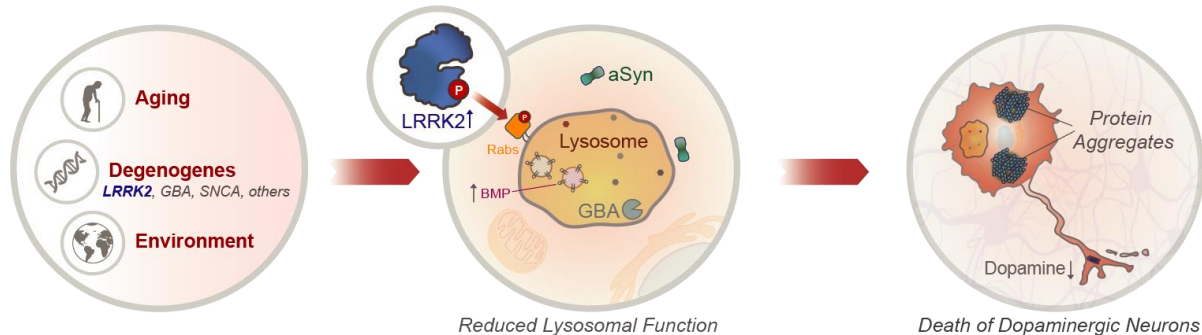


BIIB122 in Parkinson's disease

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
- **Initiated: September 2022**

Phase 2/3 AMETHYST Study initiated in CLE

ALZHEIMER'S
DISEASE

NEURO-
PSYCHIATRY

NEURO-
MUSCULAR

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**SPECIALIZED
IMMUNOLOGY**



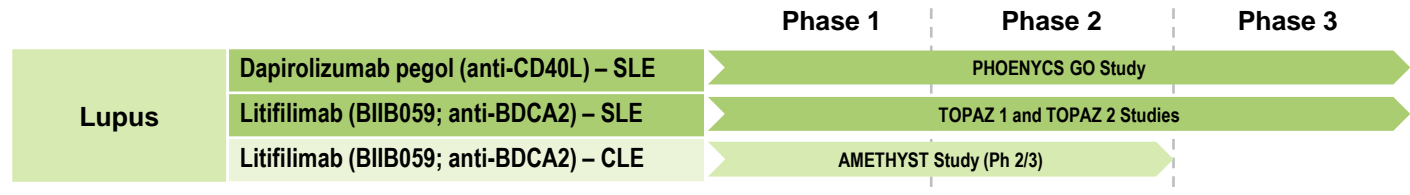
Litifilimab (BIIB059) in lupus

Initiated the Phase 2/3 AMETHYST Study evaluating litifilimab in CLE

Litifilimab two-part Phase 2 LILAC Study results published as two separate manuscripts in *The New England Journal of Medicine*

- Part A results show litifilimab significantly reduced disease activity based on active joint count in people with SLE compared to placebo
- Part B results showed litifilimab improved skin disease activity in participants with CLE compared to placebo

Litifilimab has the potential to be a first-in-class therapy in both SLE and CLE



Key expected milestones for late-stage pipeline

Q4 2022

⋮

2023

Regulatory Filings

Lecanemab in Alzheimer's disease

- U.S. Filing for AA+  PDUFA date of January 6, 2023
- Global Filings for Traditional Approval+  *U.S., E.U., and Japan* Q1 2023

Zuranolone in MDD / PPD – U.S. Filing[^]

 H2 2022

Tofersen in SOD1-ALS – U.S. Filing for AA

 PDUFA date of April 25, 2023

BIIB800 referencing RoACTEMRA[®]/ACTEMRA[®]

- E.U. Filing  EMA accepted filing in September 2022
- U.S. Filing  H2 2022

Clinical Studies

BIIB080 Phase 2 *initiation* in Alzheimer's

 H2 2022

BIIB131 Phase 2b *initiation* in AIS

 H1 2023

BIIB105 Phase 1/2 PoC *readout* in broad ALS

 H2 2023

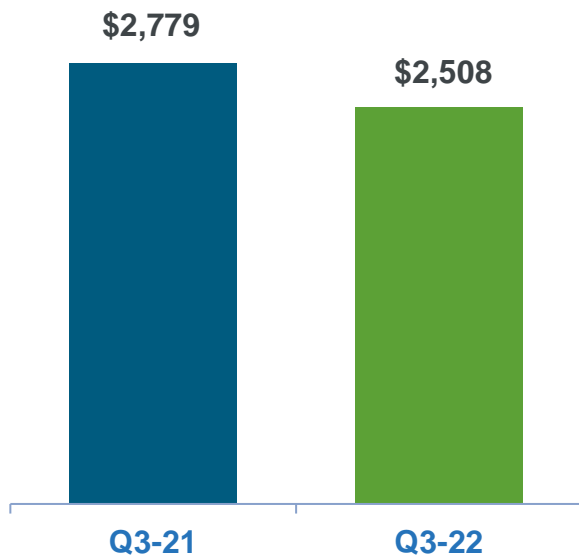
Financial Update

Michael McDonnell

Chief Financial Officer

Q3 2022 financial results

Total Revenue (\$M)

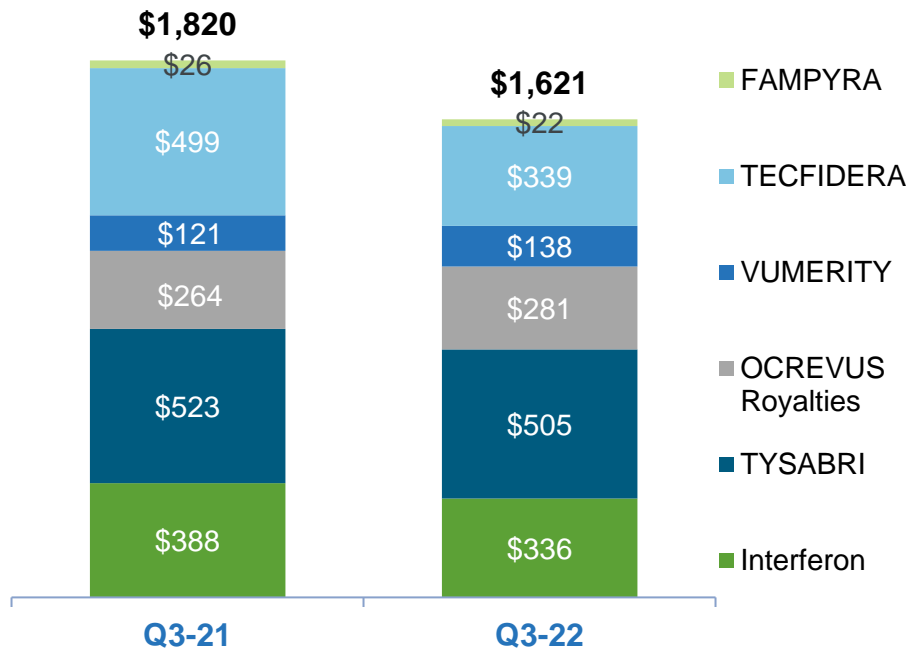


Non-GAAP Diluted EPS (\$)



Global multiple sclerosis revenue

MS Revenue (\$M)

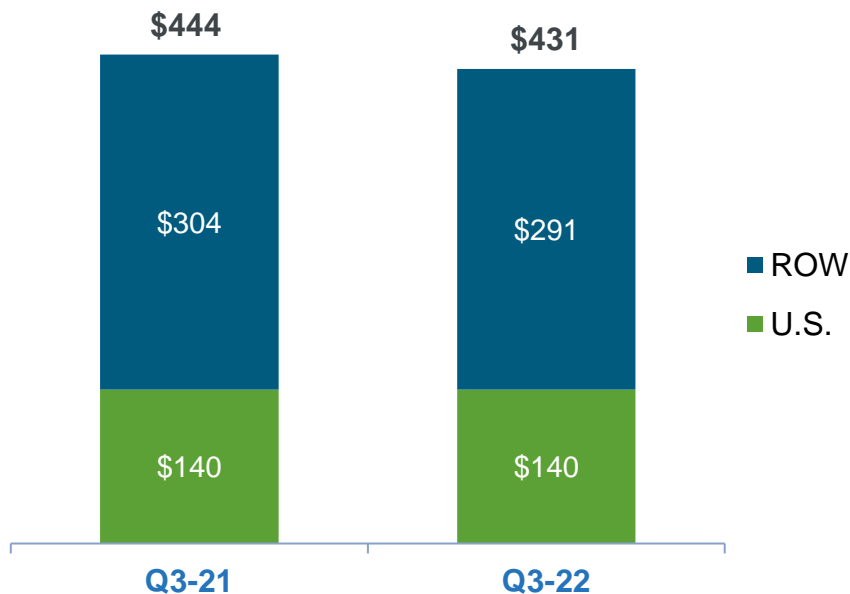


Highlights

- **Global MS revenue, including OCREVUS royalties**, declined 11% at actual currency and 9% at constant currency
- **TECFIDERA** revenue decreased 32% at actual currency and 30% at constant currency vs. prior year; impacted by the entrance of generics
- **VUMERITY** revenue increased 14% at actual currency and 15% at constant currency vs. prior year
- **TYSABRI** revenue decreased 3% at actual currency and 1% at constant currency vs. prior year
 - Subcutaneous launched in over 25 markets outside the U.S. with a conversion rate of ~40%

Global SPINRAZA revenue

SPINRAZA Revenue (\$M)

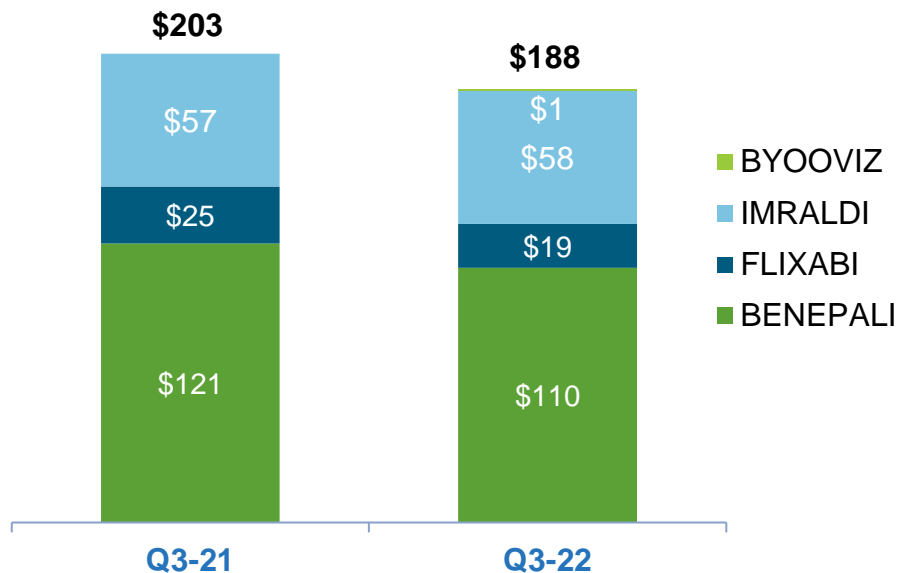


Highlights

- **Global SPINRAZA** revenue decreased 3% at actual currency and increased 2% at constant currency vs. prior year
- **U.S. SPINRAZA** revenue was flat vs. prior year
- **ROW SPINRAZA** revenue decreased 4% at actual currency and increased 2% at constant currency vs. prior year; excluding negative currency impacts, revenue increased due to volume growth in certain Asian markets as well as some positive pricing dynamics, partially offset by competition and the timing of shipments

Biosimilars revenue

Biosimilars Revenue (\$M)



Highlights

- **Biosimilars** revenue decreased 7% at actual currency and 4% at constant currency vs. prior year; volume increases more than offset by unfavorable pricing, negative currency impacts, and pricing pressure
- ~ **256,000** patients on Biogen Anti-TNF biosimilar products at end of Q3 2022*
- **BYOOVIZ** (referencing LUCENTIS®) launched in the U.S. in June 2022
- Marketing Authorization Application accepted in Europe for **BIIB800**, a biosimilar candidate referencing RoACTEMRA®

Q3 2022 revenue highlights

\$ in Millions	Q3 2022	Q3 2021	Δ Y/Y
Total Product Revenue*	\$1,962	\$2,206	(11%)
RITUXAN/GAZYVA Revenue	\$136	\$151	(10%)
OCREVUS Royalties	\$281	\$264	6%
Revenue from Anti-CD20 Therapeutic Programs	\$417	\$415	0%
Other Revenue	\$130	\$158	(18%)
Total Revenue*	\$2,508	\$2,779	(10%)

Q3 2022 financial results highlights

(\$ in Millions except EPS, Shares in Millions)	Q3 2022	Q3 2021	Δ Y/Y
Revenue	\$2,508	\$2,779	(10%)
Cost of Sales	\$470	\$512	8%
Gross Profit	\$2,039	\$2,267	(10%)
% of revenue	81%	82%	
Non-GAAP R&D Expense	\$549	\$702	22%
Non-GAAP SG&A Expense	\$562	\$651	14%
Collaboration Profit (Loss) Sharing	\$45	\$21	(114%)
Non-GAAP Amortization	\$8	\$7	(8%)
Non-GAAP Operating Income	\$875	\$885	(1%)
Non-GAAP Other Income (Expense)	(\$55)	(\$79)	31%
Non-GAAP Profit Before Taxes and JV Equity	\$820	\$806	2%
Non-GAAP Taxes	\$129	\$117	(10%)
Non-GAAP Taxes %	15.7%	14.5%	
Non-GAAP JV Equity Income (Loss)	\$0	\$9	(100%)
Non-GAAP Net Income	\$691	\$699	(1%)
Non-GAAP Net Income (Loss) Attributable to NonControlling Interests	\$0	(\$11)	(102%)
Non-GAAP Net Income Attributable to Biogen Inc.	\$691	\$710	(3%)
Weighted average diluted shares used in calculating diluted EPS	145	149	3%
Non-GAAP Diluted EPS	\$4.77	\$4.77	(0%)

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.

Balance sheet and cash flow

Balance Sheet

(as of September 30, 2022)

\$5.8B Cash and marketable securities

\$6.3B Debt

\$0.5B Net debt

Cash Flow

(Q3 2022)

\$661M Cash flow from operations

\$59M Capital expenditures

\$602M Free cash flow*

\$250M Share repurchases

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 of 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

Prior to regulatory approval: A minimal net gross margin on sales of inventory will be reflected as a reduction to R&D expense

After regulatory approval: 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

Updated full year 2022 financial guidance

	Prior FY 2022 Guidance	Updated FY 2022 Guidance
Revenue	\$9.9 billion to \$10.1 billion	\$10.0 billion to \$10.15 billion
Non-GAAP Diluted EPS	\$15.25 to \$16.75	\$16.50 to \$17.15

Please see Biogen's Q3 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



- Initiated Biogen's **1st life cycle assessment (LCA)** for MS therapies, identifying ways to reduce product water, land and carbon footprints
- Led on green chemistry with **83% of Biogen labs pursuing My Green Lab certification**, aiming to increase sustainability in scientific research
- Expanded **electric vehicle (EV) program to 13 countries** as a longstanding member of the EV100

SOCIAL



- Engaged **employees in 20 Days of Caring Deeply**, serving more than 70 non-profits with 1500+ acts of volunteer service in over 20 countries
- Launched new **Biogen Community Lab Alumni Network**, working to strengthen a more diverse talent pipeline

GOVERNANCE



- Bolstered **DE&I transparency** with reporting via Workforce Disclosure Index and Bloomberg Gender Equality Index

Announced global expansion of program to help health clinics address climate risks, reaching 2,500 under-resourced centers



Biogen-Funded Collaboration with AmeriCares and Harvard Chan C-CHANGE Recognized by the Clinton Global Initiative



Recognition for ESG leadership actions



#25 on JUST Capital's Workforce Equity and Mobility ranking

Sustainalytics

Top 5% in Biogen's sub-industry

MSCI

Top 9% in Biogen's industry

Lecanemab (A β mAb)



Neuroscience



PORTFOLIO

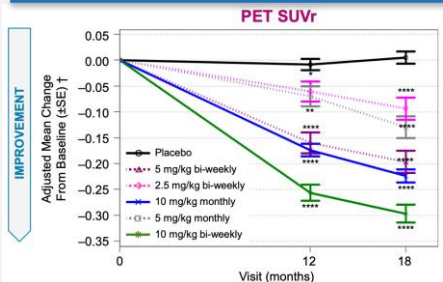
AD PIPELINE

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

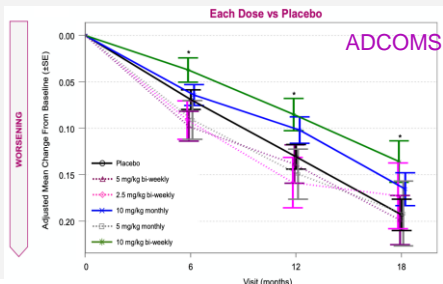
PROPOSED MECHANISM OF ACTION

- Lecanemab is a 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)

PHASE 2 CLINICAL DATA (Study 201 Phase 2b)



- (Swanson, 2018) Dose dependent reduction in amyloid PET values at all doses (Florbetapir tracer)
- At 18 months, 10-mg/kg biweekly lecanemab reduced brain amyloid (-0.306 SUVR units).
- >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 demonstrated 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), a type of adverse event associated with amyloid directed therapies, was 9.9% for the 10 mg/kg biweekly dosing.

Phase 3 CLINICAL DATA (Study 301 Clarity AD)

Clarity AD: A Phase 3 Placebo-Controlled, Double-Blind, Parallel-Group, 18-Month Study Evaluating Lecanemab (BAN2401) in Early Alzheimer's Disease (n=1766)

- Lecanemab treatment met the primary endpoint and reduced clinical decline on the global cognitive and functional scale, CDR-SB, compared with placebo at 18 months by 27%, which represents a treatment difference in the score change of -0.45 (p=0.00005) in the analysis of Intent-to-treat population. Starting as early as six months across all time points, the treatment showed highly statistically significant changes in CDR-SB from baseline compared to placebo (all p-values < 0.01)
- All key secondary endpoints were also met with highly statistically significant results compared with placebo (p<0.01)
- The total incidence of ARIA (ARIA-E and/or ARIA-H) was 21.3% in the lecanemab group and 9.3% in the placebo group

Current Status:

- Lecanemab filing granted priority review in the U.S. with a PDUFA of January 6, 2023
- Eisai plans to file for traditional approval in the U.S. and submit marketing authorizations in Japan and the E.U. by the end of Q1 2023
- AHEAD 3-45 Phase III study in preclinical AD is ongoing (n=1400)

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
- ❖ Lecanemab (Ph3) – Preclinical Alzheimer's

❖ BIIB080 (Ph2) – tau ASO

PROPOSED MECHANISM OF ACTION

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

CLINICAL STUDY OVERVIEW

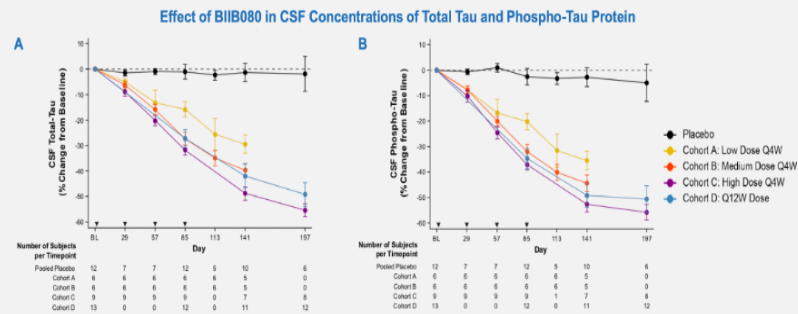
- First in Human Phase 1b Study [[NCT03186989](#)] is a two-part study evaluating the safety, tolerability, pharmacokinetics, and target engagement of BIIB080 in patients with mild Alzheimer's disease (with consistent CSF biomarkers). Part 1: a randomized double-blind, placebo controlled multiple ascending 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 (Ph1/2) – 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; 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]

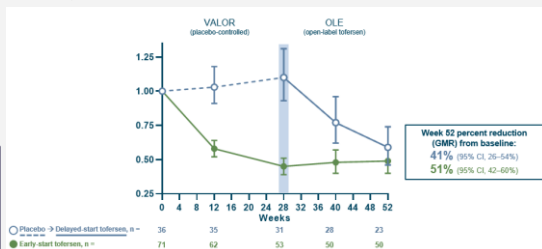
Current Status:

Regulatory filing for tofersen in SOD1-ALS accepted by the FDA under the accelerated approval pathway and granted priority review; **FDA decision expected by April 25, 2023**

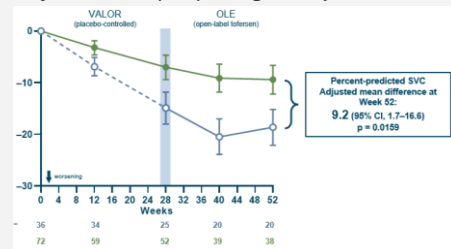
Integrated data from VALOR and its OLE

- 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 people with ALS enrolled in the study 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

* p-values are nominal

ALSFRS-R = revised ALS Functional Rating Scale; CI = confidence interval; ENCALs = European Network to Cure ALS; OLE = open label extension; PV = permanent ventilation (defined as ≥22 hours of mechanical ventilation/day for ≥21 consecutive days); 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

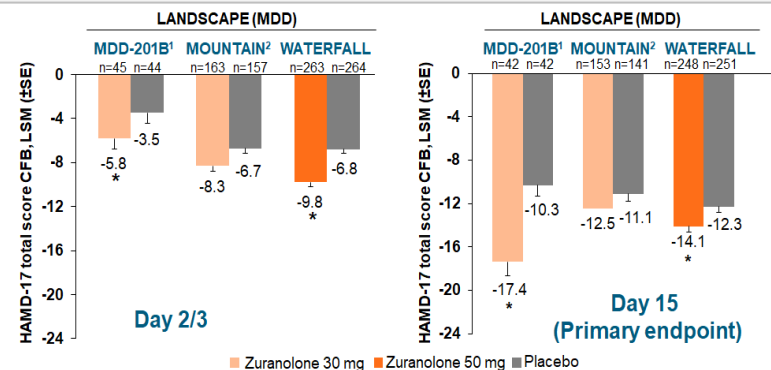
CLINICAL STUDY OVERVIEW

- 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/failed the primary endpoint at Day 15, and trends at Day 3, 8, and 12 suggested improvement and provided supportive information that the dose be increased to 50 mg. [[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 at Day 3. [[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](#)]
- **Single NDA 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.

*p<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

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

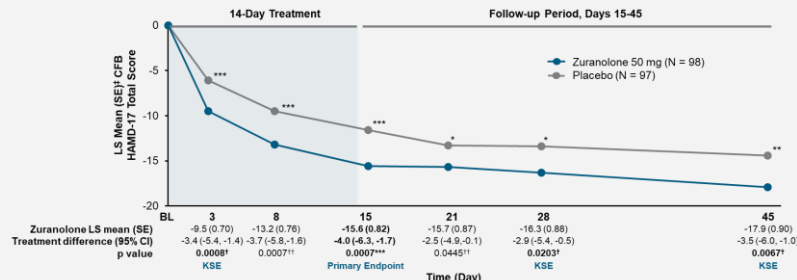
CLINICAL STUDY OVERVIEW

- 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](https://clinicaltrials.gov/ct2/show/study/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](https://clinicaltrials.gov/ct2/show/study/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:

- **Single NDA 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. Improvements in additional secondary endpoints were also observed, including CFB in HAMD-17 total score and HAMD-17 response and remission.

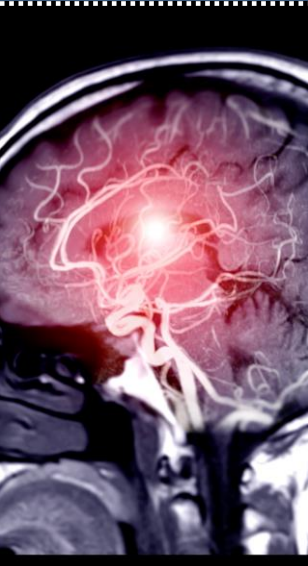
In the SKYLARK Study, zuranolone was generally well tolerated with a safety profile consistent with other LANDSCAPE and NEST clinical trials. The most common treatment-emergent adverse events observed with zuranolone in SKYLARK included somnolence, dizziness, sedation, and headache. <5% of participants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



BIIB093 (IV glibenclamide) – Large Hemispheric Infarction



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, hypoxia and brain injury, and involved in cerebral edema development

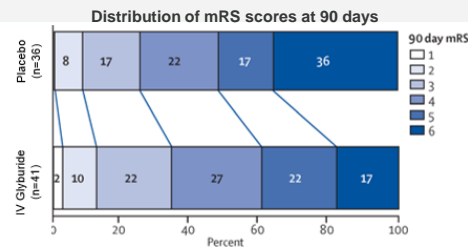
PHASE 3 CLINICAL STUDY OVERVIEW

- 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:

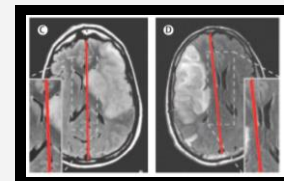
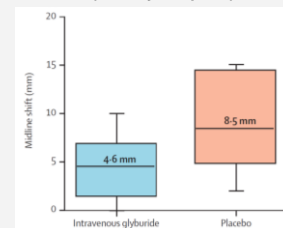
- Phase 3 CHARM study ongoing [[NCT02864953](https://clinicaltrials.gov/ct2/show/study/NCT02864953)]

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

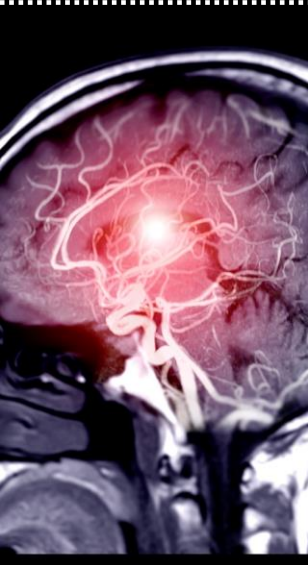
Reduction in Midline Shift- at 72-96 hours (Tertiary Endpoint)



BIIB093 (IV glibenclamide) – Brain Contusion



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

- Sulfonylurea receptor 1-transient receptor potential melastatin 4 (SUR1-TRPM4) is a cation channel, upregulated in human pericontusional endothelium and astrocytes that allows for harmful osmotic cell swelling under adenosine triphosphate-depleted conditions.

PHASE 2 CLINICAL STUDY OVERVIEW

- A Multicenter, Double-Blind, Multidose, Placebo-Controlled, Randomized, Parallel-Group, Phase 2 Study to Evaluate the Efficacy and Safety of Intravenous BIIB093 for Patients With Brain Contusion
- Study population: Brain contusion patients aged 18 to 85 years (N=160)
- BIIB093 or placebo administered as intravenous (IV) infusion over 96 hours with started within 6.5 hours of time of trauma/last known normal
- Primary endpoint is the proportion of participants with contusions expansion by Hour 96

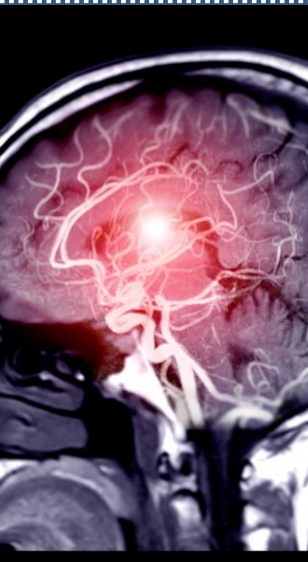
Current Status:

- Phase 2 ASTRAL study ongoing [[NCT03954041](https://clinicaltrials.gov/ct2/show/study/NCT03954041)]

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

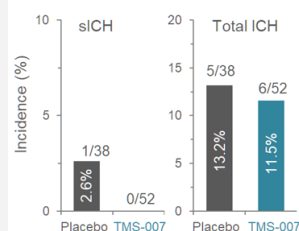
- Phase 2a, randomized, double-blind, placebo-controlled, dose escalation study to evaluate the safety, efficacy, PK, PD, and mechanisms of action of BIIB131 [[JapicCTI-183842](#)]
- Study population: Acute Ischemic Stroke adult patients (N=90) within 12 hours of symptom onset and <88 years old
- BIIB131 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:

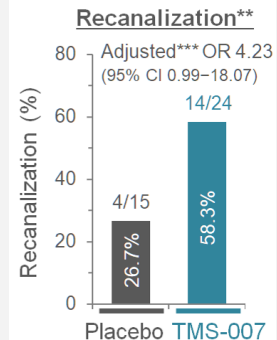
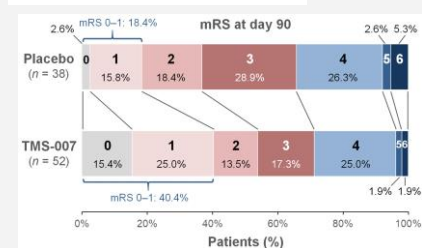
- Ph 2a study completed
- Ph 2b to be initiated in H1 2023. Double-blind, dose-ranging placebo controlled randomized study to evaluate the efficacy and safety of IV BIIB131 in AIS up to 24 hours

PHASE 2a* CLINICAL DATA

ICH events within 24 h



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)
- ❖ BIIB122 (Ph3) – LRRK2-Parkinson's disease
- ❖ BIIB122 (Ph2b) – Parkinson's disease
- ❖ BIIB094 (Ph1) – Parkinson's disease
- ❖ BIIB101 (Ph1) – Multiple System Atrophy
- ❖ 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

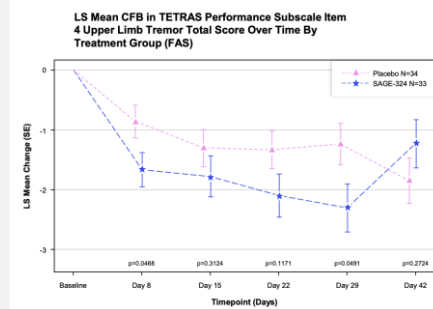
- Phase 2a, randomized, double-blind, placebo-controlled study was conducted to evaluate the efficacy, safety, and tolerability of BIIB124 [NCT04305275]
- The inclusion criteria were 18-80 years with ET diagnosis: isolated action tremor bilateral upper limb at least 3 years duration, with or without 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 ≥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)
- ❖ BIIB094 (Ph1) – Parkinson's disease
- ❖ **BIIB122 (Ph3) – LRRK2-Parkinson's disease**
- ❖ BIIB101 (Ph1) – Multiple System Atrophy
- ❖ BIIB122 (Ph2b) – Parkinson's disease
- ❖ BIIB132 (Ph1) – Spinocerebellar Ataxia Type 3

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 slow the progression of 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)

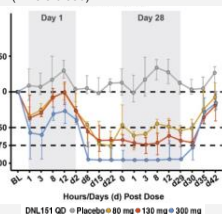
Current Status:

- 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]– **Achieved FPI Sep 2022**
- LUMA and LIGHTHOUSE studies will utilize 225 mg oral once daily BIIB122 administration

PHASE 1b CLINICAL DATA

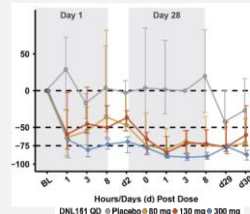
Target Engagement

Reduction of pS935 LRRK2 (Whole blood)



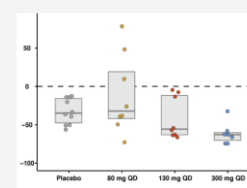
Pathway Engagement

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

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

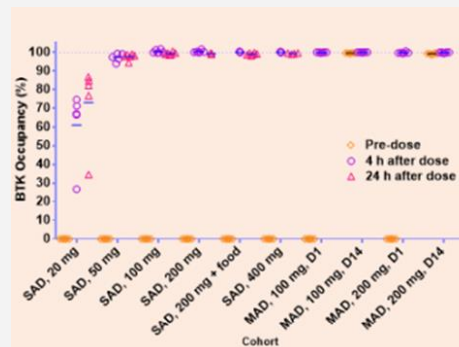
- Study ICP-CL-00112 Phase 2 in relapsing and remitting MS: is a global, placebo-controlled, double-blind, randomized trial with open-label extension
- Core randomization phase (n=160) with primary endpoint of cumulative number of new gadolinium-enhancing (GdE) T1 magnetic resonance (MRI) brain lesions 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**

Dapirolizumab Pegol (anti-CD40L)



Specialized
Immunology

PORTFOLIO

LUPUS PIPELINE

- ❖ Dapirolizumab Pegol (Ph3) – Systemic Lupus Erythematosus
- ❖ Litifiliimab (Ph3) – Systemic Lupus Erythematosus
- ❖ Litifiliimab (Ph2/3) – 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}

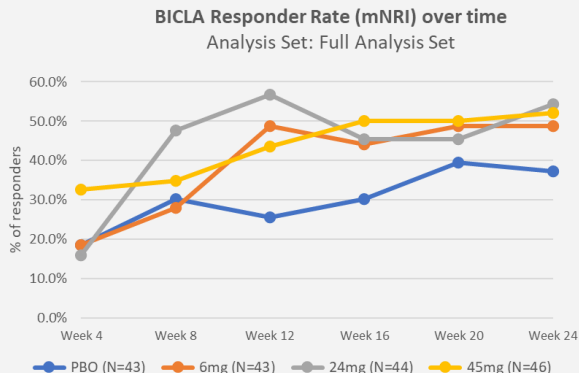
CLINICAL STUDY OVERVIEW

- 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. 42

Litifilimab (formerly BIIB059; anti-BDCA2 mAb) – SLE



PORTFOLIO

LUPUS PIPELINE

- ❖ Dapirolizumab Pegol (Ph3) – Systemic Lupus Erythematosus
- ❖ **Litifilimab (Ph3) – Systemic Lupus Erythematosus**
- ❖ Litifilimab (Ph2/3) – Cutaneous Lupus Erythematosus

PROPOSED MECHANISM OF ACTION

- Litifilimab is a humanized monoclonal antibody that binds to BDCA2, a protein predominantly expressed on plasmacytoid dendritic cells (pDCs), that negatively regulates the production of Type-I interferons (IFN-I) and other proinflammatory cytokines and chemokines by pDCs.
- 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.
- Litifilimab, targets pDC production of IFN-I via BDCA2, and is not expected to affect the IFN-I response to viral infection mediated by other immune cells.

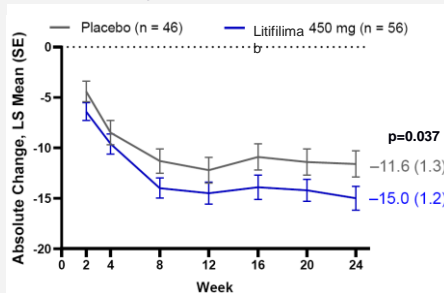
CLINICAL STUDY OVERVIEW

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

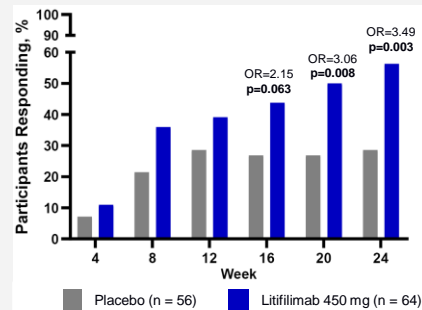
Current Status:

- 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 (AEs) in LILAC part A were similar in placebo (68%) and litifilimab (59%) treatment groups, with the majority being mild or moderate¹.
- AEs in the Infections and Infestations System Organ Class occurred in 39% and 36% of participants receiving placebo and litifilimab, respectively

Specialized Immunology



1. Furie et al., *N Engl J Med.* 2022. 2. Werth et al., *N Engl J Med.* 2022

SLE = systemic lupus erythematosus; CLE = Cutaneous Lupus Erythematosus; IgG1 = Immunoglobulin G1; pDC = plasmacytoid dendritic cell; BDCA2 = blood dendritic cell antigen 2; FPI = first patient in; IFN = Interferon

Litifilimab (formerly BII059; anti-BDCA2 mAb) – CLE



PORTFOLIO

LUPUS PIPELINE

- ❖ Dapirolizumab Pegol (Ph3) – Systemic Lupus Erythematosus
- ❖ Litifilimab (Ph3) – Systemic Lupus Erythematosus
- ❖ Litifilimab (Ph2/3) – Cutaneous Lupus Erythematosus

PROPOSED MECHANISM OF ACTION

- Litifilimab is a humanized monoclonal antibody that binds to BDCA2, a protein predominantly expressed on plasmacytoid dendritic cells (pDCs), that negatively regulates the production of Type-I interferons (IFN-I) and other proinflammatory cytokines and chemokines by pDCs.
- 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.
- Litifilimab, targets pDC production of IFN-I via BDCA2, and is not expected to affect the IFN-I response to viral infection mediated by other immune cells.

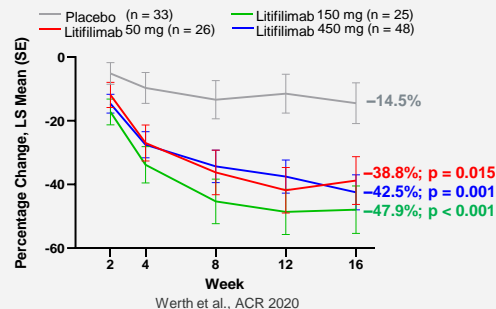
CLINICAL STUDY OVERVIEW

- Ph2 LILAC study met its primary endpoints, demonstrating a statistically significant reduction of disease activity in patients with SLE and CLE^{1,2}.
 - Litifilimab 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.
- Pivotal Phase 2/3 AMETHYST study will evaluate the efficacy and safety of litifilimab, as compared to placebo, in cutaneous lupus erythematosus (CLE).
- Litifilimab enrollment targets are set to reflect the prevalence of CLE in African American and Hispanic/Latino communities with the aim to achieve appropriate representation of these populations in the AMETHYST study.

Current Status:

- AMETHYST achieved FPI in October 2022. [[NCT05531565](https://clinicaltrials.gov/ct2/show/study/NCT05531565)]

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



- Rates of adverse events in LILAC part B were similar in the placebo (67%) and pooled litifilimab (72%) treatment groups, with the majority being mild or moderate².
- Adverse events in the Infections and Infestations System Organ Class occurred in 30% and 34% of participants receiving placebo and litifilimab, respectively

1. Furie et al., *N Engl J Med*. 2022. 2. Werth et al., *N Engl J Med*. 2022

SLE = systemic lupus erythematosus; CLE = Cutaneous Lupus Erythematosus; IgG1 = Immunoglobulin G1; pDC = plasmacytoid dendritic cell; BDCA2 = blood dendritic cell antigen 2; FPI = first patient in; CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity; IFN = Interferon

Biogen Digital Health Portfolio



PORTFOLIO FOCUS

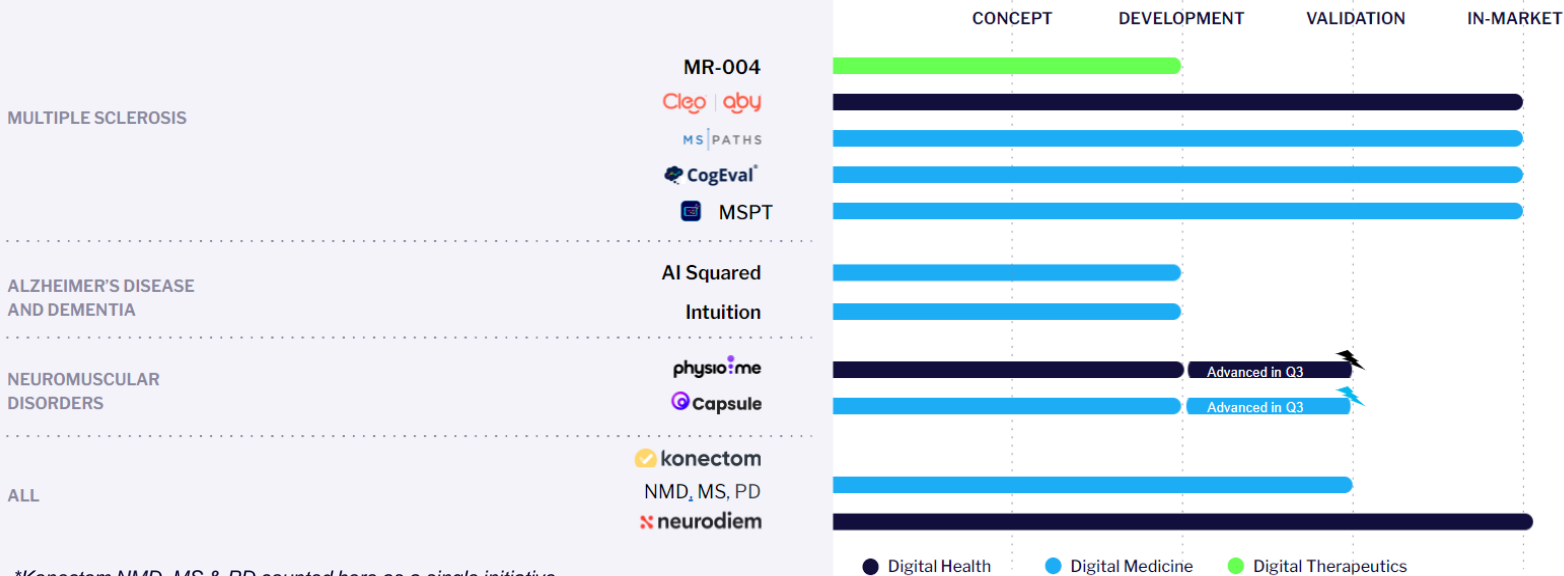
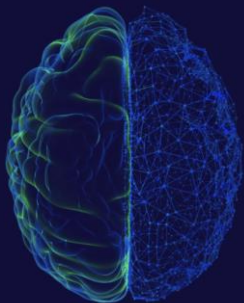
- ❖ Digital Biomarkers
- ❖ Personalized Medicine
- ❖ Patient Pathway Improvement
- ❖ Digital Therapeutics

- 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



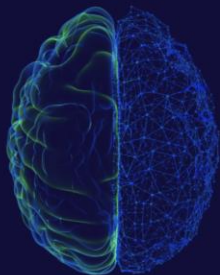
Digital Health

PORTFOLIO FOCUS

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

Disease Area: Multiple Sclerosis

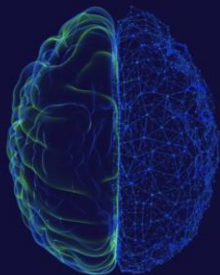
Initiative	Stage	Focus	Description
MR-004 - DTx	Development	MS Patients walking & independence	Biogen entered into a license agreement with MedRhythms to develop and commercialize MR-004, an investigational prescription digital therapeutic for the potential treatment of gait deficits in multiple sclerosis. 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 Artificial Intelligence</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 – <i>Digital Biomarkers</i>	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

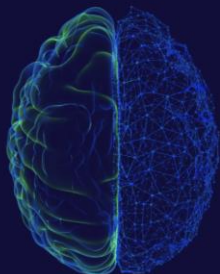
- ❖ Digital Biomarkers
- ❖ Personalized Medicine
- ❖ Patient Pathway Improvement
- ❖ Digital Therapeutics

Disease Area: Neuromuscular Disorders

Initiative	Stage	Focus	Description
Physio.me – <i>Digital Companion</i>	Validation	Patient Pathway Improvement Personalized Medicine	Digital exercise 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>	Validation	Patient Pathway Improvement	Evidence-based medical device that combines immersion through virtual reality technology and medical hypnosis to potentially alleviate anxiety related to medical 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™ [SB11¹] – referencing LUCENTIS®
- ❖ Launch commenced USA June 2022
- ❖ Approvals secured by EMA, MHRA in 2021, CA Q1 2022, AU and CH Q3 2022

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

❖ Lucentis: \$1,355M US / \$2,085M 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, pathological myopia and CNV 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 trial 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% (BCVA)/90% (CST) 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%]).

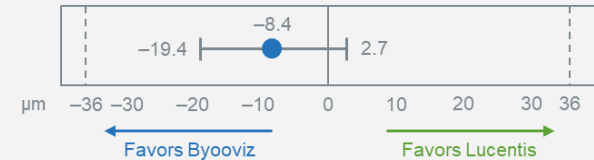
CLINICAL DATA OVERVIEW²

Difference of mean change in BCVA at Week 8



Whiskers represent the 90% CI. Dashed lines represent the predefined equivalence margins of [-3 to 3 letters].

Difference of mean change in CST at week 4



Whiskers represent the 95% CI. Dashed lines represent the predefined equivalence margin of [-36 to 36 µm].

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 Q2 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® \$6,159 M US / \$4,137M ROW¹

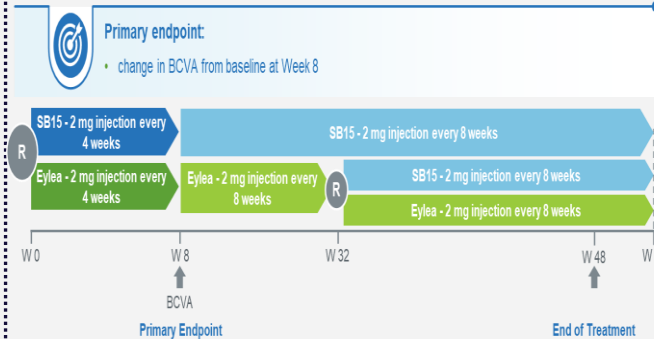
MECHANISM OF ACTION

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 56 centers across 10 countries. Study start June 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



Primary endpoint was met:

Difference of LS Mean Change between SB15 and Reference Aflibercept

LS mean difference: 0.1 letters



- Equivalence was declared: 95% CI of the difference in BCVA LS mean change between SB15 and reference from baseline to Week 8 was [-1.3 letters, +1.4 letters], i.e. contained within predefined equivalence margin of +/-3 letters
- Mean change from baseline in BCVA and CST up to Week 32 was comparable between SB15 and reference
- Interim 32-week study results also demonstrated comparable safety, immunogenicity, and pharmacokinetics of SB15 to reference aflibercept in subjects with nAMD

BIIB800 (referencing ACTEMRA®)



Biosimilars

Reference Molecule

BIOSIMILARS PIPELINE

- ❖ BIIB800 [BAT1806]¹ referencing Actemra/ - Ph3 completed
- ❖ Regulatory dossier filing accepted by EMA in Q3 2022

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

- ❖ Actemra/RoActemra \$1,873M US / \$1,954M ROW¹

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

CLINICAL DATA

A Phase 3, Randomised, Double-Blind, Active-Controlled Clinical Trial to Compare BAT1806/BII800, a Proposed Tocilizumab Biosimilar, with a Tocilizumab Reference Product in Subjects with Moderate to Severe Rheumatoid Arthritis with an Inadequate Response to Methotrexate Therapy

L. Song,¹ P. Lanquar,² G. Shen,³ D. Li,⁴ M. Al-Hussaini,⁵ J. Liu,⁶ S. Kakimoto,⁷ M. Stanitschka,⁸ X. Yang,⁹ H. X. Zhou,¹⁰ Q. Ding,¹¹ M. Mitoku,¹² J. Addison,¹³ X. Zhang¹⁴

¹Beigene, United States; ²Beigene, United States; ³Beigene, United States; ⁴Beigene, United States; ⁵Beigene, United States; ⁶Beigene, United States; ⁷Beigene, United States; ⁸Beigene, United States; ⁹Beigene, United States; ¹⁰Beigene, United States; ¹¹Beigene, United States; ¹²Beigene, United States; ¹³Beigene, United States; ¹⁴Beigene, United States



Note: Biosimilar indications may vary by product or region. ¹BAT1806 refers to the Bio-Thera Solutions product candidate name. Source: ¹Evaluate pharma Q2 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 \$1,439M US / \$777M 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

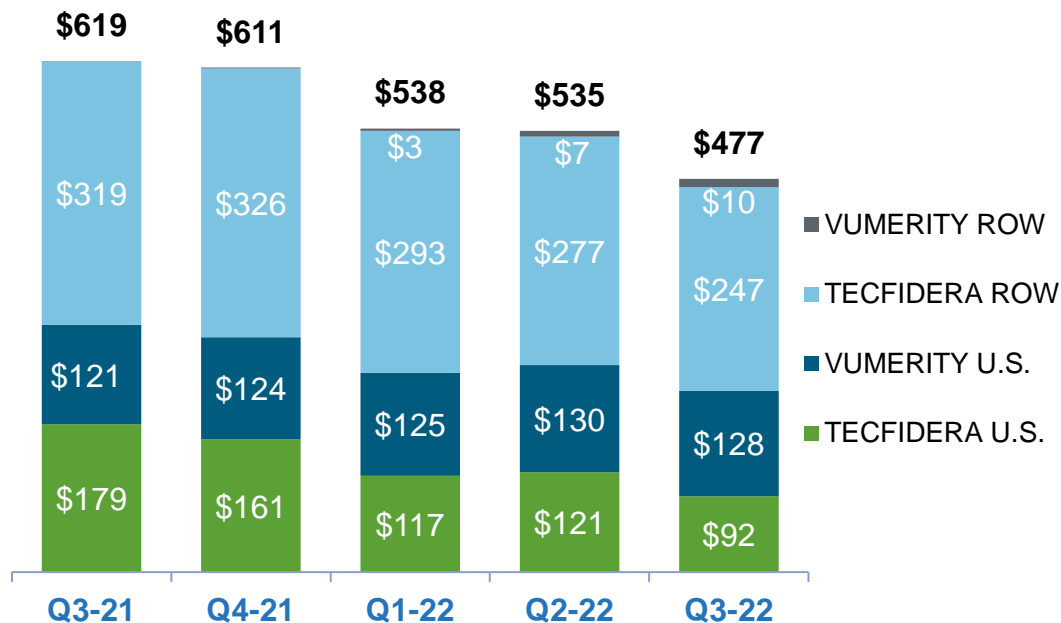
- Biogen will be the Marketing Authorization Holder
- Unlimited duration of agreement
- Global scope

Note: Biosimilar indications may vary by product or region. Source: ¹ Evaluate pharma Q2 22; ² FDA database; ³ EMA database; ⁴ FDA only; ⁵ EMA only

Global fumarate revenue



Fumarate Revenue (\$M)



Q3 2022 Highlights

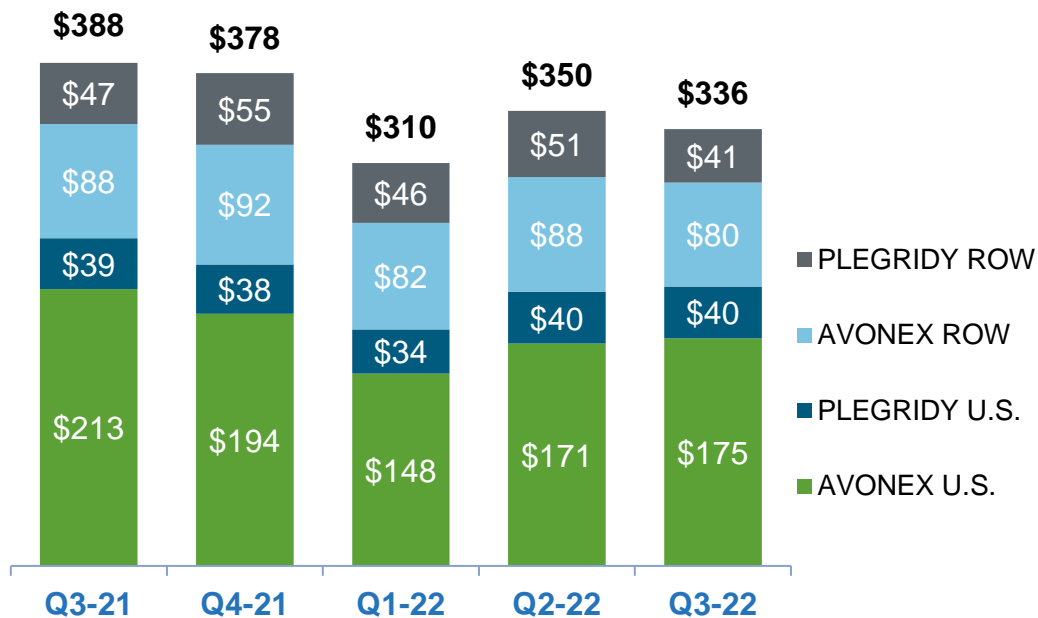
Revenue vs. Q3 2021 and Q2 2022

	<u>ΔY/Y</u>		<u>ΔQ/Q</u>
WW	- 23%	and	- 11%
ROW	- 20%	and	- 10%
U.S.	- 27%	and	- 12%

Global interferon revenue



Interferon Revenue (\$M)



Q3 2022 Highlights

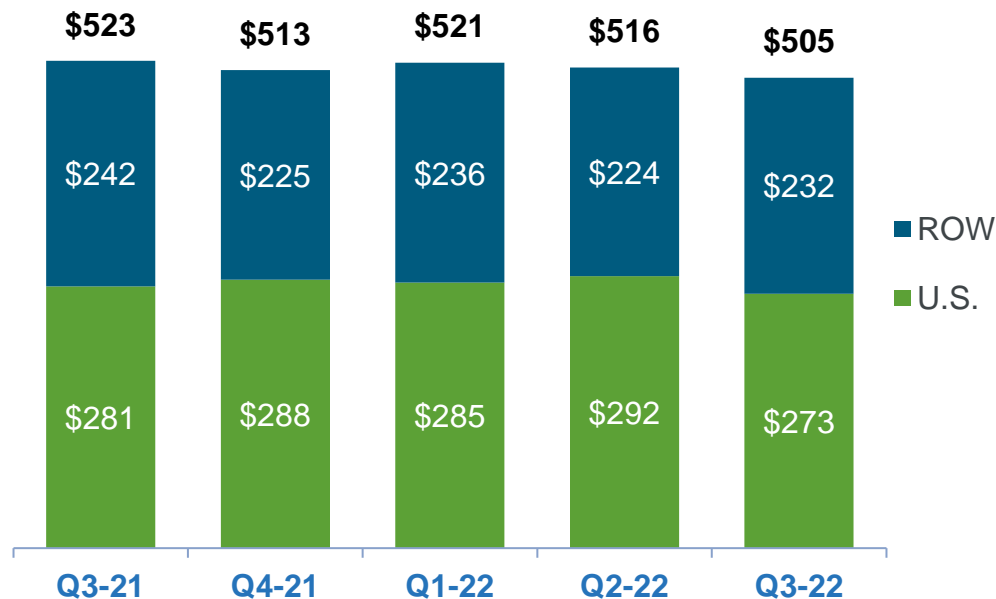
Revenue vs. Q3 2021 and Q2 2022

	$\Delta Y/Y$	and	$\Delta Q/Q$
WW	- 13%		- 4%
ROW	- 10%		- 13%
U.S.	- 15%		+ 2%

Global TYSABRI revenue



TYSABRI Revenue (\$M)



Numbers may not foot or recalculate due to rounding.

Q3 2022 Highlights

Revenue vs. Q3 2021 and Q2 2022

	<u>ΔY/Y</u>		<u>ΔQ/Q</u>
WW	- 3%	and	- 2%
ROW	- 4%	and	+ 4%
U.S.	- 3%	and	- 7%

Consolidated Statement of Income

(unaudited, in millions, except per share amounts)

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenue:				
Product, net	\$ 1,962.1	\$ 2,205.7	\$ 6,083.3	\$ 6,653.4
Revenue from anti-CD20 therapeutic programs	416.9	415.4	1,252.6	1,244.4
Other	129.5	157.8	293.5	350.1
Total revenue	2,508.5	2,778.9	7,629.4	8,247.9
Cost and expense:				
Cost of sales, excluding amortization and impairment of acquired intangible assets	469.5	511.8	1,707.4	1,449.6
Research and development	549.2	702.4	1,629.5	1,801.7
Selling, general and administrative	563.3	654.1	1,770.8	1,886.4
Amortization and impairment of acquired intangible assets	56.5	111.0	190.9	813.2
Collaboration profit (loss) sharing	45.3	21.2	(42.6)	74.5
(Gain) loss on fair value remeasurement of contingent consideration	(2.1)	(15.6)	(13.7)	(49.1)
Acquired in-process research and development	—	—	—	18.0
Restructuring charges	15.4	—	124.1	—
Gain on sale of building	(503.7)	—	(503.7)	—
Other (income) expense, net	(56.0)	502.9	(221.3)	913.4
Total cost and expense	1,137.4	2,487.8	4,641.4	6,907.7
Income before income tax expense and equity in loss of investee, net of tax	1,371.1	291.1	2,988.0	1,340.2
Income tax (benefit) expense	236.2	(25.9)	578.5	(390.7)
Equity in (income) loss of investee, net of tax	—	(1.1)	(2.6)	(17.2)
Net income	1,134.9	318.1	2,412.1	1,748.1
Net income (loss) attributable to noncontrolling interests, net of tax	0.2	(11.1)	(84.4)	560.2
Net income attributable to Biogen Inc.	\$ 1,134.7	\$ 329.2	\$ 2,496.5	\$ 1,187.9
Net income per share:				
Basic earnings per share attributable to Biogen Inc.	\$ 7.86	\$ 2.22	\$ 17.12	\$ 7.93
Diluted earnings per share attributable to Biogen Inc.	\$ 7.84	\$ 2.22	\$ 17.07	\$ 7.90
Weighted-average shares used in calculating:				
Basic earnings per share attributable to Biogen Inc.	144.4	148.0	145.8	149.9
Diluted earnings per share attributable to Biogen Inc.	144.8	148.6	146.2	150.3

GAAP to Non-GAAP Reconciliation

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

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 cash 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.

(In millions, except per share amounts)	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2022 ⁽¹⁾	2021 ⁽¹⁾⁽²⁾	2022 ⁽¹⁾	2021 ⁽¹⁾⁽²⁾
Selling, General and Administrative Expense:				
Total selling, general and administrative, GAAP	\$ 563.3	\$ 654.1	\$ 1,770.8	\$ 1,886.4
Less: other	1.5	3.0	3.5	5.2
Total selling, general and administrative, Non-GAAP	\$ 561.8	\$ 651.1	\$ 1,767.3	\$ 1,881.2
Amortization and Impairment of Acquired Intangible Assets:				
Total amortization and impairment of acquired intangible assets, GAAP	\$ 56.5	\$ 111.0	\$ 190.9	\$ 813.2
Less: impairment charges ^A	—	44.3	—	629.3
Less: amortization of acquired intangible assets	48.6	59.4	168.1	176.6
Total amortization and impairment of acquired intangible assets, Non-GAAP	\$ 7.9	\$ 7.3	\$ 22.8	\$ 7.3
Other (Income) Expense, net:				
Total other (income) expense, net, GAAP	\$ (56.0)	\$ 502.9	\$ (221.3)	\$ 913.4
Less: (gain) loss on equity security investments	(109.8)	424.2	158.1	705.9
Less: (gain) on sale of equity interest in Samsung Bioepis ^B	—	—	(1,505.3)	—
Less: litigation settlement agreed to in principle ^C	—	—	900.0	—
Less: premium paid on debt exchange or early debt redemption ^D	2.2	—	2.2	9.5
Less: other	(3.0)	—	17.0	—
Total other (income) expense, net, Non-GAAP	\$ 54.6	\$ 78.7	\$ 206.7	\$ 198.0
Income Tax (Benefit) Expense:				
Total income tax (benefit) expense, GAAP	\$ 236.2	\$ (25.9)	\$ 578.5	\$ (390.7)
Less: Neurimmune step-up tax basis ^E	—	—	83.9	(492.0)
Less: international reorganization & income tax effect related to Non-GAAP reconciling items	107.6	(142.7)	133.1	(331.4)
Total income tax expense, Non-GAAP	\$ 128.6	\$ 116.8	\$ 361.5	\$ 432.7
Effective Tax Rate:				
Total effective tax rate, GAAP	17.2 %	(8.9)%	19.4 %	(29.2)%
Less: Neurimmune step-up tax basis ^E	—	—	2.8	(36.7)
Less: impact of GAAP to Non-GAAP adjustments	1.5	(23.4)	1.1	(7.9)
Total effective tax rate, Non-GAAP	15.7 %	14.5 %	15.5 %	15.4 %

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 cash 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 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 September 30,		For the Nine Months Ended September 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	\$ —	\$ (1.1)	\$ (2.6)	\$ (17.2)
Less: amortization of equity in (income) loss of investee	—	7.8	14.4	31.0
Total equity in (income) loss of investee, Non-GAAP	\$ —	\$ (8.9)	\$ (17.0)	\$ (48.2)
Net Income (Loss) Attributable to Noncontrolling Interests, Net of Tax:				
Total net income (loss) attributable to noncontrolling interests, GAAP	\$ 0.2	\$ (11.1)	\$ (84.4)	\$ 560.2
Less: Neurimmune step-up tax basis ^E	—	—	(83.9)	492.0
Less: net distribution to noncontrolling interests	—	—	(1.5)	(4.4)
Total net income (loss) attributable to noncontrolling interests, Non-GAAP	\$ 0.2	\$ (11.1)	\$ 1.0	\$ 72.6
Net Income Attributable to Biogen Inc.:				
Total net income attributable to Biogen Inc., GAAP	\$ 1,134.7	\$ 329.2	\$ 2,496.5	\$ 1,187.9
Plus: impairment charges ^A	—	44.3	—	629.3
Plus: amortization of acquired intangible assets	48.6	59.4	168.1	176.6
Plus: restructuring charges	15.4	—	124.1	—
Plus: (gain) loss on fair value remeasurement of contingent consideration	(2.1)	(15.6)	(13.7)	(49.1)
Plus: (gain) loss on equity security investments	(109.8)	424.2	158.1	705.9
Plus: net distribution to noncontrolling interests & amortization of equity in (income) loss of investee	—	7.8	12.9	26.6
Plus: gain on sale of equity interest in Samsung Bioepis ^B	—	—	(1,505.3)	—
Plus: litigation settlement agreed to in principle ^C	—	—	900.0	—
Plus: (gain) on sale of building ^F	(503.7)	—	(503.7)	—
Plus: premium paid on debt exchange or early debt redemption ^D	2.2	—	2.2	9.5
Plus: international reorganization & income tax effect related to Non-GAAP reconciling items	107.6	(142.7)	133.1	(331.4)
Plus: other	(1.7)	3.0	20.4	5.2
Total net income attributable to Biogen Inc., Non-GAAP	\$ 691.2	\$ 709.6	\$ 1,992.7	\$ 2,360.5
Diluted Earnings Per Share				
Total diluted earnings per share, GAAP	\$ 7.84	\$ 2.22	\$ 17.07	\$ 7.90
(Less) Plus: adjustments to GAAP net income attributable to Biogen Inc. (as detailed above)	(3.07)	2.55	(3.44)	7.80
Total diluted earnings per share, Non-GAAP	\$ 4.77	\$ 4.77	\$ 13.63	\$ 15.70

⁽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.

	Q3 2022 vs. Q3 2021	YTD 2022 vs. YTD 2021
Total Revenue		
Revenue change, as reported	(9.7)%	(7.5)%
Less: impact of foreign currency translation and hedging gains / losses	(2.0)	(1.7)
Revenue change at constant currency	(7.7)%	(5.8)%
Total MS Revenue (including OCREVUS royalties)		
Revenue change, as reported	(10.9)%	(5.9)%
Less: impact of foreign currency translation and hedging gains / losses	(1.5)	(1.1)
Revenue change at constant currency	(9.4)%	(4.8)%
Total TECFIDERA Revenue		
Revenue change, as reported	(32.0)%	(21.7)%
Less: impact of foreign currency translation and hedging gains / losses	(1.8)	(1.5)
Revenue change at constant currency	(30.2)%	(20.2)%
Total VUMERITY Revenue		
Revenue change, as reported	14.0 %	41.0 %
Less: impact of foreign currency translation and hedging gains / losses	(1.2)	(0.9)
Revenue change at constant currency	15.2 %	41.9 %
Total TYSABRI Revenue		
Revenue change, as reported	(3.3)%	(0.5)%
Less: impact of foreign currency translation and hedging gains / losses	(2.1)	(1.3)
Revenue change at constant currency	(1.2)%	0.8 %
Total INTERFERON Revenue		
Revenue change, as reported	(13.3)%	(16.2)%
Less: impact of foreign currency translation and hedging gains / losses	(1.4)	(1.1)
Revenue change at constant currency	(11.9)%	(15.1)%
Total SPINRAZA Revenue		
Revenue change, as reported	(2.9)%	(8.9)%
Less: impact of foreign currency translation and hedging gains / losses	(4.4)	(3.4)
Revenue change at constant currency	1.5 %	(5.5)%
Total SPINRAZA Rest of World Revenue		
Revenue change, as reported	(4.4)%	(13.2)%
Less: impact of foreign currency translation and hedging gains / losses	(6.5)	(4.8)
Revenue change at constant currency	2.1 %	(8.4)%
Total Biosimilars Revenue		
Revenue change, as reported	(7.5)%	(5.6)%
Less: impact of foreign currency translation and hedging gains / losses	(3.9)	(5.1)
Revenue change at constant currency	(3.6)%	(0.5)%

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 September 30,		For the Nine Months Ended September 30,	
	2022	2021	2022	2021
Cash Flow:				
Net cash provided by (used in) operating activities	\$ 661.0	\$ 805.3	\$ 1,559.3	\$ 2,801.6
Net cash provided by (used in) investing activities	1,672.2	(233.6)	1,717.7	(451.0)
Net cash provided by (used in) financing activities	(1,251.9)	(746.5)	(1,739.9)	(2,096.0)
Net increase (decrease) in cash and cash equivalents	\$ 1,081.3	\$ (174.8)	\$ 1,537.1	\$ 254.6
Net cash provided by (used in) operating activities	\$ 661.0	\$ 805.3	\$ 1,559.3	\$ 2,801.6
Less: Purchases of property, plant and equipment	59.1	42.0	153.9	206.5
Free cash flow	\$ 601.9	\$ 763.3	\$ 1,405.4	\$ 2,595.1

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 nine months ended September 30, 2022, compared to the same periods in 2021, decreased primarily due to impairment charges recorded during 2021. For the three and nine months ended September 30, 2022, we had no impairment charges.

For the three and nine months ended September 30, 2021, amortization and impairment of acquired intangible assets reflects impairment charges of \$15.0 million and \$365.0 million, respectively, related to BIIB111 (timrepigene emparvovec) for the potential treatment of choroideremia and impairment charges of \$28.4 million and \$220.0 million, respectively, related to BIIB112 (cotoretigene toliparvovec) for the potential treatment of X-linked retinitis pigmentosa. During the second quarter of 2021 we announced that our Phase 3 STAR study of BIIB111 and our Phase 2/3 XIRIUS study of BIIB112 did not meet their primary endpoints. In the third quarter of 2021 we suspended further development on these programs based on the decision by management as part of its strategic review process.

For the nine months ended September 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).

^B In April 2022 we completed the sale of our 49.9% equity interest in Samsung Bioepis to Samsung BioLogics Co., Ltd (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 in cash 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 this transaction.

For the nine months ended September 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.

^C During the second quarter of 2022 we recorded a pre-tax charge of \$900.0 million related to a litigation settlement agreement to resolve a qui tam litigation relating to conduct prior to 2015.

Notes to GAAP to Non-GAAP Reconciliation

Operating Expense & Net Income Attributable to Biogen Inc.

^D In July 2022 we redeemed our 3.625% Senior Notes due September 15, 2015, prior to their maturity and recognized a net pre-tax charge of approximately \$2.2 million upon the extinguishment of these Senior Notes related to the payment of an early call premium. These charges were recognized as interest expense in other (income) expense, net in our condensed consolidated statements of income for the three and nine months ended September 30, 2022.

^E For the three and nine months ended September 30, 2022, compared to the same periods in 2021, the increases in our effective tax rates include the tax impacts on the sale of one of our buildings and the favorable prior year tax effects of changes in the value of our equity investments, where we recorded unrealized losses, and the BIIB111 and BIIB112 impairment charges. The tax effects of this change in value of our equity investments were recorded discretely as changes in value of equity investments cannot be forecasted.

For the nine months ended September 30, 2022, compared to the same period in 2021, the increase in our effective tax rate also reflects the net effects of the Neurimmune SubOne AG (Neurimmune) matters, as discussed below, and the litigation settlement agreement.

During the second quarter of 2021 we recorded a net deferred tax asset in Switzerland of approximately \$490.0 million on Neurimmune's 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.

^F In September 2022 we completed the sale of our building and land parcel located at 125 Broadway, Cambridge, MA (125 Broadway) for an aggregate sales price of approximately \$603.0 million, which is inclusive of a \$10.8 million tenant allowance. This sale resulted in a pre-tax gain on sale of approximately \$503.7 million, net of transaction costs for the three and nine months ended September 30, 2022.