Q2:2026 Business Update and Financial Results

July 29, 2026

Nasdaq: IONS

Yajaira (with family)
Living with sHTG

On Today's Earnings Call

Brett Monia, Ph.D.
Chief Executive Officer

Kyle Jenne
Chief Global Product Strategy Officer

Holly Kordasiewicz, Ph.D.
Chief Development Officer

Beth Hougen
Chief Financial Officer

Eugene Schneider, M.D.
Chief Clinical Development Officer

Eric Swayze, Ph.D.
Executive Vice President, Research

Forward-Looking Statements

This presentation includes forward-looking statements regarding our business, financial guidance and the therapeutic and commercial potential of our commercial medicines, additional medicines in development and technologies and our expectations regarding development and regulatory milestones. Any statement describing Ionis' goals, expectations, financial or other projections or guidance, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties including but not limited to those related to our commercial products and the medicines in our pipeline, and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Ionis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on our Form 10-K for the year ended December 31, 2025, and our most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of these and other documents are available at www.ionis.com.

In this presentation, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals and its subsidiaries.

Introduction

Brett Monia, Ph.D.

Chief Executive Officer

Well Positioned for Accelerating Growth

Fully integrated, commercial-stage biotechnology company

High-value innovative pipeline built on **groundbreaking RNA-targeting technology**

Successful commercial launches enabled by **breakthrough clinical results**

Clear path to **accelerating revenue growth, sustained positive cash flow** and **substantial value creation**[1]

1. Based on current expectations and timing assumptions, subject to change.

Building Commercial Momentum

Providing multi-billion-dollar revenue potential for Ionis[1]

First Broad Patient Population Launch Underway

Tryngolza® (olezarsen) injection

First FDA-approved treatment to prevent AP in sHTG

Encouraging early launch progress

EU sHTG marketing application under review[2]

Continued Strong FCS Patient Demand

Tryngolza® (olezarsen) injection

First FDA-approved treatment for FCS

H1:26 U.S. net sales of $32M

Global FCS launch underway[2]

HAE Launch Driving Revenue Growth

DAWNZERA™ (donidalorsen) 80 mg / 0.8 mL injection

Positioned to transform the HAE treatment paradigm

H1:26 U.S. net sales of $42M

Global launch underway[3]

On Track for First Independent Neurology Launch

Zilganersen in AxD

First disease-modifying treatment for Alexander disease[4]

PDUFA September 22, 2026

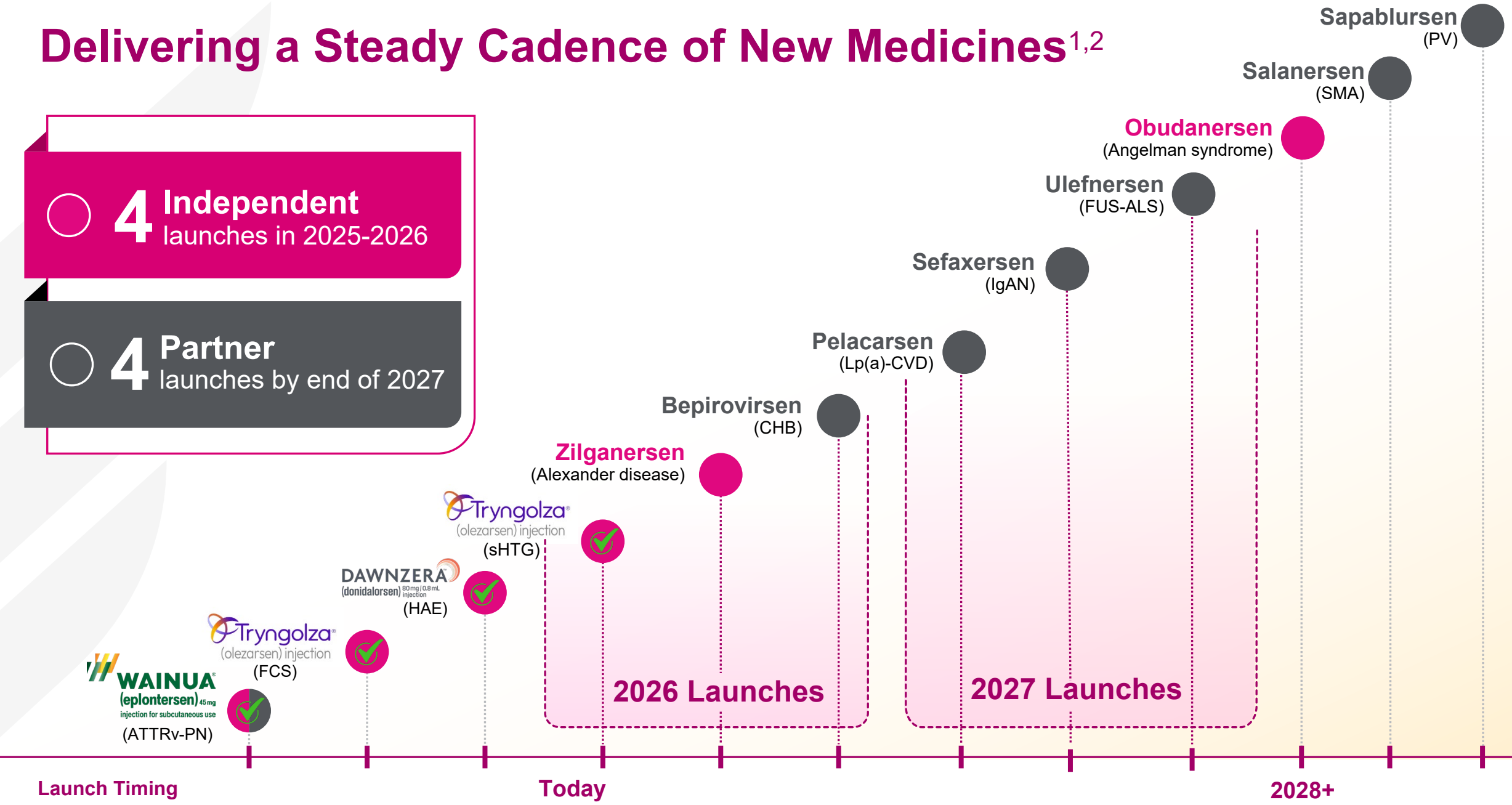
Global regulatory filings planned in 2027[5]

1. Timing expectations and peak sales estimates based on current assumptions and subject to change. 2. Sobi is responsible for commercializing TRYNGOLZA in the EU. 3. Otsuka is responsible for commercializing DAWNZERA in the EU. 4. Investigational medicine, based on data from Phase 1-3 study of zilganersen. 5. Recordati is responsible for commercializing Zilganersen ex-U.S. See press release here.

Delivering a Steady Cadence of New Medicines[1,2]

4 Independent launches in 2025-2026

4 Partner launches by end of 2027



1. Assuming approval. 2. Based on current timing assumptions, subject to change.

Accelerating Value through Commercial Execution

Kyle Jenne

Chief Global Product Strategy Officer

Strong Foundation for TRYNGOLZA Launch in sHTG[1]

Increasing FCS Demand Continued in Q2:2026

Robust efficacy and safety

- Significant and sustained triglyceride reductions
- Substantial reduction in acute pancreatitis events

Convenience of once-monthly self-administration with an autoinjector

EU FCS launch underway[2]

Strong Q-o-Q Increase in Demand[3]

Q2:2026 TRYNGOLZA FCS product sales of $5M reflect updated WAC price effective April 1, 2026

1. See Full Prescribing Information. 2. Approved in the EU as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS), commercialized by Sobi.
3. Q2:2026 vs Q1:2026.

Tryngolza®
(olezarsen) injection

NOW APPROVED

Indicated as an adjunct to diet to reduce triglycerides (TG) and the risk of acute pancreatitis in adults with severe hypertriglyceridemia
(sHTG: TG greater than or equal to 500 mg/dL)

IONIS

TRYNGOLZA is now approved in the U.S.; see Full Prescribing Information.

TRYNGOLZA: sHTG Launch Off to Encouraging Start with Exceptional Initial Commercial Execution[1,2]

- Landmark approval as the **first-ever medicine to prevent acute pancreatitis** in sHTG[1]
- Leveraging strong foundation **established with FCS launch**

- **Prescriptions** from **cardiologists, endocrinologists** and **lipidologists,** plus **primary care physicians**
- **Encouraging reimbursement progress** including **patients with triglycerides above 500 mg/dL**

- **Positive physician** and **patient feedback**
- **Simplicity** of **self-administration** with a patient-friendly **autoinjector**
- 50 and 80mg doses **provide dosing flexibility**

- **First mover** advantage
- Under regulatory review in **EU for sHTG**
- Reaffirming **2026 TRYNGOLZA net product sales $100-110M**[2]

Annual Peak Product Revenue Opportunity[3]

>$3B

1. See Full Prescribing Information. 2. Sobi is responsible for ex.U.S. commercialization. 3. Estimates based on current assumptions and subject to change.

DAWNZERA Launch Gaining Momentum[1]

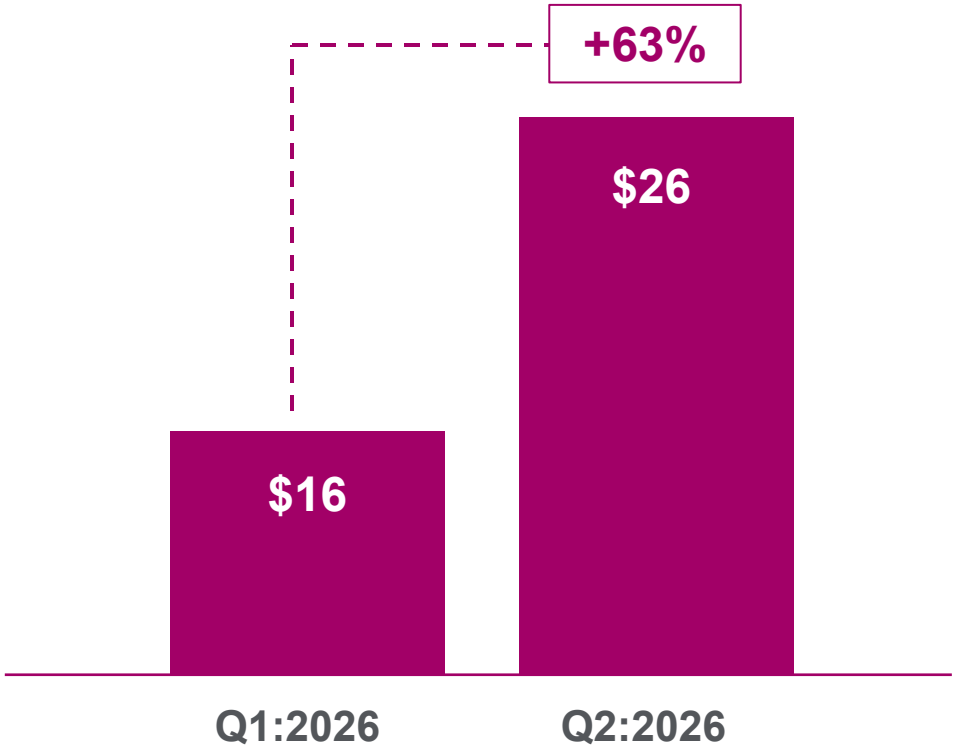
Delivering on What HAE Patients Need Most

First and **Only RNA-Targeted Treatment** to **Prevent HAE Attacks**

Indicated for prophylaxis to prevent attacks of HAE in adult and pediatric patients ≥12 years old

- **Prescriptions written for all patient segments:**
  - Switches from other long-term prophylactic treatments
  - Previously on-demand treatment only
  - Treatment naïve
- **Meaningful share of prophylactic market captured in <1 year**
- **Growing number of repeat prescribers**
- **Global launch underway, expanding in EU markets[2]**

Generated $42 million in H1:2026



DAWNZERA, U.S. Product Sales, net (millions)

1. DAWNZERA is approved in the U.S. for hereditary angioedema in adults and pediatric patients 12 years of age and older; see Full Prescribing Information. 2. Otsuka is responsible for commercializing DAWNZERA in the EU.

Zilganersen: Ionis' First Independent Neurology Launch[1,2]

PDUFA September 22

Substantial Unmet Need

Alexander disease is a **rare**, **progressive** and **often fatal** neurological condition

No approved disease-modifying treatments

Groundbreaking Phase 3 Data

First time an investigational **medicine** has shown a **positive disease-modifying impact in Alexander disease**

Demonstrated **statistically significant** and **clinically meaningful benefit** on the **primary endpoint of change in gait speed**

Well-Established Patient Community

Strong partnership with the Alexander disease **patient community**

Strategy to Reach Patients

Evaluation, diagnosis and **treatment management**

Access and **adherence**

Expanding global access through Recordati

1. Assuming approval. 2. Timing expectations based on current assumptions and subject to change.

Building Momentum Across Independent Launches

Top-Tier Team

Strong Launch Execution

Multiple Opportunities for Continued Growth

Delivering Important Pipeline Achievements

Holly Kordasiewicz, Ph.D.

Chief Development Officer

TRYNGOLZA:

Positioned to be the New Standard of Care for Severe Hypertriglyceridemia[1]

Groundbreaking clinical results[2]:

- **Highly statistically significant** and **clinically meaningful mean reductions** in **fasting triglycerides** of **up to 72%** on top of standard of care
  - **86%** of patients reached **TGs <500 mg/dL**
  - Up to **54%** of patients' **TGs normalized** (≤150 mg/dL)
- **First treatment** to **significantly reduce acute pancreatitis** events in **people with sHTG**
  - Up to **91%** reduction in **AP events** vs. placebo
- **Favorable safety** and **tolerability**

First and Only FDA approved medicine to reduce triglycerides and risk of acute pancreatitis in sHTG[3]

1. Timing expectations based on current assumptions and subject to change. 2. Marston NA, Bergmark BA, Alexander VJ, et al. Olezarsen for managing severe hypertriglyceridemia and pancreatitis risk. *N Engl J Med.* 2026;394(5):429-441. doi:10.1056/NEJMoa2512761. 3. TRYNGOLZA is now approved in the U.S.; see Full Prescribing Information.

Building a Leading Cardiometabolic Pipeline[1,2]

2
Wholly Owned Medicines in Clinical Development

4
Partnered Medicines in Clinical Development

6
Medicines in Clinical Development

Approved Medicine[3]

Tryngolza® (olezarsen) injection

1. Timing and expectations based on current assumptions and subject to change. 2. Assuming approval. 3. TRYNGOLZA is now approved in the U.S.; see Full Prescribing Information.

Late-Stage Ionis-Owned Neurology Opportunities: Zilganersen and Obudanersen[1]

Zilganersen
for the Treatment of Alexander Disease

First and **only** investigational **medicine** to demonstrate **clinically meaningful disease-modifying impact**

~1 in 1-3 million people with AxD; ~300 people in the U.S.[2]

Potential to broaden access outside the U.S. with Recordati

U.S. and EU Orphan designation; U.S. Fast Track designation

Granted Priority Review; **PDUFA September 22, 2026**

Obudanersen
for the Treatment of Angelman Syndrome

Significant unmet need with no approved disease-modifying treatments

HALOS long-term extension data continues to support development

>100k people in major geographies[4]

Granted Breakthrough Therapy designation

Pivotal Phase 3 REVEAL study **fully enrolled**; On track for **data H2:2027**[3]

1. Formerly ION582. 2. Yoshida T, Sasaki M, Yoshida M, et al. Nationwide survey of Alexander disease in Japan and proposed new guidelines for diagnosis. J Neurol. 2011;258(11):1998-2008. 3. Based on current timing assumptions, subject to change. 4. Luk HM, Lo IFM. *Eur J Med Genet.* 2016;59:315–319.

Leading the Way in the Treatment of Neurological Diseases[1,2]

8
Wholly Owned Medicines in Clinical Development

4
Partnered Medicines in Clinical Development

12
Medicines in Clinical Development

Approved Medicines[3-5]

SPINRAZA® (nusinersen) injection 12 mg/5 mL

QALSODY® (tofersen) 100 mg/15 mL injection

WAINUA® (eplontersen) 45 mg injection for subcutaneous use

1. Timing and expectations based on current assumptions and subject to change. 2. Assuming approval. 3. SPINRAZA.com. 4. QALSODY.com. 5. WAINUA.com.

2026 Key Value-Driving Events[1]

Clinical Events

Phase 3

Bepirovirsen
B-Well data
(CHB)

Eplontersen
CARDIO-TTRansform data
(ATTR-CM)

Sefaxersen
IMAGINATION data
(IgAN)

Obudanersen
Enrollment completion
(Angelman syndrome)

Pelacarsen
Lp(a) HORIZON data
(Lp(a)-CVD)

Ulefnersen
FUSION data
(FUS-ALS)

Sapablursen
Phase 3 initiation
(PV)

Salanersen
Phase 3 initiation
(SMA)

Phase 2

Diranersen
CELIA data
(Alzheimer's disease)

Tominersen
GENERATION HD2 data
(Huntington's disease)

Tonlamarsen
Phase 2 data
(Uncontrolled hypertension)

Regulatory Actions

Donidalorsen
EU approval
(HAE)

TRYNGOLZA
U.S. approval
EU submission
(sHTG)

Zilganersen
U.S. submission
U.S. approval
(AxD)

High Dose Nusinersen
U.S. approval
EU approval
(SMA)

Bepirovirsen
Submission
Approval
(CHB)

Pelacarsen
U.S. submission
(Lp(a)-CVD)

Eplontersen
U.S. submission
(ATTR-CM)

Product Launches

DAWNZERA
EU
(HAE)

TRYNGOLZA
U.S.
(sHTG)

Zilganersen
U.S.
(Alexander disease)

Bepirovirsen
U.S. & Japan
(CHB)

1. Timing expectations are based on current assumptions and are subject to change, timing of partnered program catalysts based on partners' most recent publicly available disclosures.

Q2:2026 Financial Performance

Beth Hougen

Chief Financial Officer

H1:2026 Financial Highlights[1]

Revenues $514M

Commercial Revenue: $226M

- $32M in TRYNGOLZA product sales
- $42M in DAWNZERA product sales
- 27% increase year-over-year (YoY)

R&D Revenue: $288M

- Significant YoY increase driven by multiple payments as partnered programs advance[3]

Operating Expenses[2] $645M

R&D Expenses[2]: $377M

- Majority funding late-stage programs

SG&A Expenses[2]: $262M

- YoY increase fueling ongoing and planned launches

Operating Loss[2] ($131M)

- Reflects strong revenue generation from multiple sources and disciplined expense management

Cash & Short-term Investments $2.1B

- Enabling continued investments in our commercial medicines, planned launches and wholly owned pipeline

1. For the second half of 2026 ended June 30, 2026. 2. Non-GAAP – please see reconciliation to GAAP in Q2:2026 press release. 3. Excludes the $280 million upfront payment for the global license of sapablursen to Ono Pharmaceutical Co., Ltd. Received in the second quarter of 2025.

On Track to Achieve our 2026 Financial Guidance [1,2]

Revenue
$875-$900M
>30% vs 2025[2]

Numerous diverse revenue sources

TRYNGOLZA net product sales $100-110M

DAWNZERA net product sales $110-120M

Operating Loss
$425-475M[3]
Similar to 2025[2]

Investing in multiple launches, including broad sHTG indication

Improved operating leverage

Cash
>$1.6B

Supports investments for launches, pipeline and technology

On track to achieve 2028 cashflow breakeven

1. Based on current assumptions, subject to change. 2. Excludes the $280 million upfront payment for the global license of sapablursen to Ono Pharmaceutical Co., Ltd. Received in the second quarter of 2025. 3. Non-GAAP – please see reconciliation to GAAP in Q2:2026 press release.

Conclusion

Brett Monia, Ph.D.

Chief Executive Officer

Driving Accelerating Growth[1,2]

2028 Cash Flow Breakeven

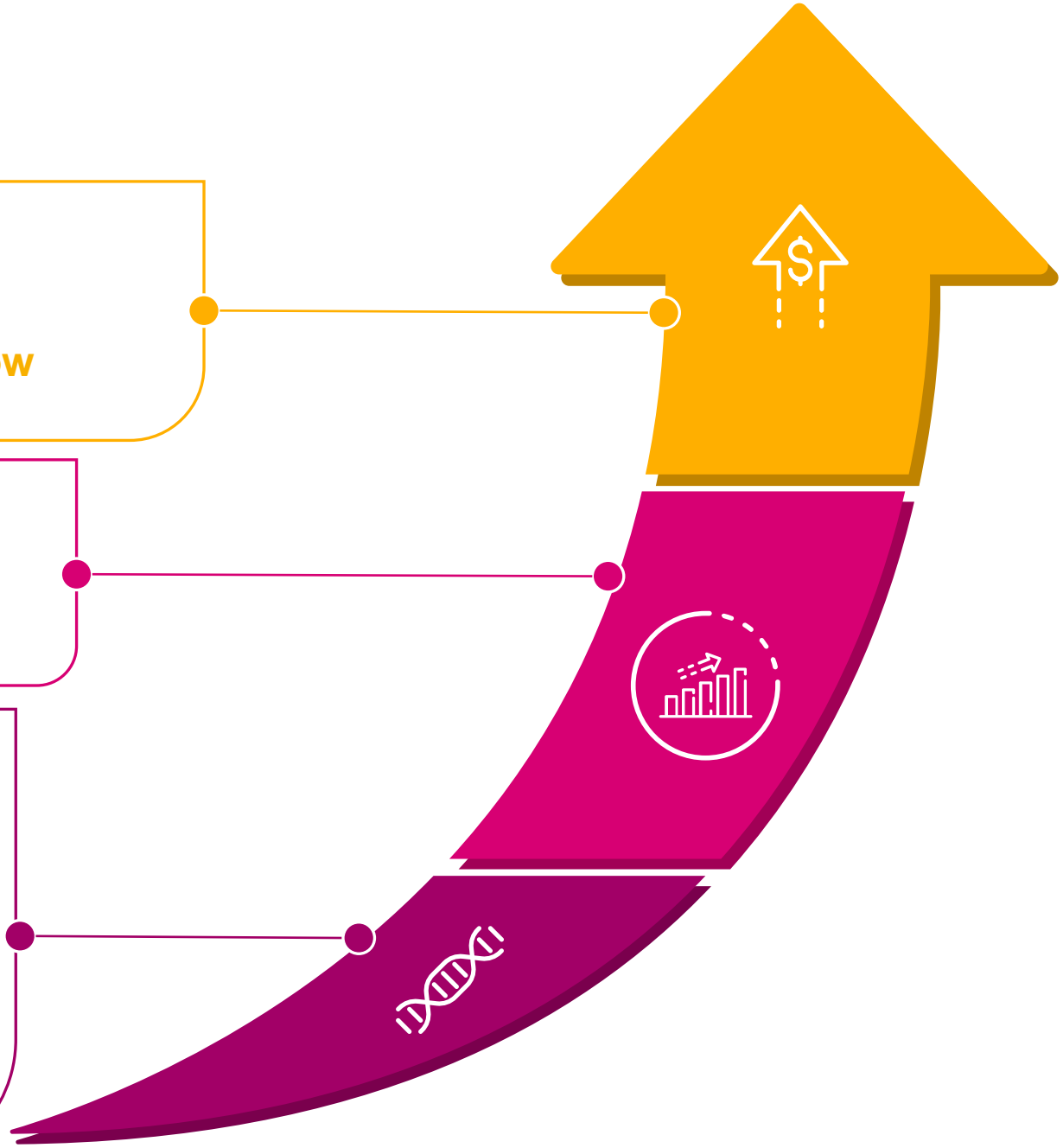
Clear Path to Sustained Positive Cash Flow

Accelerating Revenue Growth

Fully-integrated commercial stage biotechnology company

Positive clinical trial results enabling steady cadence of approvals and launches

Established **leadership in cardiometabolic and neurology drug discovery and development**

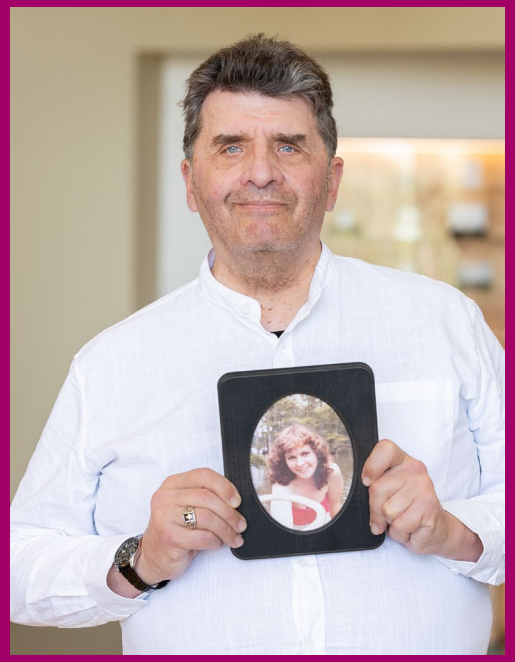


1. Based on current estimates, subject to change. 2. Assuming approvals.

Breakthrough Therapies Driving Accelerating Growth












Q&A

1,2

Accelerating Growth through Life-Changing Medicines