Q3:2026 Business Update and Financial Results

November 9, 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

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.

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Introduction

Brett Monia, Ph.D.

Chief Executive Officer

Positioned for Growth through Commercial Execution and Pipeline Progress

Expanded our Marketed Medicines[1]

- TRYNGOLZA for severe hypertriglyceridemia
- ZANVASTRO for Alexander disease
- HIBSAGO for chronic hepatitis B

Reported Positive Phase 3 Data

- Sefaxersen for IgA nephropathy[2]
- Ulefnersen for FUS-ALS

Announced Phase 3 Data Misses

- Pelacarsen for Lp(a) driven-CVD
- Eplontersen for ATTR cardiomyopathy

Reaffirming 2026 Total Revenue, Operating Loss and Cash Guidance; Reducing TRYNGOLZA[3]

- TRYNGOLZA product sales guidance lowered to ~$50M
- DAWNZERA product sales guidance unchanged
- Substantial R&D revenue



Jared
living with sHTG

1. U.S. Prescribing Information: tryngolza.com, zanvastro.com, hibsago.com. 2. Interim Phase 3 data, study remains ongoing. 3. Based on current expectations, subject to change.

Accelerating Value through Commercial Execution

Kyle Jenne

Chief Global Product Strategy Officer

TRYNGOLZA: Launch Underway for First and Only FDA Approved Medicine to Reduce TGs and Risk of AP in sHTG[1]

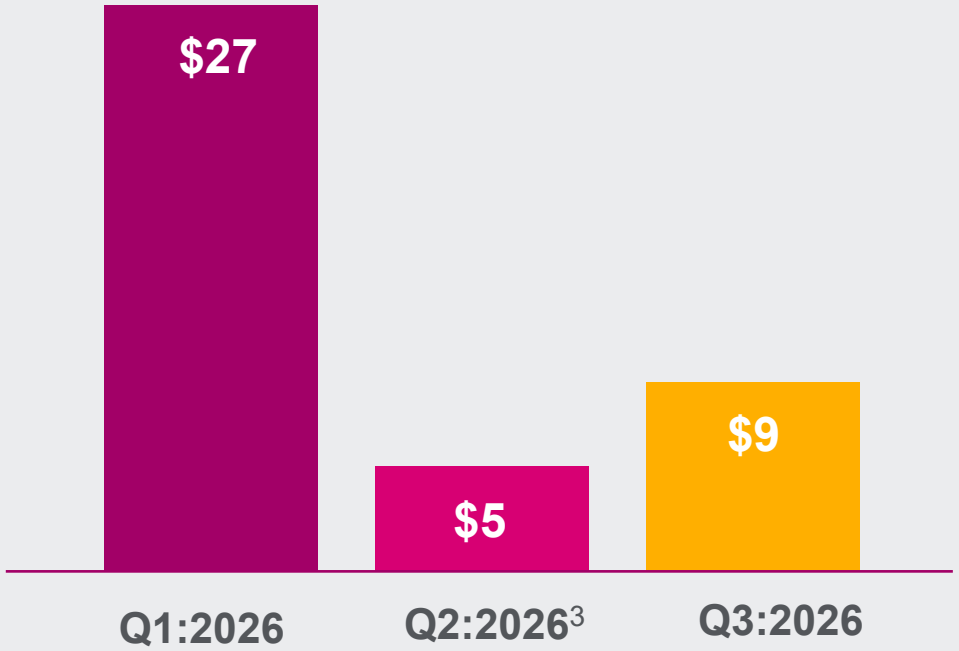


Robust efficacy and safety

- Significant and sustained triglyceride reductions
- Substantial reduction in acute pancreatitis events
- Favorable safety and tolerability profile

Convenience of once-monthly self-administration with an autoinjector

Generated $41 million through Q3:2026[2]



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

1. See Full TRYNGOLZA Prescribing Information. 2. Q1'26 and Q2'26 results product sales reflect familial chylomicronemia syndrome (FCS) indication. Q3'26 product sales reflect expanded sHTG indication. 3. Price adjustment effective April 1, 2026.

TRYNGOLZA: Establishing a New Treatment Paradigm for sHTG[1]



Encouraging Early Launch Fundamentals[2]

Strong HCP enthusiasm and **intent to prescribe**

Prescribing consistent with **broad sHTG label**

Prescribing across all expected specialties, including **cardiology, endocrinology and lipidology**

HCP's value flexibility of **50 mg** and **80 mg** doses

1. See Full TRYNGOLZA Prescribing Information. 2. Through September 30, 2026.

Key Execution Priorities Designed to Increase and Streamline Prescribing

Broaden the Prescriber Base

Increasing education and **engagement efforts** with **high-priority specialists**

~1,500

HCPs have prescribed across all anticipated specialties[1]

1. From sHTG approval through September 30, 2026.

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Increase the Depth of Prescribing

Help **early prescribers gain experience**, identify **additional** appropriate **patients** and **expand treatment** within practices

24%

of **prescribers** have **written more than one prescription**[1]

1. From sHTG approval through September 30, 2026.

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Expand and Streamline Access

Educate HCP offices on **payer requirements** & reimbursement process

Work with payers to **establish additional coverage** policies

33%

of **commercial lives** on formulary; **all coverage aligned with broad TRYNGOLZA label**[1]

1. From sHTG approval through September 30, 2026.

TRYNGOLZA: Significant Opportunity for Underserved sHTG Patients

Substantial Unmet Need

Fasting triglycerides **≥500 mg/dL** and **increased risk** of potentially life-threatening acute pancreatitis (AP)

Limited benefit from other treatments, including **fibrates** and **omega-3s**

Significant Market Opportunity[1]

>3 million people with sHTG in the U.S.

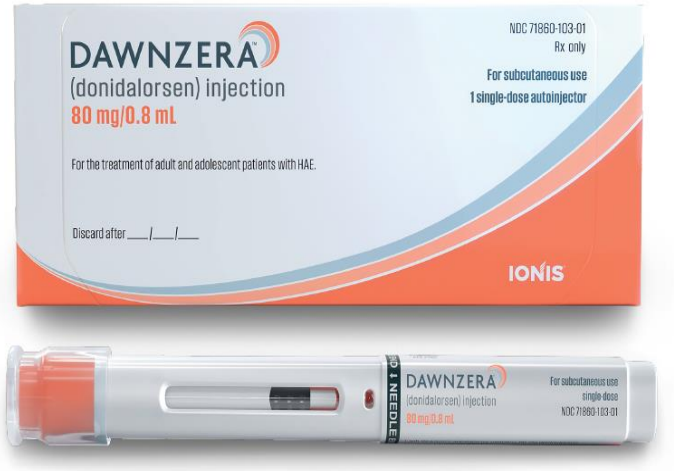
- Includes ~1 million people with high-risk sHTG: TGs ≥880 mg/dL or ≥500 mg/dL + AP history and/or comorbidities
- **Early launch focus** on these **high-risk patients**

1. Sanchez et al. *Lipids in Health and Disease* 2021;20:72; Christian et al., *Am J Cardiol* 2011;107:891-897; Saadatagah et al. *J Am Heart Assoc*. 2021;10(11):e019343.

DAWNZERA Launch Continues to Gain Momentum[1]

Delivering on What HAE Patients Need Most

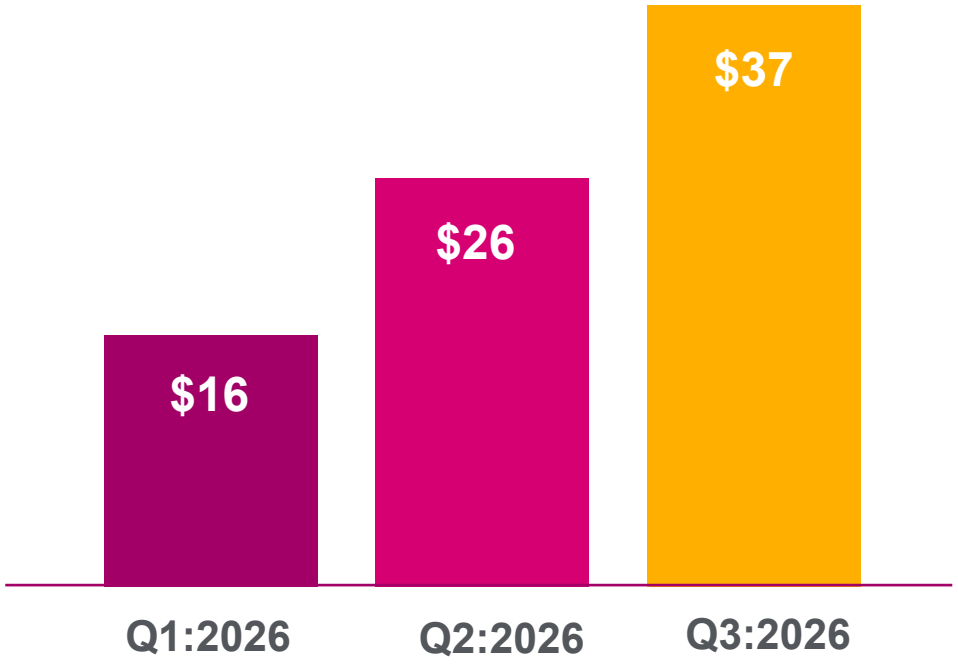
First and **Only RNA-Targeted Treatment** to **Prevent HAE Attacks**



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**
- **Growing number of repeat prescribers**
- **Global launch underway, expanding in EU markets**[2]

Generated $79 million through Q3:2026



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

1. See Full DAWNZERA Prescribing Information. 2. Otsuka is responsible for commercializing DAWNZERA in the EU.

Zanvastro™
(zilganersen)

NOW APPROVED

The first and only disease-modifying therapy approved by the FDA for the treatment of pediatric and adult patients with Alexander disease[1]

1. See Full ZANVASTRO Prescribing Information.

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ZANVASTRO: Ionis' First Independent Neurology Launch[1]

Substantial Unmet Need

Alexander disease (AxD): An ultra-rare, progressive and often fatal neurological disorder

First approved disease-modifying treatment

Broad Label

Enables treatment for children and adults with AxD

Early Enthusiasm from AxD Community

Excitement across HCPs and caregivers for ZANVASTRO

Strong partnership with the Alexander disease patient community

Launch Priorities

Transition clinical study and EAP patients to commercial therapy

Support physicians in starting treatment for diagnosed patients

Identify new patients through disease awareness

Establish coverage and access

1. See Full ZANVASTRO Prescribing Information.

Clear Commercial Priorities Across Launches

First Broad Patient Population Launch Underway

Tryngolza® (olezarsen) injection

Convert HCP enthusiasm into broader, repeat prescribing while expanding payer coverage

HAE Launch Driving Commercial Revenue Growth

DAWNZERA® (donidalorsen) injection

Continue building momentum across all patient segments

First Independent Neurology Launch Underway

Zanvastro™ (zilganersen)

Help HCPs initiate treatment for patients, including working with payers to ensure access

Delivering Important Pipeline Achievements

Holly Kordasiewicz, Ph.D.

Chief Development Officer

TRYNGOLZA: First and Only FDA Approved Medicine to Reduce TGs and Risk of AP in sHTG

Reductions in Fasting Triglycerides

Up to **72%** at 6 months

placebo-adjusted mean reduction[1]
(p<0.0001)

Phase 3 placebo-controlled data

Up to **79%** in up to 2 years

mean reduction[2]

Open-label extension data

Reduction in Adjudicated Acute Pancreatitis Events

Up to a **91%**

reduction in acute pancreatitis events compared to placebo at 12 months[3]

Phase 3 placebo-controlled data

Patients who Achieved TGs below 500 mg/dL

90%

in up to 2 years[2]

Open-label extension data

Patients who Achieved TGs below 150 mg/dL

Nearly **60%**

in up to 2 years[2]

Open-label extension data

Favorable safety and tolerability, no new safety findings in OLE[1,2]

1. *The New England Journal of Medicine*, "Olezarsen for Managing Severe Hypertriglyceridemia and Pancreatitis Risk." Marston, et al. 2. Open-label extension (OLE) data presented at ESC 2026.
3. From USPI. Data based on the 50 mg dose at 12 months. See Full TRYNGOLZA Prescribing Information.

ZANVASTRO: Ionis' First Independent Launch from Leading Neurology Pipeline[1]

ZANVASTRO for the treatment of Alexander disease

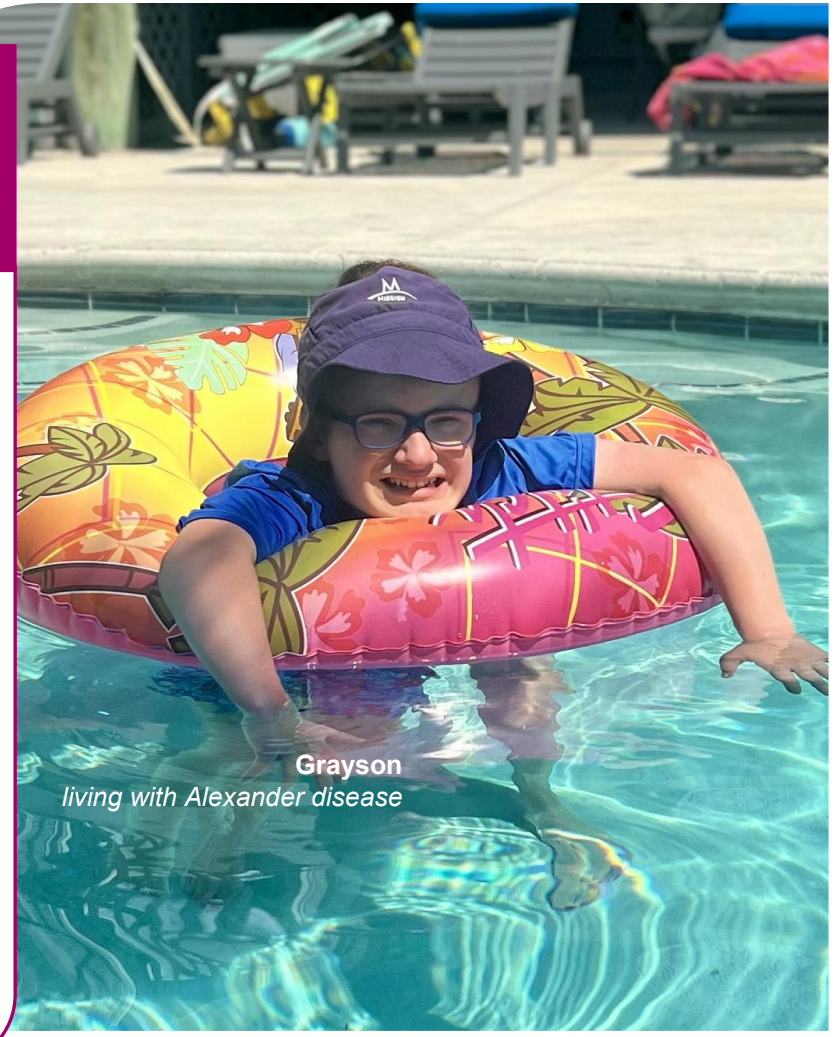
First and **only disease modifying treatment approved** for Alexander disease

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Positive pivotal study data:

- Statistically significant stabilization of motor function
- Favorable trends across key symptoms
- Favorable safety and tolerability

Awarded a **Rare Pediatric Disease Priority Review Voucher**



Grayson
living with Alexander disease

1. See Full ZANVSTRO Prescribing Information.

Obudanersen: A Promising Investigational Medicine for Angelman Syndrome

The Opportunity

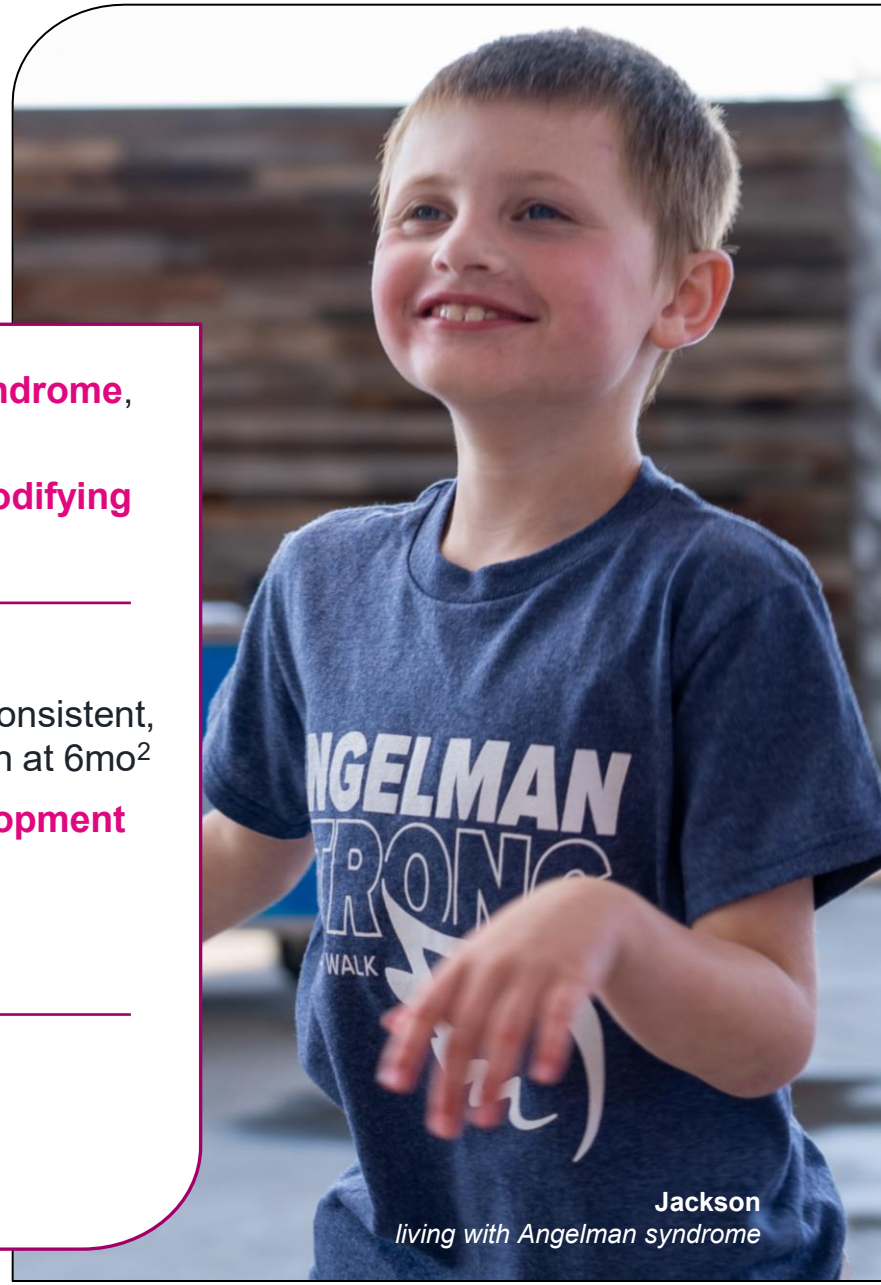
- **>100k people** in major geographies with **Angelman syndrome**, a severe, rare neurodevelopmental disorder[1]
- **Significant unmet need** with **no approved disease-modifying treatments**

Key Clinical Highlights

- **Positive results seen in the HALOS Ph2 study**, with consistent, meaningful improvements in key areas of clinical function at 6mo[2]
- **Long-term extension data** continues to **support development**
- **Granted Breakthrough Therapy designation**

Next Steps

- Pivotal Phase 3 REVEAL study **now fully enrolled**
- UPD/ID CHAMPION **study underway**
- On track for Phase 3 **data** in **H2 2027**[3]



Jackson
living with Angelman syndrome

1. Luk. *Eur. J. Méd. Genet.* (2016). 2. Based on data generated to date from the Phase 1/2a HALOS study of obudanersen. 3. Based on current assumptions, subject to change.

Partnered Medicines Amplify Our Opportunities[1]

	HIBSAGO™ (CHB)[3]	Sefaxersen (IgAN)	Ulefnersen (FUS-ALS)
Program Status	**Approved** in the **U.S.**, **Japan** and **Canada; Under** regulatory **review** in **additional markets**	**Positive interim Phase 3 data; Potential 2027 U.S. approval**[1]	**Positive topline Phase 3 data; Potential 2027 U.S. approval**[1]
Patient Population[2]	**~240M patients** worldwide	**>400k patients** worldwide	**~1% of all ALS cases** worldwide
Value Proposition	**First-in-class** treatment offering **unprecedented functional cure rates** compared to current standard of care	**First RNA-targeted treatment for IgAN**; addresses the underlying pathophysiology of alternative complement pathway activation[4]	**First-disease-modifying potential treatment** to address amyotrophic lateral sclerosis (ALS) caused by mutations in the *FUS* gene, a fatal neurodegenerative disorder

1. Based on current assumptions, subject to change. Sefaxersen approval timing subject to the outcome of the discussion with health authorities. 2. Market data on file. 3.See Full HIBSAGO Prescribing Information. 4. Among investigational medicines in Phase 3 development.

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2026 Progress and First Look at 2027 Key Value-Driving Events[1]

Phase 3 **Clinical Events**

2026

HIBSAGO
B-Well data
(CHB)

Eplontersen
CARDIO-TTRansform data
(ATTR-CM)

Sefaxersen
IMAgINATION
interim 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)

2027

Obudanersen
REVEAL data
(Angelman syndrome)

Sefaxersen
IMAgINATION data
(IgAN)

Diranersen
Phase 3 initiation
(Alzheimer's disease)

Regulatory **Actions**

2026

DAWNZERA
EU approval
(HAE)

TRYNGOLZA
U.S. approval
EU submission
EU approval
(sHTG)

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

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

HIBSAGO
Submissions
U.S. & Japan
Approval
(CHB)

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

2027

Sefaxersen[2]
U.S. approval
(IgAN)

HIBSAGO
EU approval
China approval
(CHB)

Ulefnersen
U.S. approval
(FUS-ALS)

Product **Launches**

2026

DAWNZERA
EU
(HAE)

TRYNGOLZA
U.S.
(sHTG)

ZANVASTRO
U.S.
(AxD)

HIBSAGO
Japan
U.S.
(CHB)

TRYNGOLZA
EU
(sHTG)

2027

HIBSAGO
EU & China
(CHB)

Sefaxersen[2]
U.S.
(IgAN)

Ulefnersen
U.S.
(FUS-ALS)

1. Based on current assumptions and are subject to change, timing of partnered program catalysts based on partners' most recent publicly available disclosures. 2. Subject to the outcome of the discussion with health authorities.

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Q3:2026 Financial Performance

Beth Hougen

Chief Financial Officer

Q3:2026 YTD Financial Highlights[1]

Revenues $757M

Commercial Revenue: $363M

- $41M in TRYNGOLZA product sales
- $79M in DAWNZERA product sales
- 23% increase year-over-year (YoY)

R&D Revenue: $394M

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

Operating Expenses[2] $975M

R&D Expenses[2]: $569M

- Majority funding late-stage programs

SG&A Expenses[2]: $397M

- YoY increase fueling launches

Operating Loss[2] ($218M)

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

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Cash & Short-term Investments $1.9B

- Supports investments in launches, pipeline and technology

1. For the nine months ended September 30, 2026. 2. Non-GAAP – please see reconciliation to GAAP in Q3:2026 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.

Reaffirming 2026 Total Revenue, Operating Loss and Cash Guidance[1,2]

Revenue

$875-900M

TRYNGOLZA net product sales
~$50M
(lowered from $100-110M)

DAWNZERA net product sales
$110-120M
(unchanged)

Substantial R&D Revenue

Operating Loss

$425-475M[2]

Reflects strong revenue generation from multiple sources and prudent expense management

Cash

>$1.6B

Supports investments in launches, pipeline and technology

1. Based on current assumptions, subject to change. 2. Non-GAAP – please see reconciliation to GAAP in Q3:2026 press release.

Conclusion

Brett Monia, Ph.D.

Chief Executive Officer

Driving Accelerating Growth[1]









1. Based on current estimates, subject to change.

Q&A

Breakthrough Therapies Driving Accelerating Growth



