Corporate Presentation

October 2026

Nasdaq: IONS

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.

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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) injection

Positioned to transform the HAE treatment paradigm

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

Global launch underway[3]

First Independent Neurology Launch Underway

Zanvastro™ (zilganersen)

First disease-modifying treatment for Alexander disease

Broad label, enabling treatment for children and adults

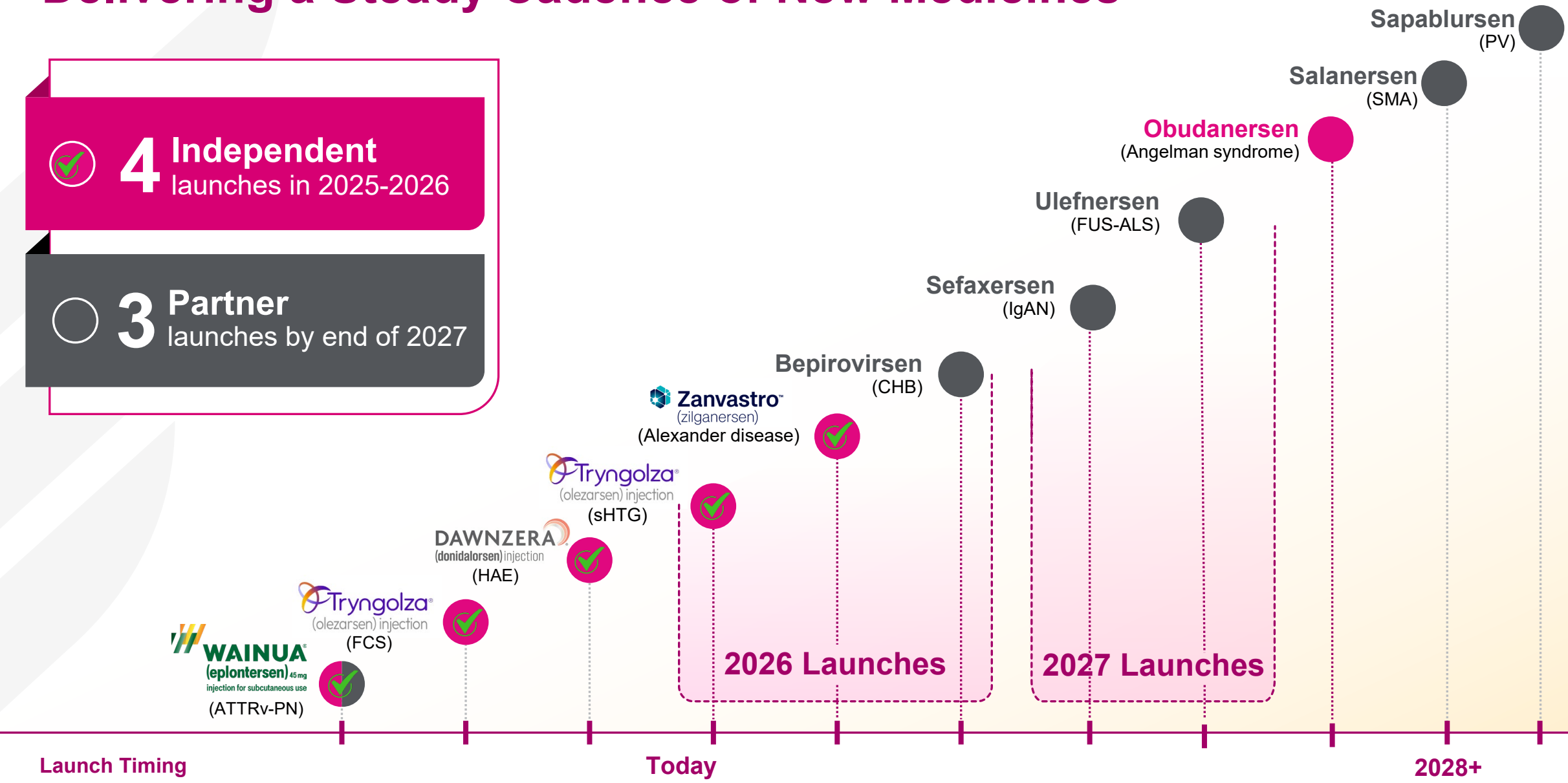
Global regulatory filings planned in 2027[4]

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. 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

3 Partner launches by end of 2027



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

Delivering Transformational Medicines in Focused Therapeutic Areas



Cardiometabolic

First- or best-in-class medicines that target cardiometabolic diseases, the leading causes of death globally

Rare and prevalent patient populations in focused disease areas



Neurology

First- or best-in-class medicines to address a broad range of diseases with high unmet need

Potential for Multiple Blockbusters[1]

1. Based on current estimates, subject to change.

Building a Leading Cardiometabolic Pipeline[1,2]

2
Wholly Owned Medicines

3
Partnered Medicines

5
Medicines

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.

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)

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

TRYNGOLZA: sHTG Launch Off to Encouraging Start[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**[2]
- **2026 TRYNGOLZA net product sales guidance $100-110M**[3,4]

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. 4. Guidance provided as of July 29, 2026 in conjunction with Q2'2026 earnings.

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.

Leading the Way in the Treatment of Neurological Diseases with an Advancing Pipeline[1,2]

8
Wholly Owned Medicines

5
Partnered Medicines

13
Medicines

Approved Medicines[3-6]

Zanvastro™ (zilganersen)

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. ZANVASTRO is now approved in the U.S.; see Full Prescribing Information. SPINRAZA.com. 4. QALSODY.com. 5. WAINUA.com.

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

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ZANVASTRO: Ionis' First Independent Neurology Medicine Launch[1]

ZANVASTRO for the treatment of Alexander disease

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

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Broad label, enabling treatment **for children and adults** with Alexander disease

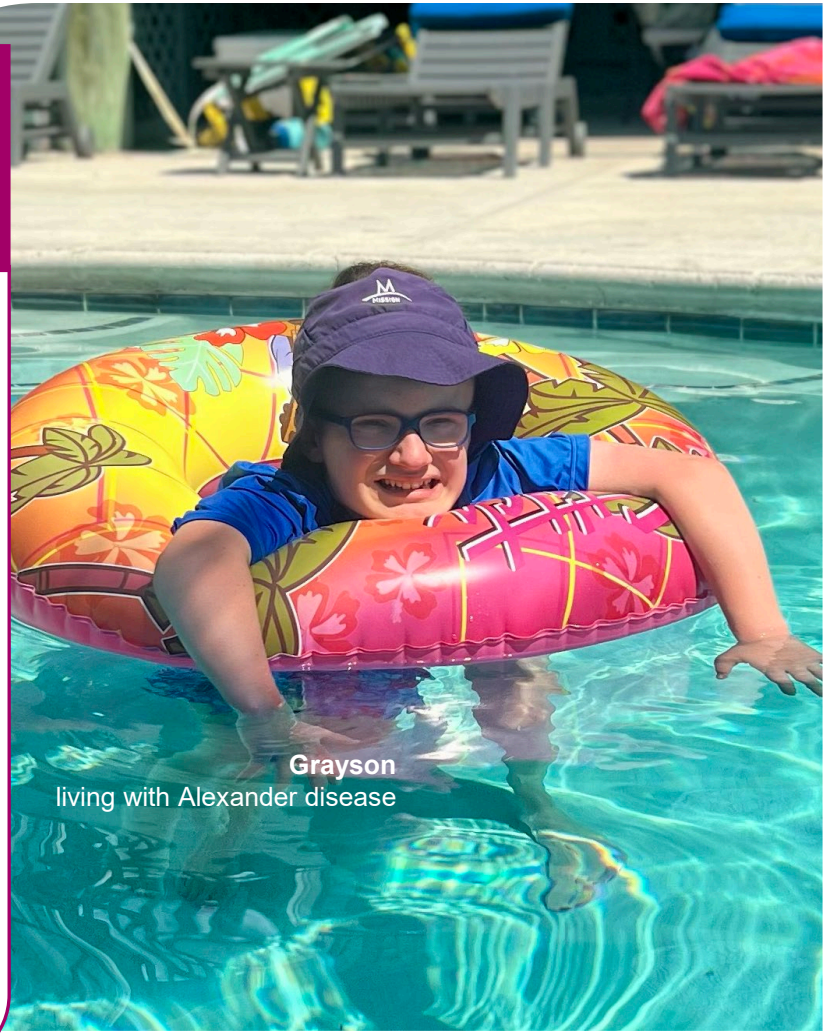
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Positive pivotal study data: statistically significant stabilization of motor function, favorable trends across key symptoms and favorable safety

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Commercializing outside the U.S. with Recordati[2]

Awarded a **Rare Pediatric Disease Priority Review Voucher** in connection with ZANVASTRO approval



Grayson
living with Alexander disease

1. ZANVASTRO is now approved in the U.S.; see Full Prescribing Information. 2. Assuming approval.

ZANVASTRO: Ionis' First Independent Neurology Launch[1]

Substantial Unmet Need

Alexander disease: An **ultra-rare**, **progressive** and **often fatal** neurological disorder

First approved disease modifying treatment

Broad Label

ZANVASTRO indication enables **treatment for children and adults** with Alexander disease

Well-Established Patient Community

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

Strategy to Reach Patients

Identification, diagnosis and **treatment management**

Education, access and **support**

Expanding **global access** through **Recordati**[2]

1. ZANVASTRO is now approved in the U.S.; see Full Prescribing Information. 2. Assuming approval.

Obudanersen: A Promising Investigational Medicine for Angelman Syndrome

The Opportunity

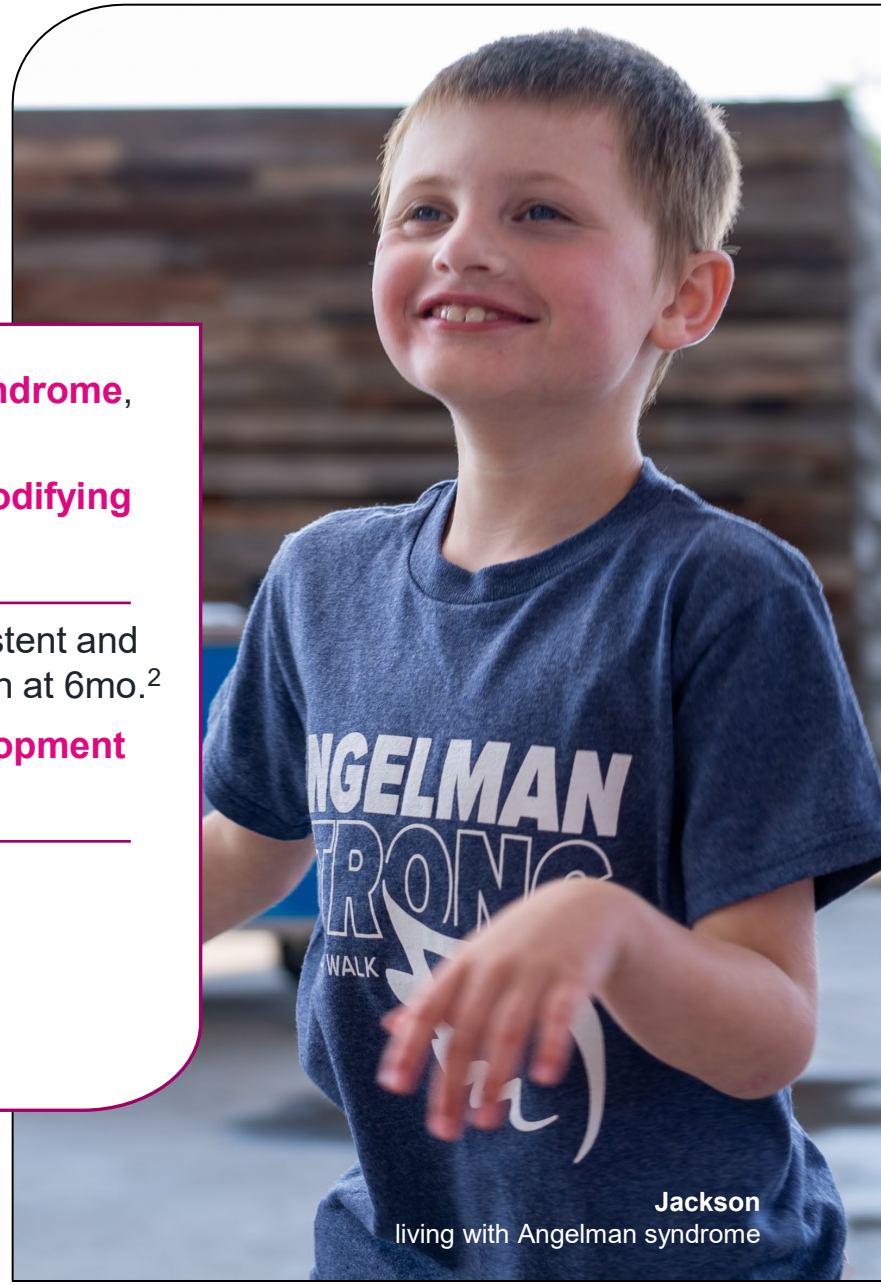
- **>100k people** in major geographies with **Angelman syndrome**, a severe, rare neurodevelopmental disorder[1]
- **Significant unmet need** with **no approved disease-modifying treatments**

Key Clinical Highlights

- **Positive results seen in the HALOS study**, with consistent and 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**
- On track for Phase 3 **data expected in H2 2027**[3]
- UPD/ID CHAMPION **study initiation expected in 2026**

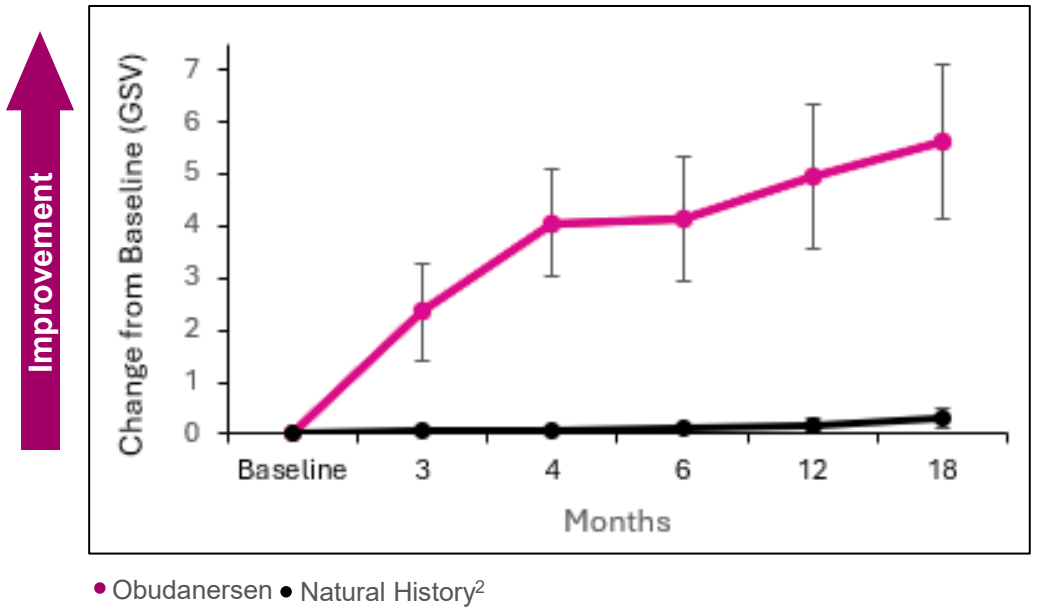


Jackson
living with Angelman syndrome

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.

Expressive Communication: Continued Improvement Observed on Bayley-4 at 18 Months[1]

Change on Bayley-4 Expressive Communication Obudanersen vs. Natural History



Improvements on Bayley-4 measure of expressive communication exceed natural history[2]

Consistent improvements across additional assessment tools measuring expressive communication

GSV, Growth scale values 1. ≥2 years of age medium (40mg) and high (80mg) dose groups, n=35-40 for obudanersen treatment. Excludes patients who dose escalated or had a gap in dosing between MAD and LTE. 2. Natural history data compiled from two studies: www.clinicaltrials.gov/study/NCT04507997 and www.clinicaltrials.gov/study/NCT00296764 and includes Bayley-3 to Bayley-4 conversion by Pearson.

Responder Analysis: Continued Benefit in Multiple Domains Assessed in the HALOS Study[1-3]

HALOS

	Responders on Bayley-4 Expressive Communication	Responders on ≥ 1 Bayley-4 Domains	Responders on ≥ 2 Bayley-4 Domains	Responders on ≥ 3 Bayley-4 Domains
6 months	61%	95%	84%	68%
12 months	64%	97%	89%	75%
18 months	71%	97%	83%	71%

Responders are defined as having a change from baseline of >20% the standard deviation plus the expected change for growth from natural history[4]

Nearly All Study Participants Responded to Obudanersen Treatment on ≥ 1 Bayley-4 Domains through 18 Months

1. Medium and high dose groups,≥2 years of age, n=35-38. Excludes patients who dose escalated or had a gap in dosing between MAD and LTE. 2. Bayley N. Aylward GP. *Bayley Scales of Infant and Toddler Development-Fourth Edition*. NCS Pearson. (2019). 3. Analysis reflects data from participants in the obudanersen HALOS study aged 2-34 years old who received either 40mg or 80mg obudanersen for the entirety of the study. Participant data for those who dose-escalated during the study and with data from out-of-window visits are excluded. 4. Natural history studies: www.clinicaltrials.gov/study/NCT04507997 and www.clinicaltrials.gov/study/NCT00296764 and includes Bayley-3 to Bayley-4 conversion by Pearson.4.

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Extending the SMA Franchise



SPINRAZA® (nusinersen) injection 12 mg/5 mL

Nusinersen High Dose

- Now approved in U.S., EU and Japan

Salanersen

- Designed with a novel Ionis chemistry to achieve strong efficacy & once-yearly dosing
- Interim Phase 1 data showed that once-yearly dosing with both doses tested was well tolerated and led to substantial slowing of neurodegeneration
- Improved economics over SPINRAZA[2]

Salanersen Phase 3 program underway

- STELLAR-1 study underway in presymptomatic infants genetically diagnosed with SMA

1. Timing expectations based on current assumptions and subject to change. 2. SPINRAZA is approved in the U.S. for or the treatment of spinal muscular atrophy in pediatric and adult patients; see Full Prescribing Information.

Diranersen: A Differentiated Approach in Targeting Tau

Tau is a potentially attractive target in Alzheimer's disease:

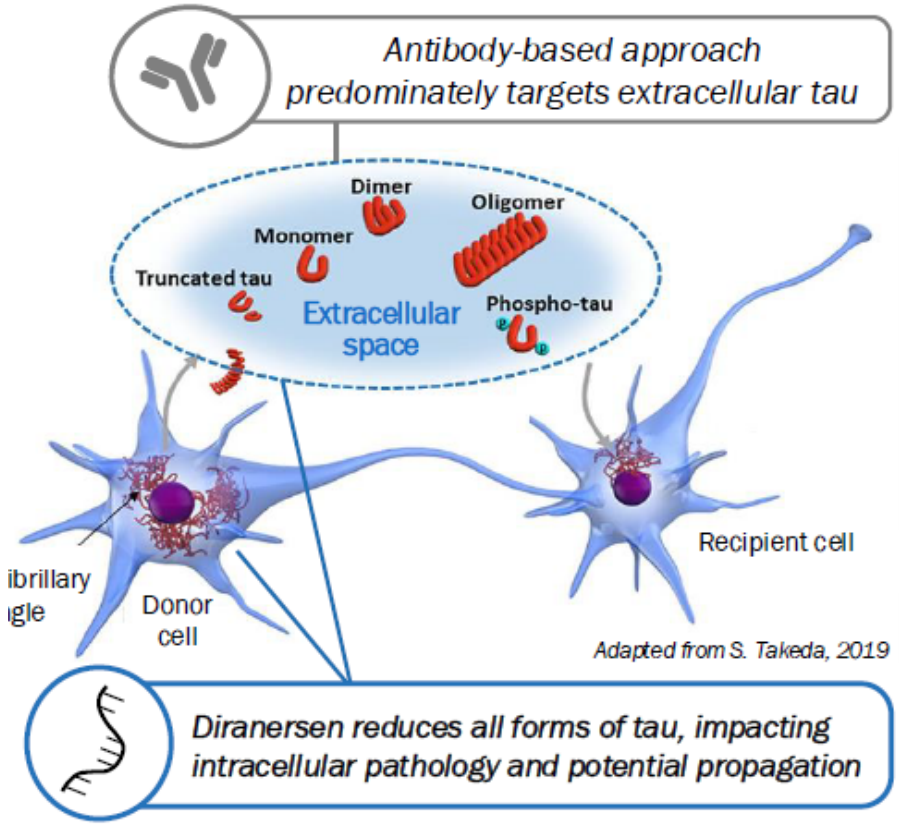
- AD is a progressive neurodegenerative disease characterized by cerebral accumulation of amyloid plaques and tau NFTs[1]
  - The burden of tau NFTs is closely linked to neurodegeneration and clinical decline[2]

To date, antibody approaches for tau have not shown clinical benefit

- Antibodies target tau predominately outside the cell
- No reduction in baseline tau PET has been demonstrated by anti-tau antibodies

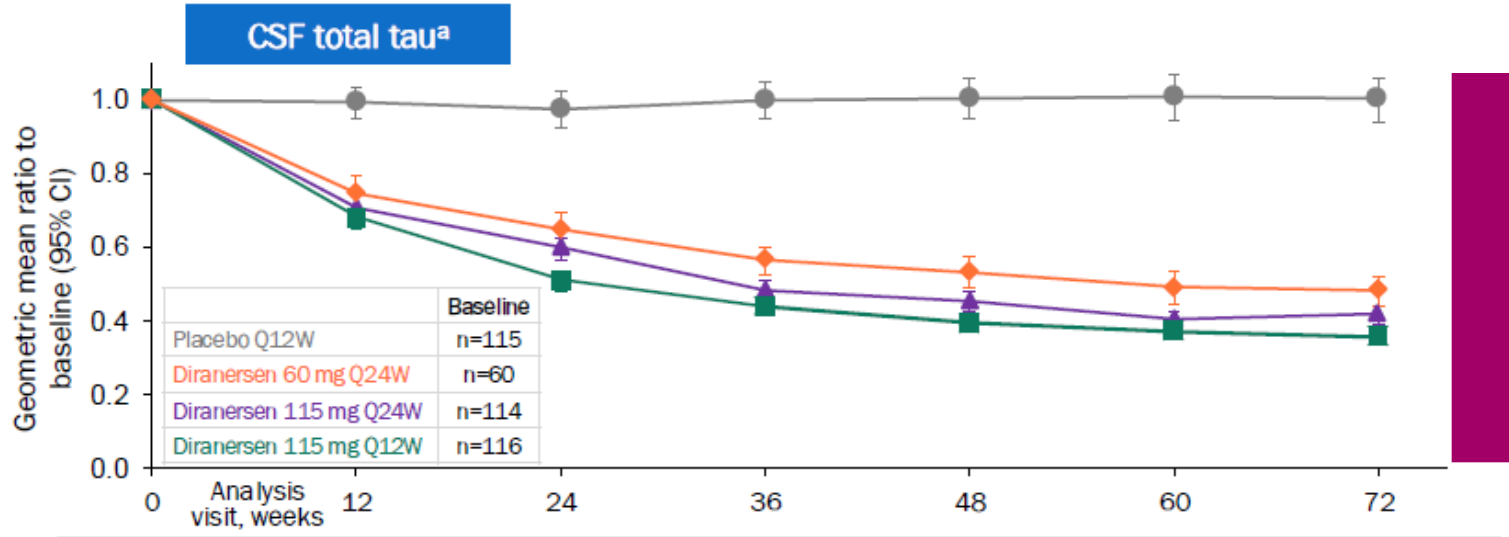
Diranersen is designed to reduce the production of all forms of tau within the neuron

- Diranersen reduces the translation of MAPT into tau protein
- Addresses both extracellular and intracellular tau
- Enables downstream reduction of tau pathology in the brain

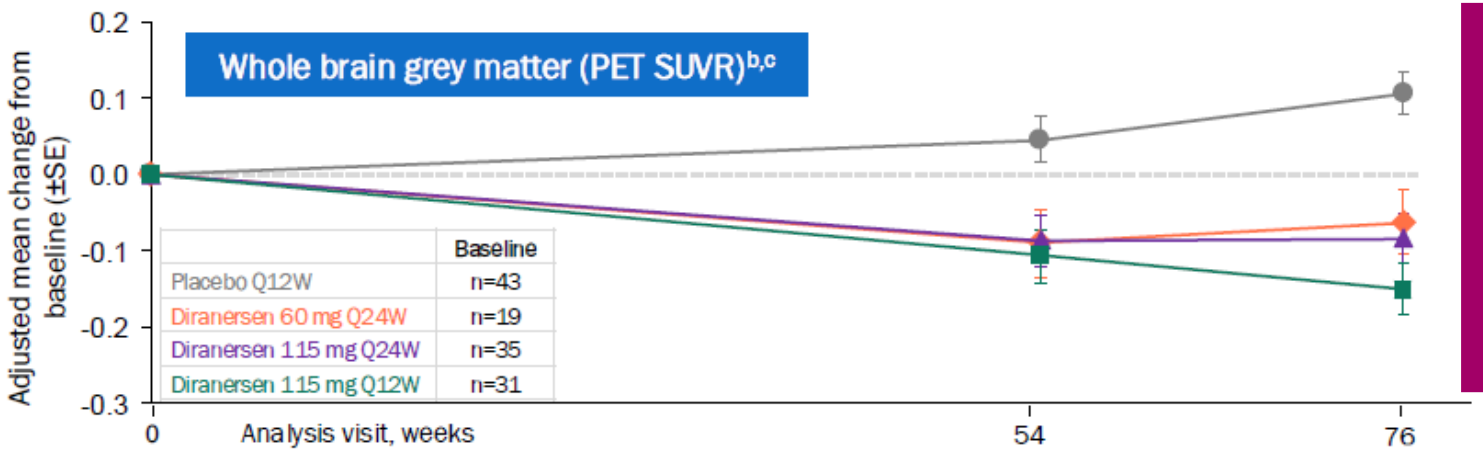


Biogen licensed diranersen and is responsible for ongoing develop and commercialization; 1. Selkoe DJ, Hardy J. EMBO Mol Med. 2016;8(6):595-608. 2. Bejanin A, et al. Brain. 2017;140(12):3286-3300. AD = Alzheimer's disease; MAPT = microtubule-associated protein tau; NFT= neurofibrillary tangles; PET = positron emission tomography.

Diranersen is the Only Tau Directed Agent to Show Substantial Tau Reduction in the CSF and Brain[1]



- **50-65% reduction** from baseline in soluble total tau in CSF across dose arms at week 72
- Confirms target engagement



- **First reported substantial reduction in tau PET** by an anti-tau agent in a Phase 2 study
- Suggests reduction in tau pathology in the brain

MMRM with treatment, visit, and treatment by visit; adjusted for baseline biomarker, baseline biomarker by visit, MMSE, clinical stage, and age. 1. In Phase 2 CELIA Study. a) Lumipulse CSF t-tau assay. b) MK-6240 was the tau PET tracer; reference region was inferior cerebellum. d) Brain regions assessed: medial temporal cortex, lateral temporal cortex, temporal cortex, frontal cortex, parietal cortex, anterior cingulate cortex, posterior cingulate cortex, occipital cortex, whole brain grey matter. CSF = cerebrospinal fluid; MMRM = Mixed Models for Repeated Measures; PET = positron emission tomography; Q12W = every 12 weeks; Q24W = every 24 weeks; SUVR = standardized uptake value ratio.

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Phase 2 CELIA Study Results: 60mg Q24W Demonstrated a Promising Efficacy Profile Across Multiple Endpoints

Diranersen 60mg Q24W	CDR-SB	ADAS-COG*	MMSE	ADCS-ADL-MCI	ADCOMS	iADRS
	26%	42%	50%	0%	23%	30%

Anti-Amyloids	CDR-SB	ADAS-COG*	MMSE	ADCS-ADL-MCI	ADCOMS	iADRS
Emerge *NCT02484547*	22%	27%	18%	42%	NA	NA
Engage *NCT02477800*	12%	11%	6%	18%	NA	NA
Clarity AD *N Engl J Med 2023*	27%	26%	NA	36%	24%	NA
Trailblazer ALZ 2 NCT04437511	29%	20%	16%	NA	NA	22%

- CDR-SB and ADCOMS inline with anti-amyloid agents[1]
- Robust cognitive effects – markedly higher improvement than anti-amyloid treatments
  - ✓ 42% for ADAS-COG 13
  - ✓ 50% for MMSE
  - ✓ 30% for iADRS
- No separation on ADCS-ADL-MCI at 76 weeks – follow up continues

* All are ADAAs-COG13 except ADAS-COG14 in Clarity AD; 1. Based on historical data, not a direct comparison based on head-to-head studies. ; iADRS= modified integrated Alzheimer's Disease Rating Scale.

Diranersen Targeting Tau for Alzheimer's Disease Advancing to Phase 3[1-2]

Diranersen:

- ✓ **Encouraging emerging clinical profile** with **unprecedented impact on tau reduction and cogitative**
  - ✓ With 94% of patients who completed the study continuing in the LTE
- ✓ A **well tolerated safety profile** where ARIA is not anticipated with tau-targeting MoA
- ✓ The potential for **twice yearly administration**

Next Steps

- Ongoing long-term extension study
- Ongoing analyses of the data expected to be presented and published
- Biogen continuing to engage with medical community and regulators on Phase 3 trial planning

1. Phase 2 data presented at AAIC 2026. 2. Biogen licensed and is responsible for ongoing development and commercialization of diranersen worldwide.

DAWNZERA Launch Gaining Momentum[1]

Delivering on What HAE Patients Need Most

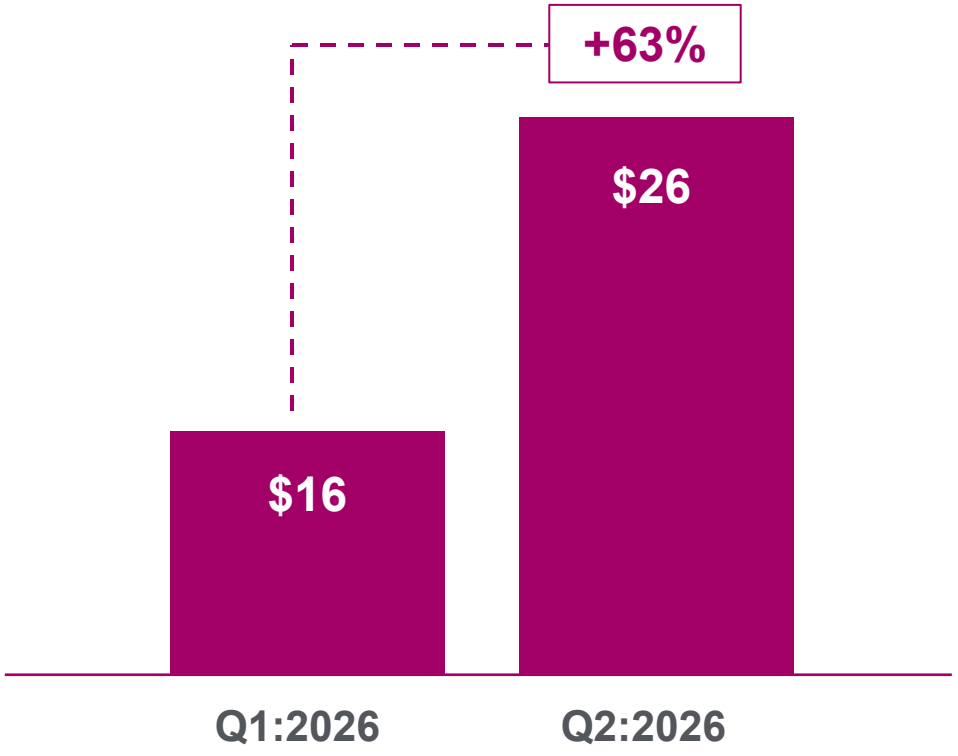
First and **Only RNA-Targeted Treatment** to **Prevent HAE Attacks**



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.

U.S. HAE Market Dynamics Underscore DAWNZERA's Potential[1,2]

- **~7,000** people with HAE in the U.S.[3]
- **~75%** of people with HAE in the U.S. are on LTPs
- **~1,000** allergists/ immunologists treat **90%** of HAE patients
- **~20%** of people with HAE have historically switched treatments annually
- **>90%** of people with HAE are interested in trying a new prophylactic therapy[4]

DAWNZERA Peak Sales Potential: >$500M[5]

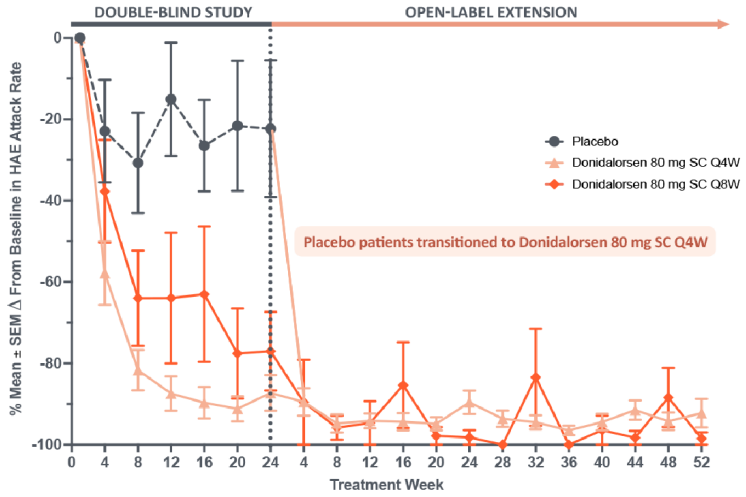
1. DAWNZERA is approved in the U.S. for hereditary angioedema in adults and pediatric patients 12 years of age and older; see Full Prescribing Information. 2. Market data on file. 3. Riedl et al. 2023 *J ALLERGY CLIN IMMUNOL PRACT* VOLUME 11, NUMBER 8; Sylvestre et al 2021 *J ALLERGY CLIN IMMUNOL PRACT* VOLUME 9, NUMBER 12; Nieto et al 2023 World Allergy Organization Journal. 4. Ionis-sponsored Harris Poll results. 5. Based on current estimates.

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DAWNZERA's Robust Efficacy Profile and Switch Data[1-3]

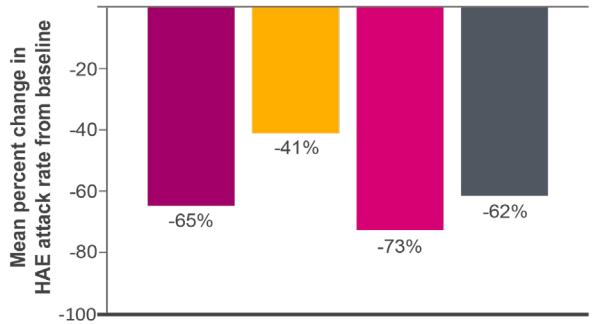
94%

Total Mean Reduction in HAE Attack Rates across Q4W and Q8W over 1 year in OLE[2]



62%

Mean Reduction in HAE Attack Rates After Switching from Prior Treatment



Prior LTP:	Lanadelumab	C1INH	Berotralstat	Total
n =	31	22	11	64
Baseline, mean ± SD =	0.69 ± 1.09	0.61 ± 0.96	1.80 ± 1.92	0.85 ± 1.28
Week 16 (donidalorsen Q4W), mean ± SD =	0.24 ± 0.33	0.36 ± 0.69	0.48 ± 0.53	0.33 ± 0.51

84%

of switch patients surveyed **preferred DAWNZERA**

Reasons participants chose for preferring DAWNZERA:

Efficacy 63%

chose **"it works better to control my HAE"**

Tolerability 50%

chose **"less injection-site pain or reaction"**

Convenience 65%

chose **"less time for administration"**

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.Data on file; HAE attack rate reduction as of data cut-off of January 27, 2025. 3. Riedl MA, Yarlas A, Bordone L, et al. Patient-reported outcomes in the Phase III OASIS-HAE Study of Donidalorsen for Hereditary Angioedema.

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Partnered Medicines Amplify Our Opportunities

Multiple Positive Phase 3 Readouts in 2026[1]

	Bepirovirsen (HBV) H1:26	Sefaxersen (IgAN) 2026	Ulefnersen (FUS-ALS) 2026
Addressable Population[2]	**~300M patients** worldwide	**>400k patients** worldwide	**1% of all ALS cases** worldwide
Value Proposition	**1st and only investigational medicine** shown potential to achieve clinically meaningful functional cure[3] **Granted Priority Review**; PDUFA October 26, 2026	**1st investigational RNA-targeted medicine** to treat IgAN by addressing the underlying pathophysiology of alternative complement pathway activation[4] **Positive topline interim data reported in September 2026**	**First-in-class potential** to address amyotrophic lateral sclerosis (ALS) caused by mutations in the *FUS* gene, a fatal neurodegenerative disorder **Positive topline data reported in September 2026**

1. Based on current assumptions, subject to change. 2. Market data on file. 3. That is currently in Phase 3 development and when combined with oral nucleoside/nucleotide analogues (NAs). 4. Among investigational medicines in Phase 3 development.

Bepirovirsen: Poised to be an Important Advance for Millions of People Living with Chronic Hepatitis B[1]

Unprecedented Functional Cure Rates in Phase 3 Program[3]

- 19% functional cure rate in the overall study population; 26% in patients with lower viral activity, compared to 0% with standard of care
- 49% achieved a surface antigen level of ≤100 IU/mL one year after end of treatment in exploratory analysis
- Acceptable safety and tolerability profile

>240M

People Worldwide Live with Chronic Hepatitis B[2]

Initial Launch anticipated H2:2026[4]

- **October 26, 2026 PDUFA**
- **Approved in Japan**
- **Under review in EU, China and Canada**

Estimated Peak Sales >$2.5B[5]

Eligible for:

- ✓ Additional milestone payments
- ✓ Tiered royalties of 10-12% on net sales

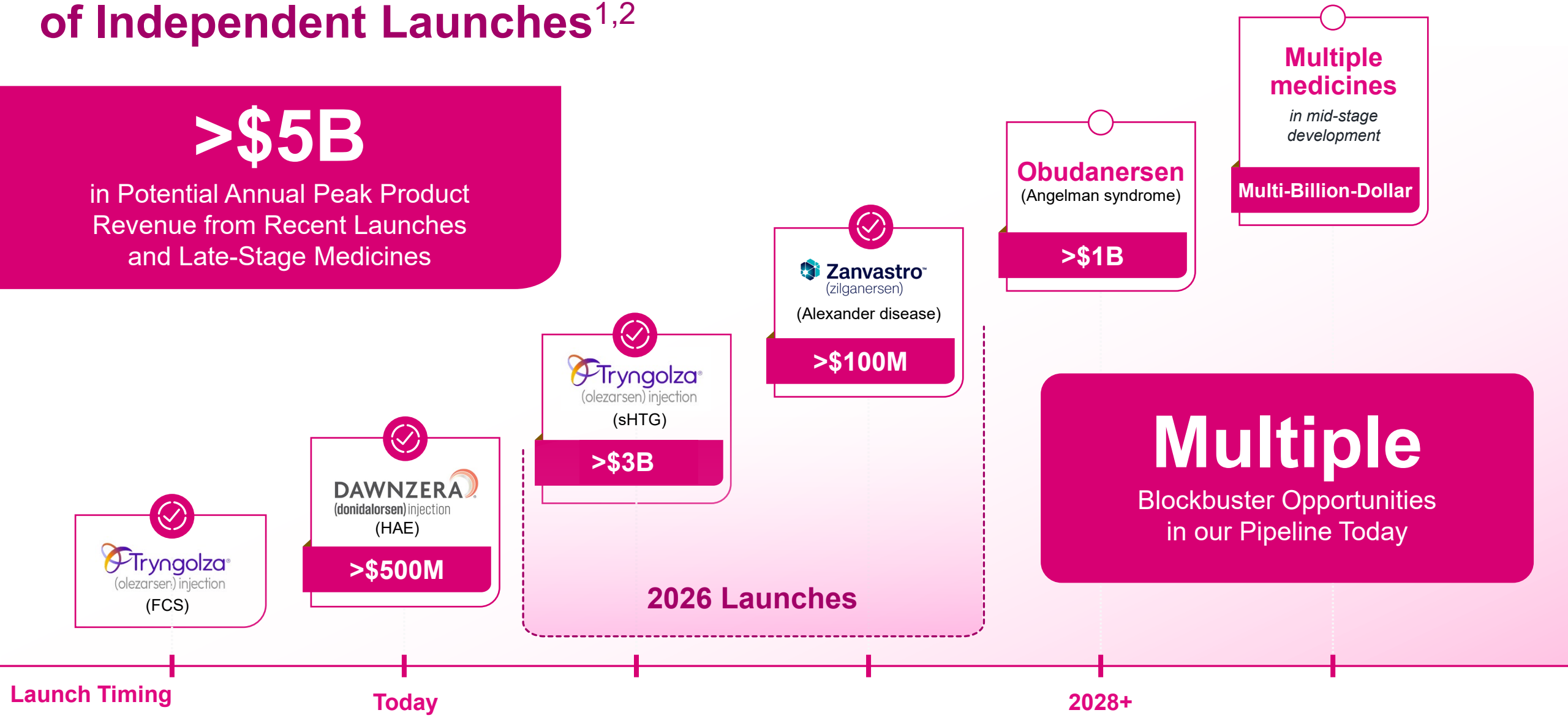
1. GSK licensed bepirovirsen and as a result is responsible for development and commercialization, assuming approval. 2. Market data on file. 3. Phase 3 data published *New England Journal of Medicine*. 4. Timing expectations based on current assumptions and subject to change. 5. Peak sales estimates subject to change and based on public disclosure made by the respective partner

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Accelerating Revenue from Steady Cadence of Independent Launches[1,2]

>$5B

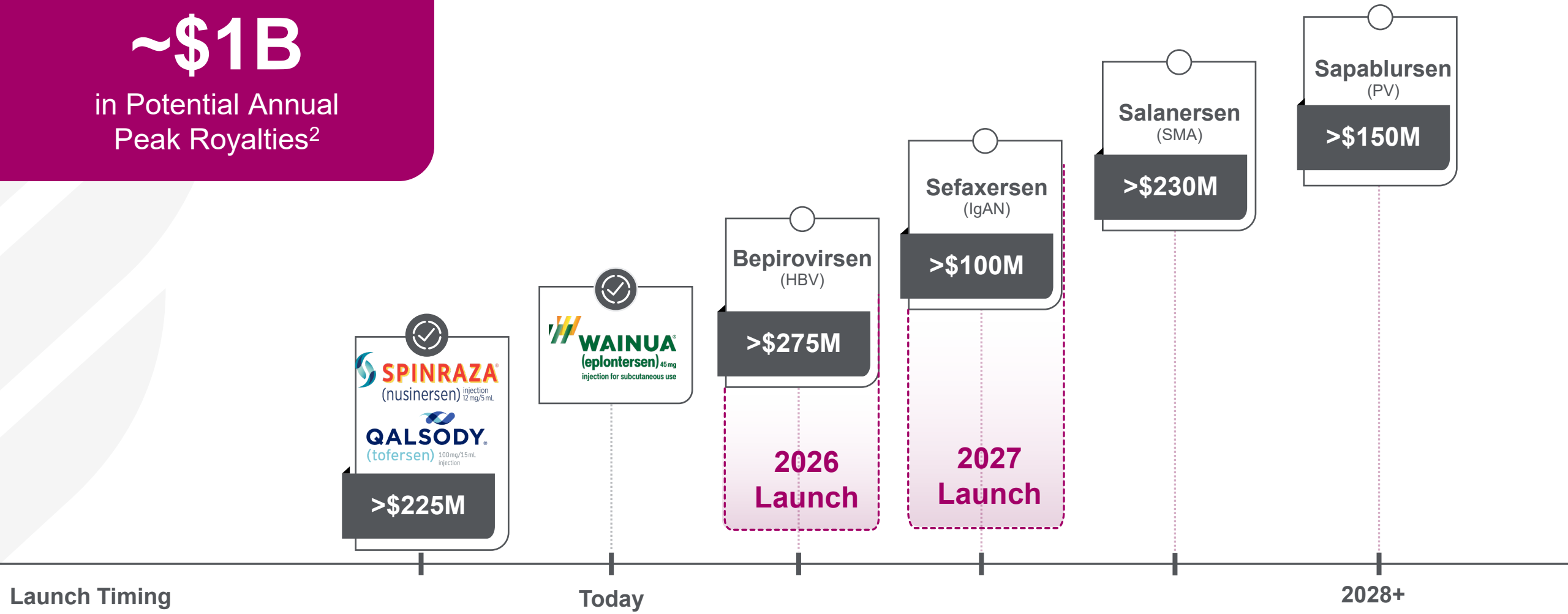
in Potential Annual Peak Product Revenue from Recent Launches and Late-Stage Medicines



1. Assuming approval. Estimated timing of potential U.S. approval based on current assumptions and subject to change. 2. Peak sales estimates based on current estimates and subject to change.

Royalty Growth Opportunities from Approved and Late-Stage Partnered Medicines[1,2]

~$1B
in Potential Annual Peak Royalties[2]



1. Assuming approval. Estimated timing of potential U.S. approval based on current assumptions and subject to change. 2. Peak sales estimates based on current estimates and subject to change. Partnered royalties based on public disclosure made by the respective partner and Ionis' contractual royalty rates for each medicine.

Significant Upside Potential from Late-Stage Partnered Programs

>$1.7B
in Remaining
Partner Payments

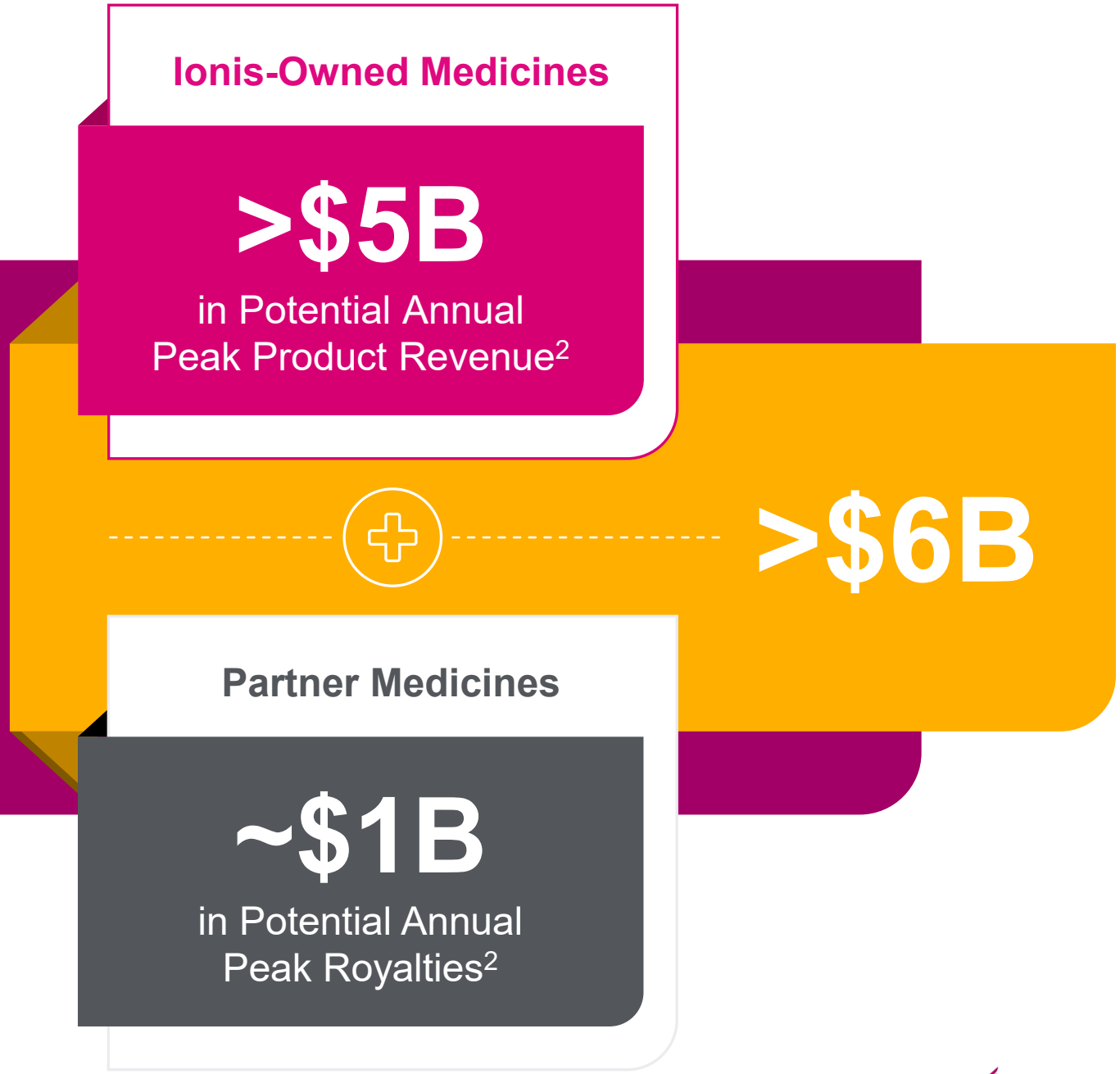
Royalties

Nearly All Partner Revenue Drops to the Bottom Line as Profit

	Total Remaining Milestone Payments[2]	Royalties[2]
Sapablursen PV	**$660M**	Mid-teens
Salanersen SMA	**>$500M**	Tiered, mid-teens to mid-20%
Sefaxersen IgAN	**>$390M**	Tiered, high-teens to 20%
Bepirovirsen HBV	**>$200M**	Tiered, 10-12% on net sales
WAINUA ATTRv-PN	-	US: mid-20% OUS: Tiered up to high teens

1. Based on current timing assumptions, subject to change. 2. As reported in 2025 10-K form and/or Q2 2026 Form 10-Q.

Marketed Products and Planned Launches Provide Substantial Revenue Growth Opportunity[1]



1. Assumes additional approvals through 2028. Estimated timing of potential U.S. approval based on current assumptions and subject to change. 2. Peak sales estimates based on current estimates and subject to change. Partnered royalties based on public disclosure made by the respective partner and Ionis' contractual royalty rates for each medicine.

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

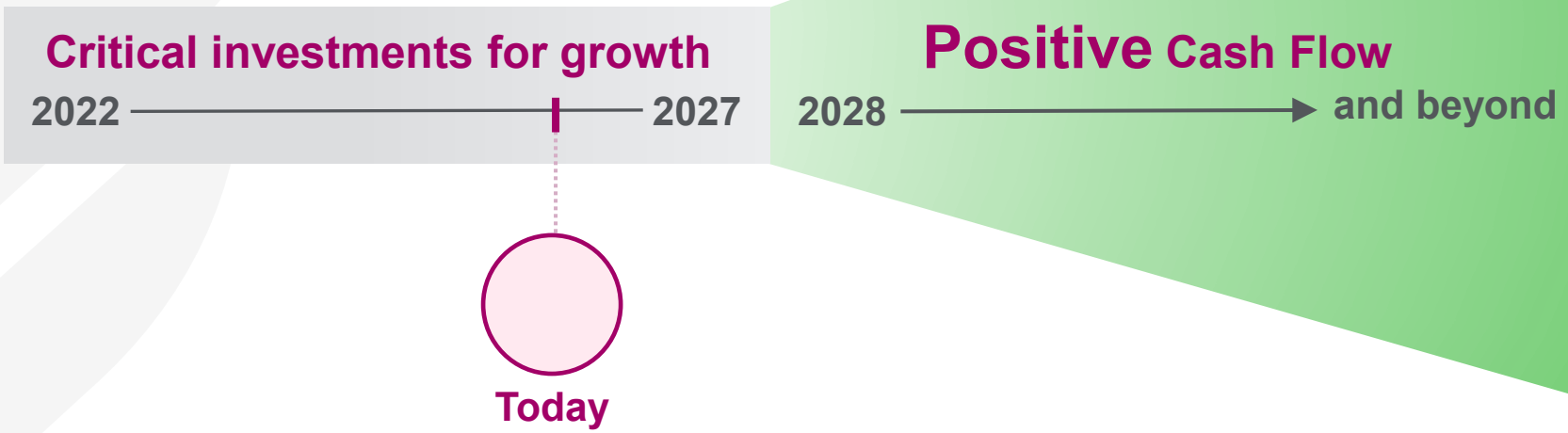
Cash
>$1.6B

Supports investments for launches, pipeline and technology

On track to achieve 2028 cashflow breakeven

1. Based on current assumptions, subject to change. Guidance provided as of July 29, 2026 in conjunction with Q2'2026 earnings. 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.

Ionis is Committed to Goal of Sustained Positive Cash Flow[1]



Key Drivers

- New product launches
- Growing royalty revenue
- Solid financial foundation
- Disciplined expense management

1. Based on current assumptions, subject to change.

Driving Accelerating Growth[1,2]

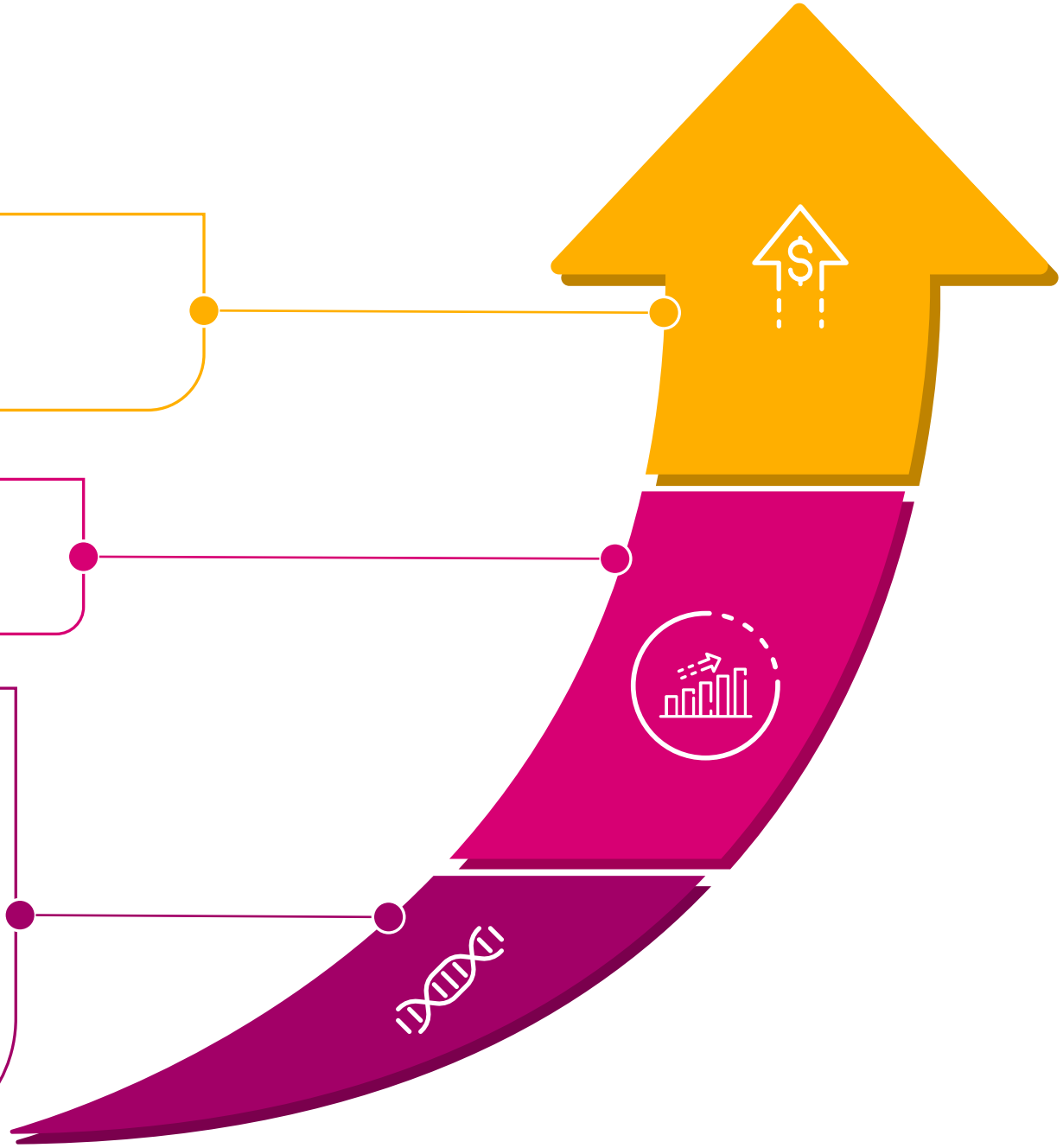
Sustained Positive Cash Flow

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.

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

- **DAWNZERA** — EU approval (HAE)
- **TRYNGOLZA** — U.S. approval; EU submission (sHTG)
- **ZANVASTRO** — U.S. submission; U.S. approval (AxD)
- **High Dose Nusinersen** — U.S. approval; EU approval (SMA)
- **Bepirovirsen** — Submission; Japan Approval; U.S. Approval (CHB)
- **Pelacarsen** — U.S. submission (Lp(a)-CVD)
- **Eplontersen** — U.S. submission (ATTR-CM)

Product Launches

- **DAWNZERA** — EU (HAE)
- **TRYNGOLZA** — U.S. (sHTG)
- **ZANVASTRO** — 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.

Ionis Corporate Responsibility Strategy Supports Long-term Value Creation

Ionis Corporate Responsibility Strategic Pillars

Innovate to improve the lives of people with serious disease

We innovate across the business and work tirelessly to discover, develop and deliver important new medicines for people with serious diseases.

Empower our people and communities

We are committed to fostering an inclusive culture that drives excellence, embraces diversity and supports our communities.

Operate responsibly and sustainably

We operate with integrity to help create a better, more sustainable future for all through environmental stewardship and responsible business practices and stakeholder interactions.



Accelerating Growth through Life-Changing Medicines