



# The Next Chapter: Accelerating Value Through Innovation

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# 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. Any statement describing Ionis' goals, expectations, financial or other projections, 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, 2023, 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](http://www.ionis.com).

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

Ionis Pharmaceuticals® is a registered trademark of Ionis Pharmaceuticals, Inc. TRYNGOLZA™ is a trademark of Ionis Pharmaceuticals, Inc. QALSODY® is a registered trademark of Biogen. SPINRAZA® is a registered trademark of Biogen. WAINUA™ is a registered trademark of the AstraZeneca group of companies.

# Ionis: Pioneered the Field of Oligonucleotide Therapeutics

A Rich History  
**Discovering**  
and **Developing**  
Transformational  
RNA-Targeted  
**Medicines**



Created **Industry Leading Medicinal Chemistry** and **Manufacturing Capabilities**



**Optimized** and **Validated Delivery** to Liver and CNS for Human Therapeutics



**Optimized** and **Validated** Multiple Mechanisms of Action Including RNase H and Splicing



Led the Way in **Discovering** and **Developing First-in-Class Medicines** for Serious Diseases

# 2020: Charted Transformation to Unlock Substantial Value

## 2020 Goals



**Prioritize and advance wholly owned pipeline for commercial success**



**Build commercial capabilities**



**Expand and diversify our technology**



**Independently bring medicines to patients**

# Strong Execution Positions Ionis to Unlock Substantial Value

## 2020 Goals



**Prioritize and advance wholly owned pipeline for commercial success**



**Advanced 10 wholly owned medicines** with transformational potential into mid- and late-stage development



**Build commercial capabilities**



**Innovative and scalable commercial organization** in place



**Expand and diversify our technology**



**Advances in medicinal chemistry** delivered numerous positive clinical data readouts and product launches



**Independently bring medicines to patients**



**First launch underway**, with 3 additional launches planned over next 3 years<sup>1</sup>

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

# Innovative, Scalable Commercial Organization for Global Launches



# Ionis Today: Fully Integrated, Commercial-Stage Biotechnology Company



## More to Come ...

Rare and prevalent opportunities in focused disease areas

- > Neurology
- > Cardiology

Multi-billion-dollar revenue potential<sup>3</sup>

 **Tryngolza™**  
(olezarsen) 80 mg injection

## First Independent Ionis Launch

First FDA-approved treatment for adults with familial chylomicronemia syndrome (FCS), adjunct to diet<sup>2</sup>

 **WAINUA™**  
(eplontersen)

## First Ionis-branded Medicine

Co-commercializing with AstraZeneca<sup>1</sup>

## Rich History

Discovered & developed transformational medicines

 **SPINRAZA®**  
(nusinersen) injection 12 mg/5 mL

 **QALSODY®**  
(tofersen) 100 mg/15 mL injection

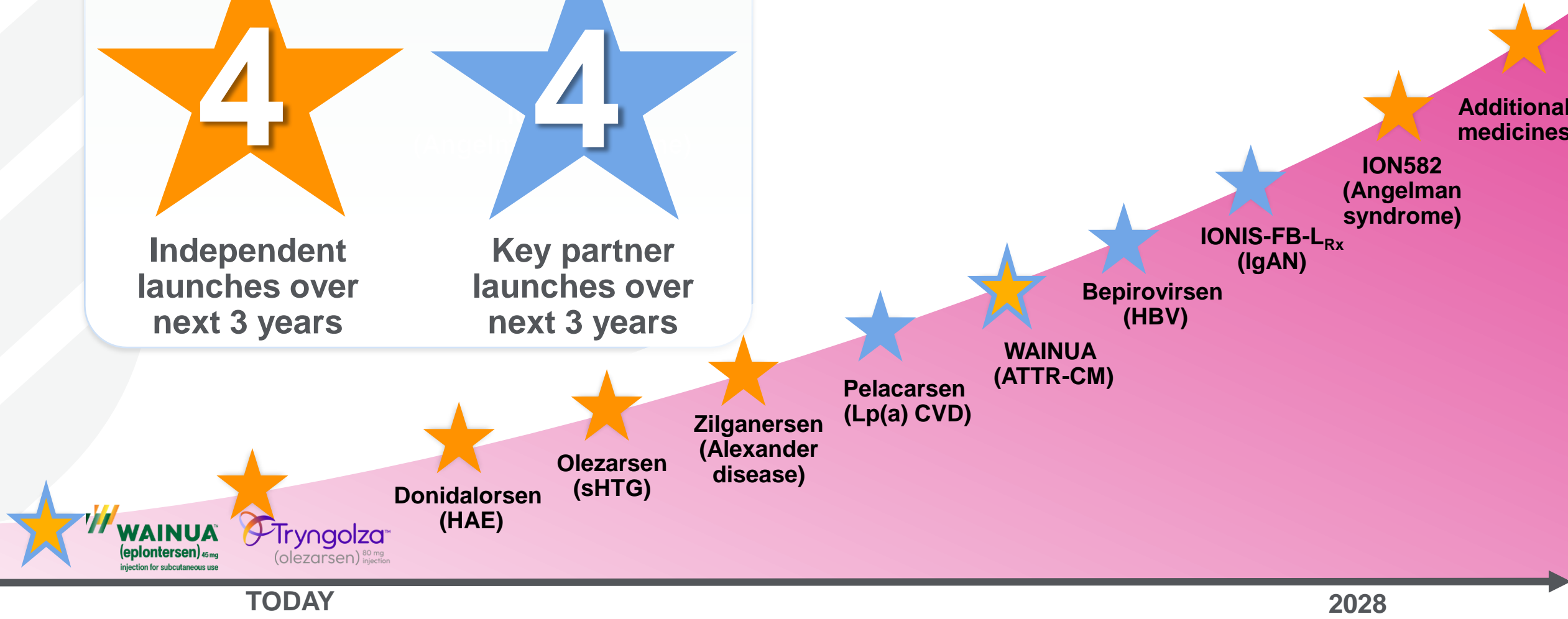
1. WAINUA co-developing and commercializing for ATTRv-PN and ATTR-CM in U.S. with AstraZeneca, [wainua.com](http://wainua.com). 2. TRYNGOLZA is approved in the U.S. for Familial Chylomicronemia Syndrome in adults; see [Full Prescribing Information](#). 3. Peak sales estimates based on current estimates and subject to change. Partnered peak sales based on public disclosure made by the respective partner and Ionis' contractual royalty rates for each medicine.

# Inflection 2025: Poised to Deliver a Steady Cadence of New Medicines

## Numerous Near-Term Growth Drivers<sup>1,2</sup>

**4**  
Independent launches over next 3 years

**4**  
Key partner launches over next 3 years



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



# Bringing Benefit to Millions of Patients Through Ionis Innovation<sup>1</sup>

RARE AND PREVALENT OPPORTUNITIES IN DISEASES WITH HIGH NEED

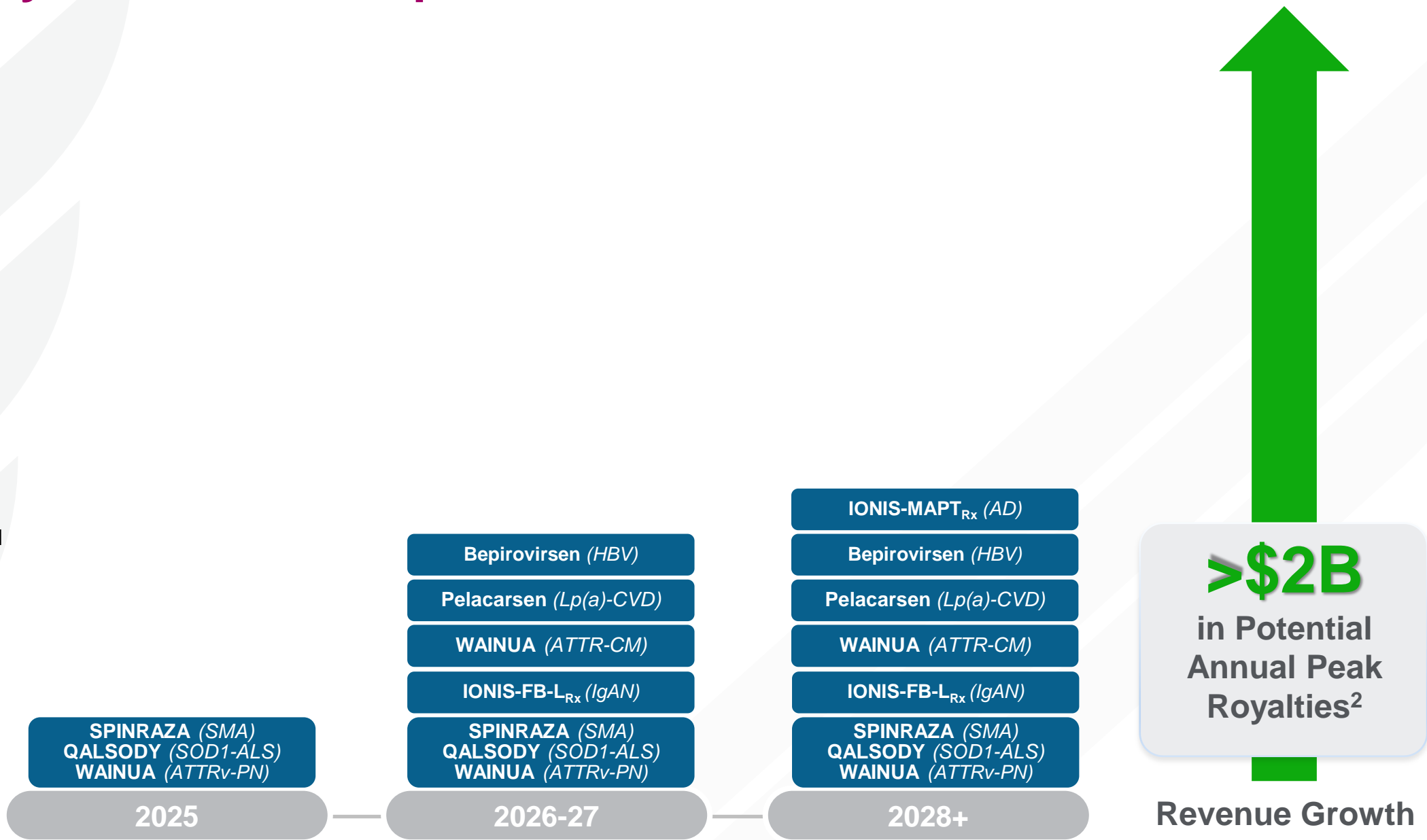


ATTRv-PN      FCS      sHTG      HAE  
ATTR-CM      Lp(a)-CVD      SMA      SOD1-ALS  
HBV      Angelman syndrome      IgAN  
FUS-ALS      Alexander disease

1. Market data on file, assuming approval.

# Steady Cadence of Expected Launches to Power Revenue Growth<sup>1</sup>

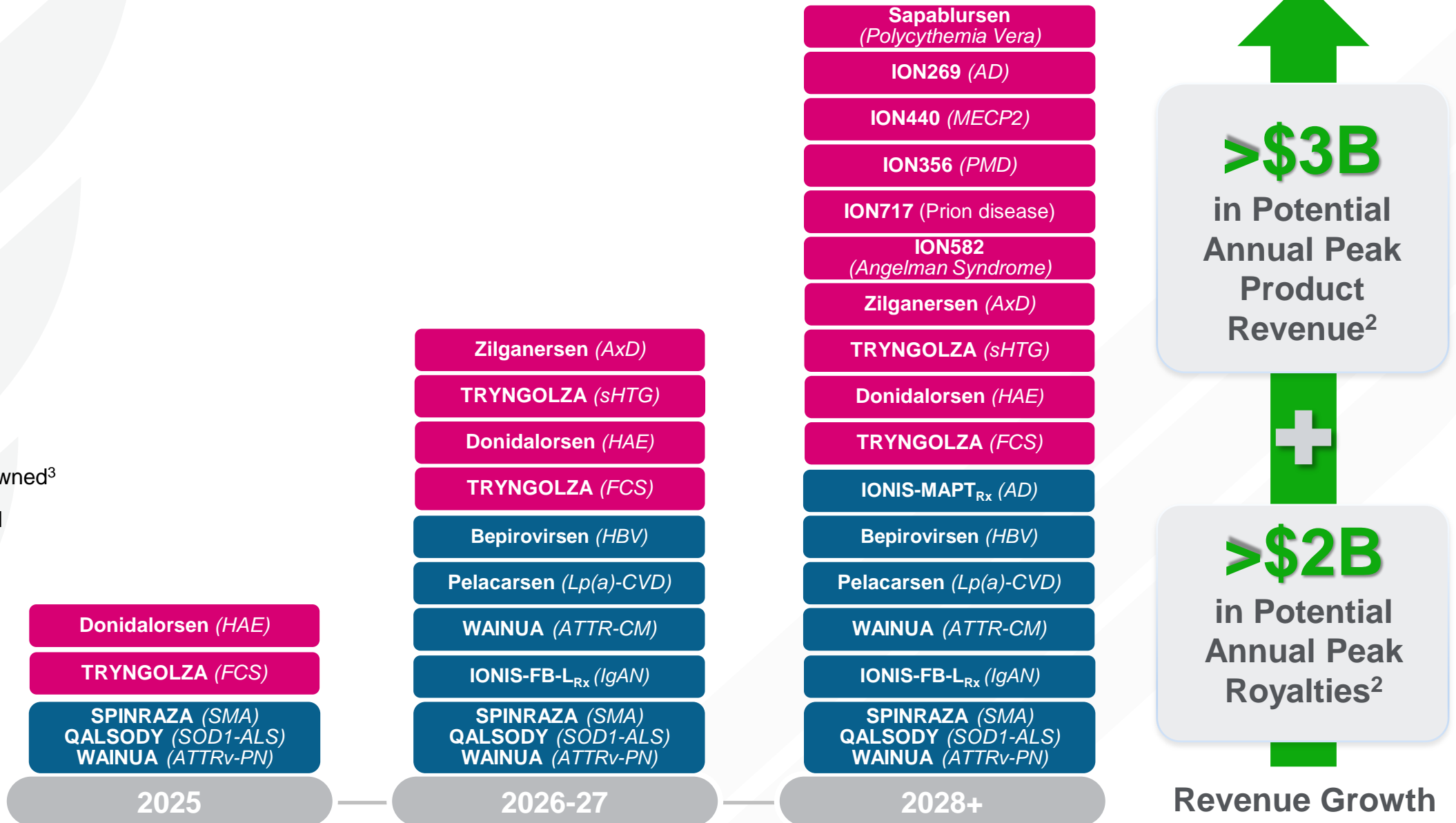
● Partnered



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.

# Steady Cadence of Expected Launches to Power Revenue Growth<sup>1</sup>

- Wholly Owned<sup>3</sup>
- Partnered



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. 3. Granted Otsuka exclusive rights to commercialize donidalorsen in Europe and Asia Pacific regions. Granted Theratechnologies exclusive rights to commercialize TRYNGOLZA and donidalorsen in Canada.

# Steady Cadence of Expected Launches to Power Revenue Growth<sup>1</sup>

**>\$5B**  
in Potential  
Annual Peak  
Product Revenue  
+  
Royalties<sup>2</sup>

- Wholly Owned<sup>3</sup>
- Partnered

Donidalorsen (HAE)  
TRYNGOLZA (FCS)  
SPINRAZA (SMA)  
QALSODY (SOD1-ALS)  
WAINUA (ATTRv-PN)

2025

Zilganersen (AxD)  
TRYNGOLZA (sHTG)  
Donidalorsen (HAE)  
TRYNGOLZA (FCS)  
Bepirovirsen (HBV)  
Pelacarsen (Lp(a)-CVD)  
WAINUA (ATTR-CM)  
IONIS-FB-L<sub>Rx</sub> (IgAN)  
SPINRAZA (SMA)  
QALSODY (SOD1-ALS)  
WAINUA (ATTRv-PN)

2026-27

Sapablursen (Polycythemia Vera)  
ION269 (AD)  
ION440 (MECP2)  
ION356 (PMD)  
ION717 (Prion disease)  
ION582 (Angelman Syndrome)  
Zilganersen (AxD)  
TRYNGOLZA (sHTG)  
Donidalorsen (HAE)  
TRYNGOLZA (FCS)  
IONIS-MAPT<sub>Rx</sub> (AD)  
Bepirovirsen (HBV)  
Pelacarsen (Lp(a)-CVD)  
WAINUA (ATTR-CM)  
IONIS-FB-L<sub>Rx</sub> (IgAN)  
SPINRAZA (SMA)  
QALSODY (SOD1-ALS)  
WAINUA (ATTRv-PN)

2028+

**>\$3B**  
in Potential  
Annual Peak  
Product Revenue<sup>2</sup>

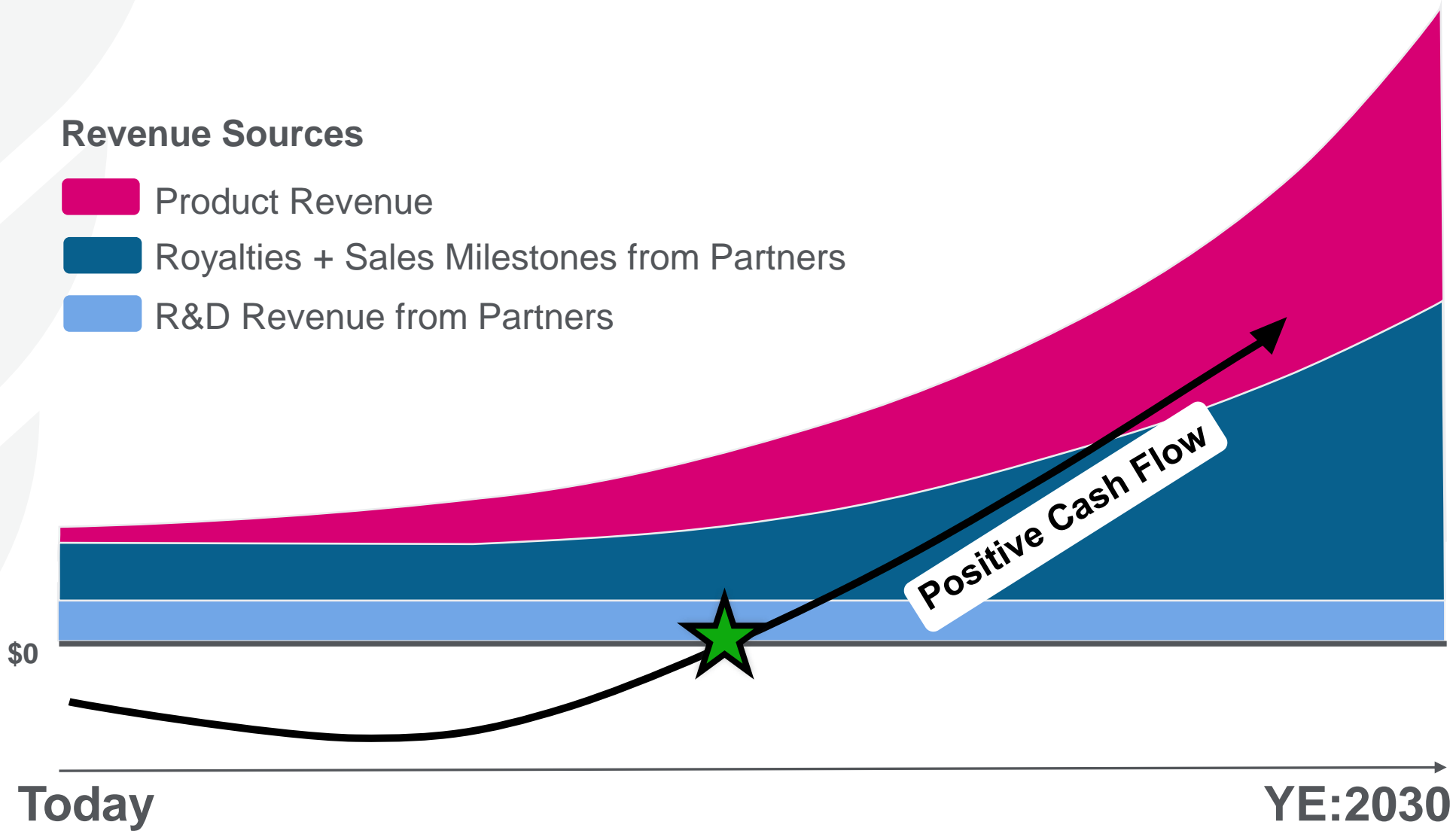
+

**>\$2B**  
in Potential  
Annual Peak  
Royalties<sup>2</sup>

Revenue Growth

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# Clear Path to Positive Cash Flow Powered by Accelerating Revenue Growth<sup>1</sup>



1. Based on current estimates, subject to change.

# Innovative Scientific Platform for Future Medicines

## Expanding Technology Platform

### Broad Range of Technologies

ASO | siRNA | DNA Editing

### Optimizing Potency and Durability

Systemic and Local Applications

## Optimizing Delivery

### Targeted Delivery (e.g., LICA)

Cardiac Muscle

Skeletal Muscle

Blood Brain Barrier

## Expanding Therapeutic Opportunities

### Established Franchises

Cardiovascular

Neurology

### New Therapeutic Areas

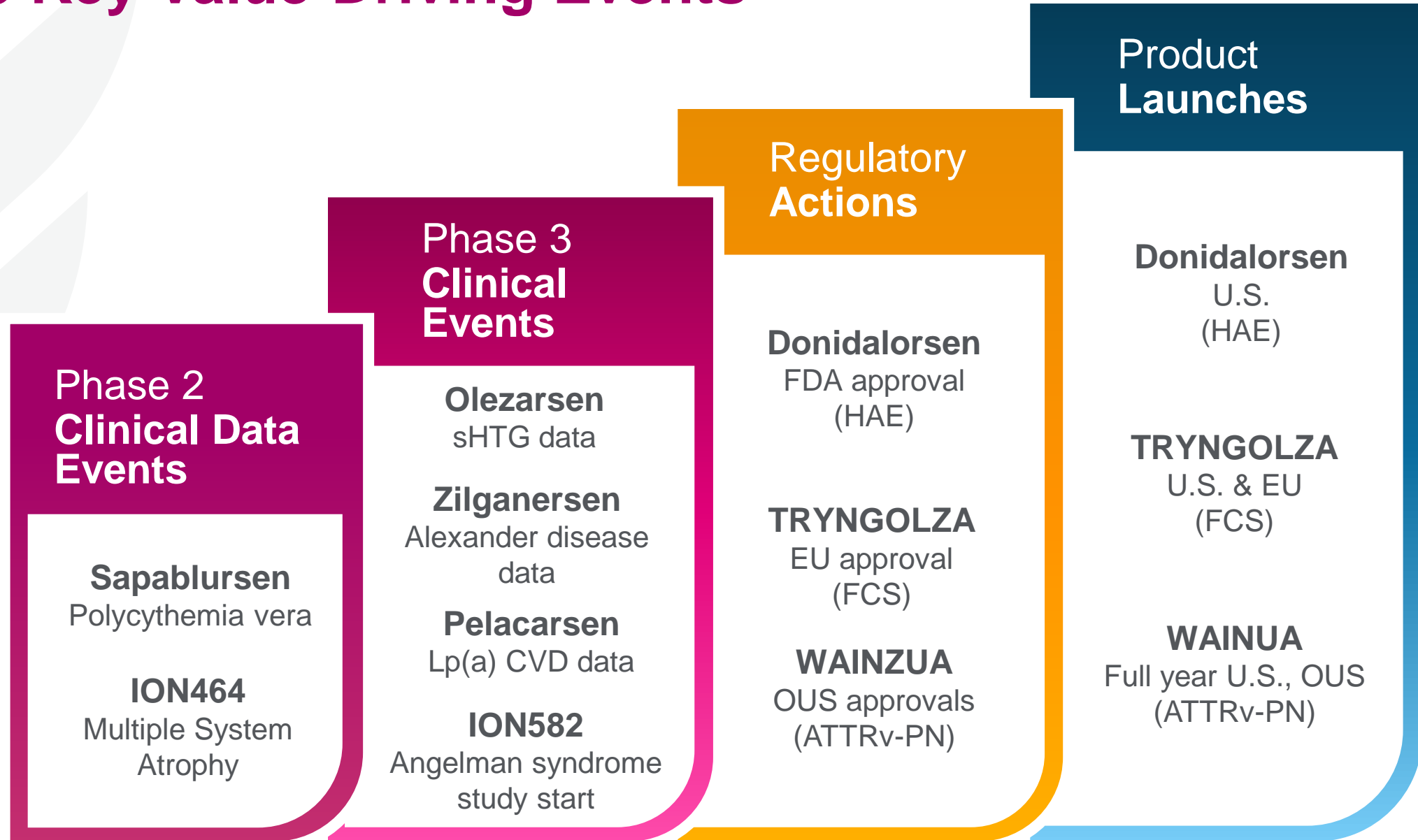
Pulmonary | Renal

## Technology Advances Expected in 2025

- Achieve clinical POC for Ionis MsPA & siRNA platform
- Advance 1<sup>st</sup> Bicycle-siRNA into clinical development
- Initiate IND-enabling studies for:
  - skeletal muscle program
  - 1<sup>st</sup> BBB candidate (CNS)

Leading Medicinal Chemistry Platform

# 2025 Key Value-Driving Events<sup>1</sup>



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.

# Accelerating Value Through Innovation



**Proven and prolific discovery and development engine**



**Pipeline delivering at all stages**



**Scalable innovative commercial organization**



**Clear path to positive cash flow<sup>1</sup>**



**Improving the lives of millions of patients with transformational medicines<sup>2</sup>**





The IONIS logo is centered at the top of the image. It features the word "IONIS" in a bold, magenta, sans-serif font. A registered trademark symbol (®) is located to the upper right of the "S". Above the letter "N", there is a stylized graphic element consisting of three parallel, slanted lines in shades of orange and red, resembling a flame or a wing.

**IONIS<sup>®</sup>**

The background of the image is a black and white photograph of several hands stacked together in a circle. Each hand is holding a small, light-colored stone or pebble. The word "HOPE" is engraved or written on each of these stones. The stones vary in shape, with some being circular and others heart-shaped. The overall composition is centered and conveys a sense of unity and shared purpose.

**Delivering Accelerated Value**