



PHARMING GROUP N.V.

# Corporate Overview

## September 2026

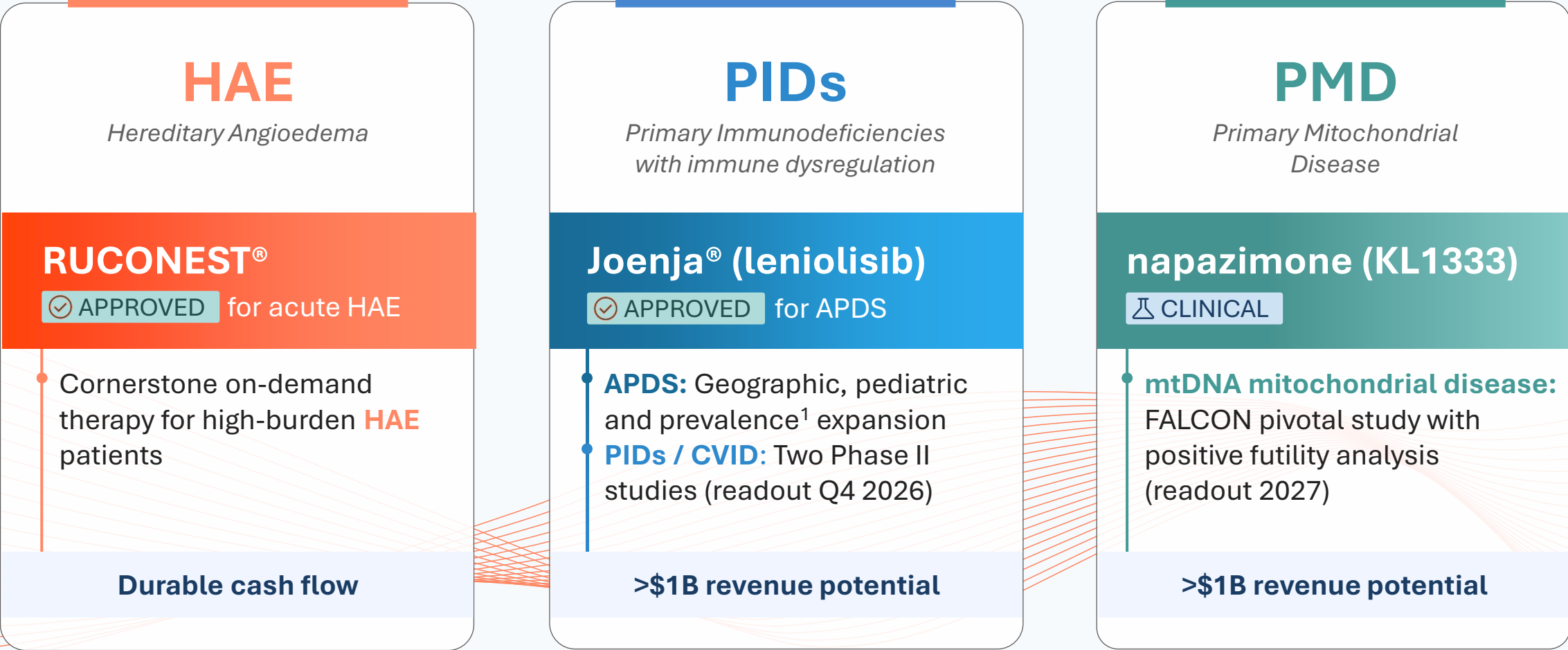
NASDAQ: **PHAR**

EURONEXT Amsterdam: **PHARM**

# Forward-looking statements

This presentation may contain forward-looking statements. Forward-looking statements are statements of future expectations that are based on management's current expectations and assumptions and involve known and unknown risks and uncertainties that could cause actual results, performance, or events to differ materially from those expressed or implied in these statements. These forward-looking statements are identified by their use of terms and phrases such as "aim", "ambition", "anticipate", "believe", "could", "estimate", "expect", "goals", "intend", "may", "milestones", "objectives", "outlook", "plan", "probably", "project", "risks", "schedule", "seek", "should", "target", "will" and similar terms and phrases. Examples of forward-looking statements may include statements with respect to timing and progress of Pharming's preclinical studies and clinical trials of its product candidates, Pharming's clinical and commercial prospects, and Pharming's expectations regarding its projected working capital requirements and cash resources, which statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to the scope, progress and expansion of Pharming's clinical trials and ramifications for the cost thereof; and clinical, scientific, regulatory, commercial, competitive and technical developments. In light of these risks and uncertainties, and other risks and uncertainties that are described in Pharming's 2025 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2025, filed with the U.S. Securities and Exchange Commission, the events and circumstances discussed in such forward-looking statements may not occur, and Pharming's actual results could differ materially and adversely from those anticipated or implied thereby. All forward-looking statements contained in this presentation are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. Readers should not place undue reliance on forward-looking statements. Any forward-looking statements speak only as of the date of this presentation and are based on information available to Pharming as of the date of this presentation. Pharming does not undertake any obligation to publicly update or revise any forward-looking statement as a result of new information, future events or other information.

# Strong commercial foundation with high-value pipeline



**2026 Revenue guidance US\$375–395M**

These product candidates are under investigation, and their safety and efficacy have not been established. There is no guarantee that these products will receive health authority approval or become commercially available for the uses being investigated. **HAE:** Hereditary Angioedema, **PIDs:** Primary Immunodeficiencies, **PMD:** Primary Mitochondrial Disease, **CVID:** Common Variable Immunodeficiency 1. Walsh et al., Scalable generation and functional classification of genetic variants in inborn errors of immunity to accelerate clinical diagnosis and treatment, Cell (2025), <https://doi.org/10.1016/j.cell.2025.05.037>

# Vision for the future

Develop a leading global rare disease company with a diverse portfolio and presence in large markets, leveraging proven and efficient clinical development, supply chain, and commercial infrastructure



## RUCONEST® for HAE

# RUCONEST – durable market position in high-burden HAE

## **Differentiated value proposition**

- Targets the root cause of HAE across all pathways
- Efficacy and reliability of IV self administration

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**Mostly used by patients experiencing more severe / frequent attacks**

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**Highly specific manufacturing process**

**Overwhelming majority of RUCONEST patients remain on therapy one year into oral competitor launch**

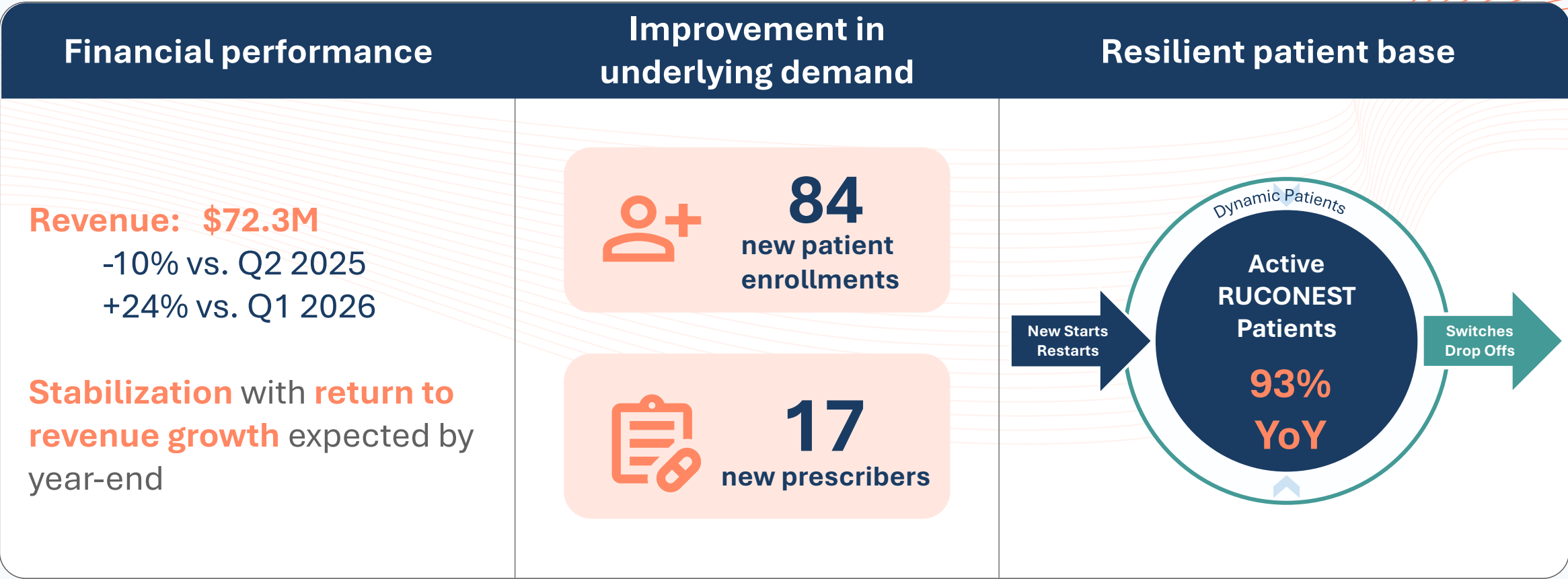
# RUCONEST – rapid, reliable, complete attack resolution



References: 1. RUCONEST. Prescribing information. Pharming Healthcare Inc; 2020. 2. Bernstein JA, et al. Ann Allergy Asthma Immunol. 2017;118(4):452-453. 3. Riedl MA, et al. Adv Ther. Published online May 20, 2026. doi:10.1007/s12325-026-03625-0.

The most common adverse reactions (incidence  $\geq 2\%$ ) were headache, nausea and diarrhea. The most serious adverse reaction reported in clinical trials was anaphylaxis.

# RUCONEST Q2 performance



# RUCONEST® Post Hoc Analysis: Rapid Attack Relief & Resolution

Adv Ther  
<https://doi.org/10.1007/s12325-026-03625-0>



## ORIGINAL RESEARCH

### Post Hoc Analysis of Recombinant C1 Inhibitor Clinical Data Using Contemporary Endpoints for Hereditary Angioedema

Marc A. Riedl · Nihal Narsipur · Douglas Jones · Raffi Tachdjian · Anurag Relan · Hannah Kilvert · Emily Aiello · Ketsia Habimana · Neil Roskell · Adam Gough · Joseph R. Harper · H. Henry Li · Amanda Harrington

Received: February 25, 2026 / Accepted: April 22, 2026  
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#### ABSTRACT

**Introduction:** Contemporary trials of medications to treat hereditary angioedema (HAE) attacks define efficacy endpoints using Patient Global Impression of Severity (PGI-S) and

Patient Global Impression of Change (PGI-C) scales; these differ from the visual analog scale (VAS) and treatment effect questionnaire (TEQ) used in legacy recombinant human C1 esterase inhibitor (rhC1-INH) studies. This post hoc analysis aimed to evaluate pooled rhC1-INH trial data, mapped to contemporary HAE clinical trial endpoints and designs.

**Methods:** Pooling data from three rhC1-INH trials for acute HAE attacks (NCT00225147, NCT01188564, NCT00262301), this analysis applied results from a bookmarking study to convert TEQ and VAS measurements to PGI-S and PGI-C scales. Kaplan–Meier estimates were calculated for time to complete resolution (TTCR; defined as “none” on PGI-S) and time to onset of symptom relief (TOSR; defined as “a little better” on PGI-C at  $\geq 2$  consecutive time

**Prior Presentation:** This manuscript is based on a previously presented poster: Riedl M, Narsipur N, Jones D, et al. Re-analysis of recombinant C1 inhibitor (rhC1-INH) clinical data with contemporary time-to-event endpoint definitions. Poster presented at: American College of Allergy, Asthma & Immunology (ACAAI) 2025 Annual Scientific Meeting; November 6–10, 2025; Orlando, FL. Poster R098.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s12325-026-03625-0>.

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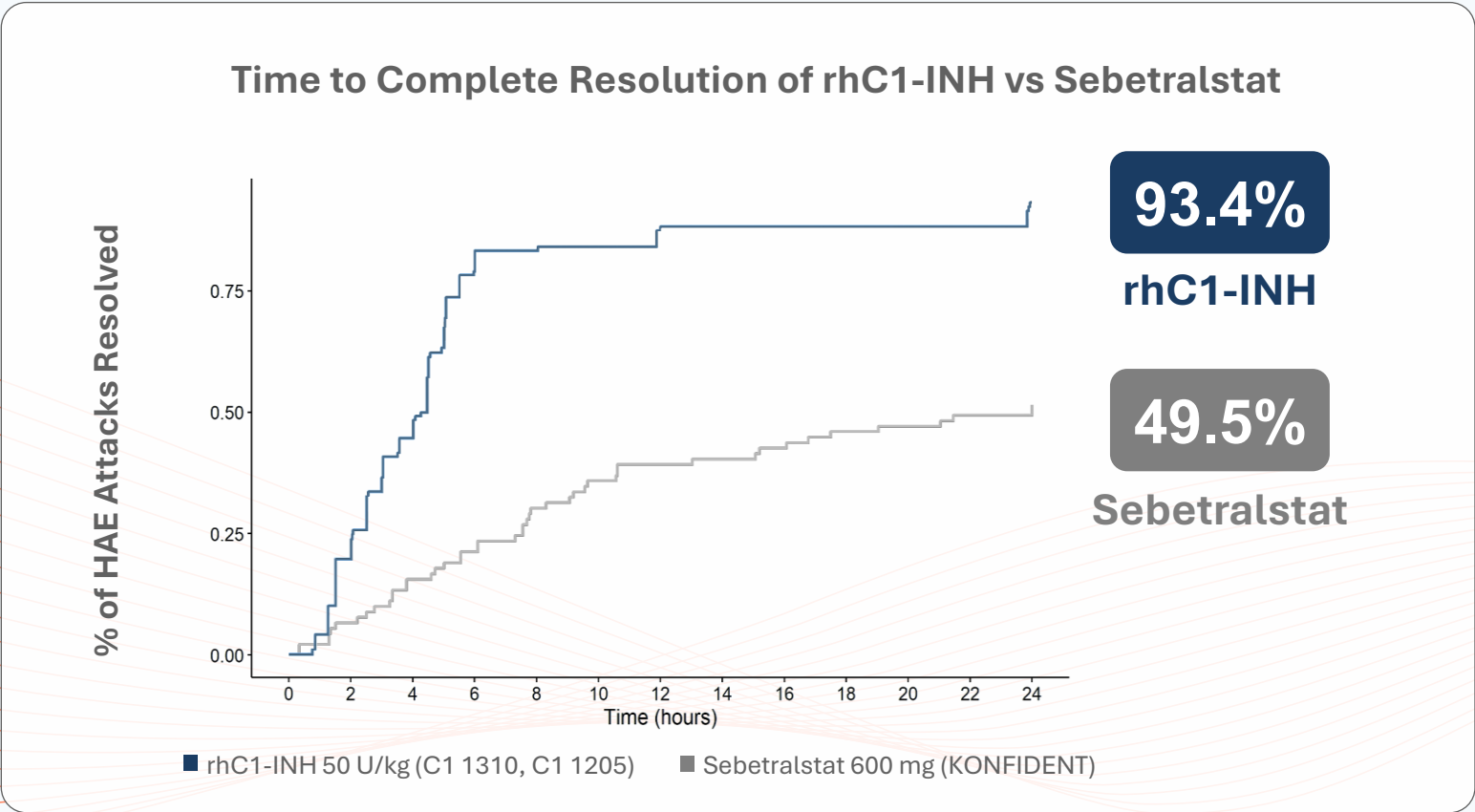
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## Key takeaways\*

- **Severe to very severe baseline attack severity:** All patients in rhC1-INH and saline trial arms had severe attacks at baseline (12–23% severe and 77–88% very severe attacks).
- **Rapid onset of symptom relief:** Median time to onset of symptom relief was 0.75 hours with rhC1-INH compared with 8 hours with placebo ( $P < 0.001$ ).
- **Substantially faster complete attack resolution:** Median time to complete resolution was 4.5 hours with rhC1-INH versus 24 hours with placebo ( $P < 0.001$ ).
- **High proportion of early resolution:** Following rhC1-INH treatment, 75% of attacks resolved within 6 hours, 82% within 12 hours, and 90% within 24 hours.

\* Source: Riedl MA, et al. Post Hoc Analysis of Recombinant C1 Inhibitor Clinical Data Using Contemporary Endpoints for Hereditary Angioedema. *Advances in Therapy*. 2026. Previously presented at ACAAI 2025 Annual Scientific Meeting, Orlando, FL.

# rhC1-INH demonstrated significantly shorter time to complete resolution compared to sebetralstat



Patients on rhC1-INH were

**4.5x  
more likely**

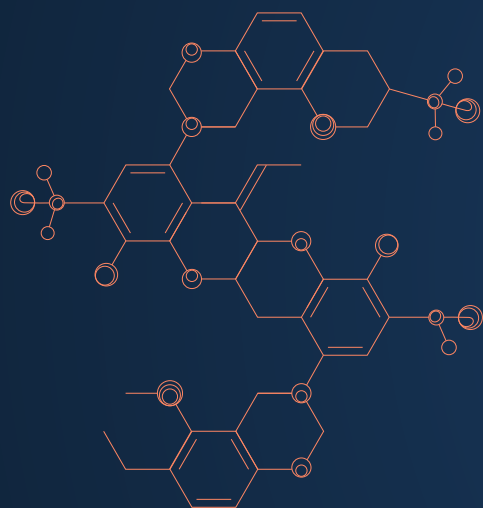
to achieve complete symptom resolution than sebetralstat\*

**Reference:** Anderson J, et al. Indirect treatment comparison (ITC) of recombinant C1 inhibitor and sebetralstat for hereditary angioedema on-demand therapy. *Ann Allergy Asthma Immunol.* 2025;135(5 Suppl 1):S29.<sup>†</sup>

\*HR = 4.5 (95% CI: 2.8 – 7.2; *P*-value < 0.05); Derived from an MAIC by taking the ratio of slopes of rhC1-INH and Sebetralstat treatment curves adjusting for attack location and prophylaxis use based on a 24-hour observation period. HR for subgroup, sensitivity, and scenario analysis were consistent and ranged from 3.64 to 7.36

Study limitations listed in slide footnote and may be provided upon request

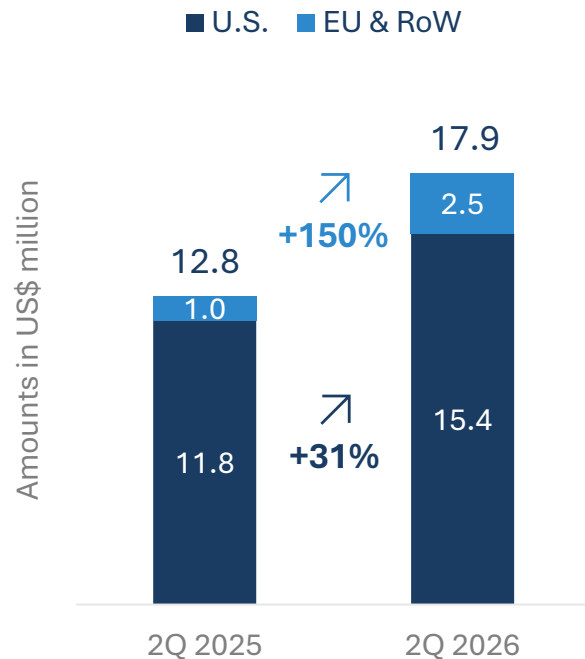
CI, Confidence Interval; HR, Hazard Ratio; MAIC, Matched Adjusted Indirect Treatment Comparison



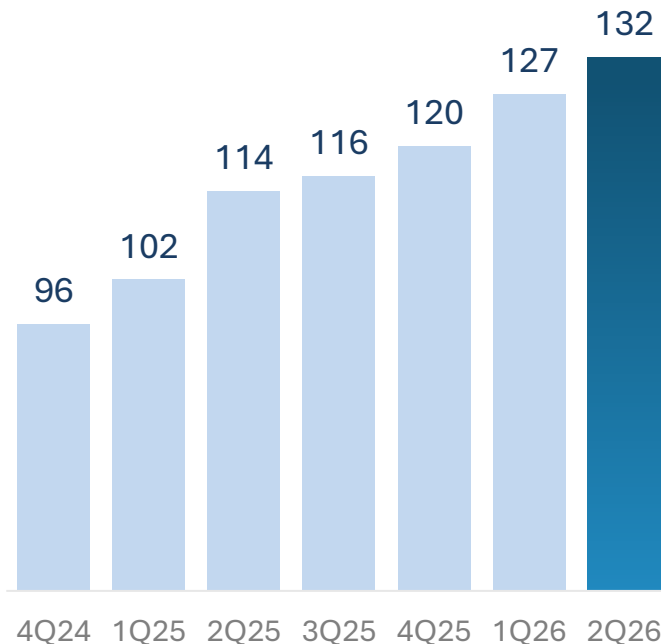
## Joenja<sup>®</sup> (leniolisib) APDS & PID indications

# Joenja Q2 update – strong global momentum in APDS ahead of geographic and pediatric expansion expected this year

Joenja revenue (global)



U.S. patients on Joenja



Revenue +40%

132 patients on therapy in US  
(+16% vs 2Q25)

+16 U.S. patients identified

Geographic expansion  
accelerating

# Joenja<sup>®</sup> for APDS - pediatric label expansion

## U.S. FDA approval received September 11, 2026

**60 eligible patients identified in the U.S.**

Children aged 4 to 11, at least 27 kg

PDUFA date – October 24, 2026

sNDA approved – September 11, 2026

New 40 mg and 50 mg twice-daily dosing

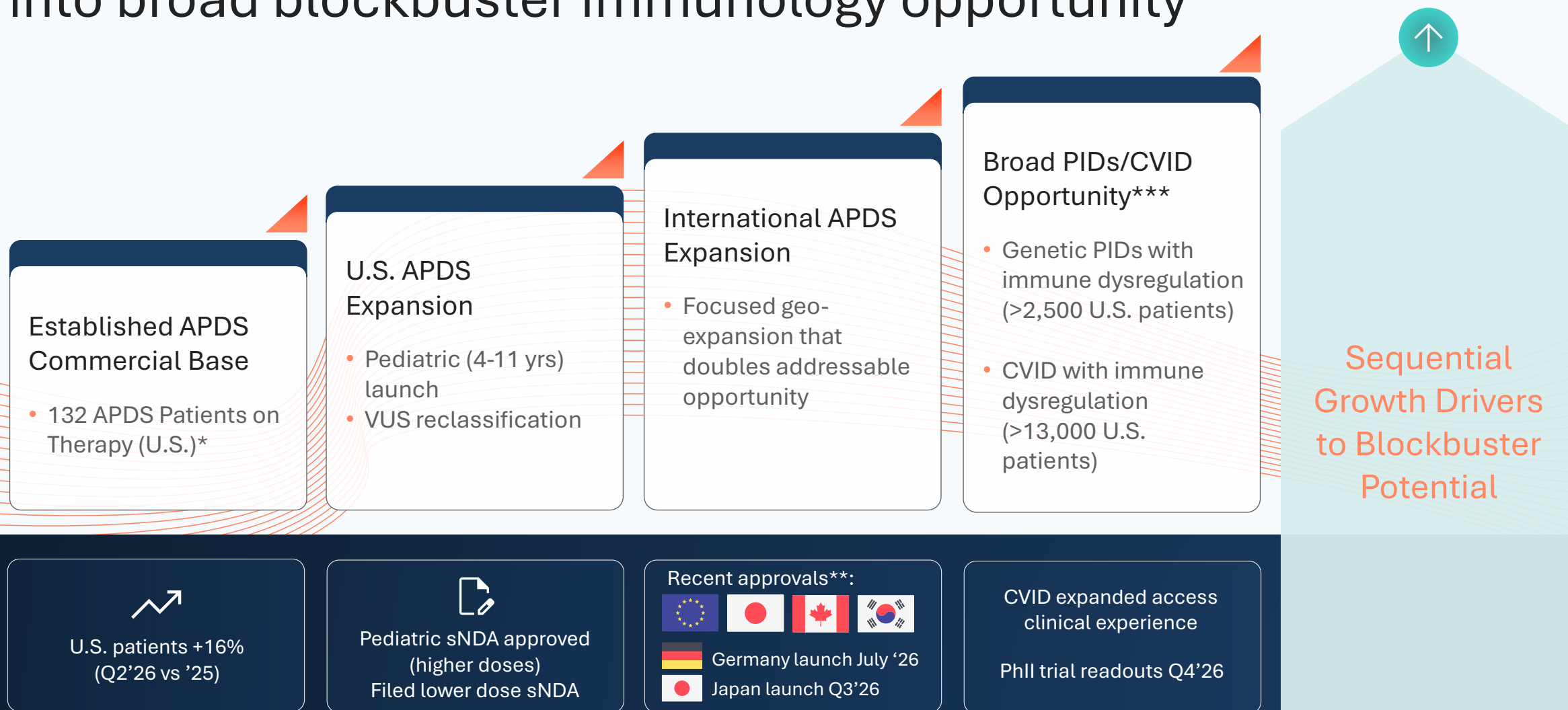
Available to eligible patients in October

Children aged 4 to 11, 13 kg to less than 27 kg

Separate sNDA filed July 30, 2026

Covers lower doses

# Joenja expansion from APDS foundation into broad blockbuster immunology opportunity



U.S. patients +16%  
(Q2'26 vs '25)



Pediatric sNDA approved  
(higher doses)  
Filed lower dose sNDA

Recent approvals\*\*:



Germany launch July '26  
Japan launch Q3'26

CVID expanded access  
clinical experience

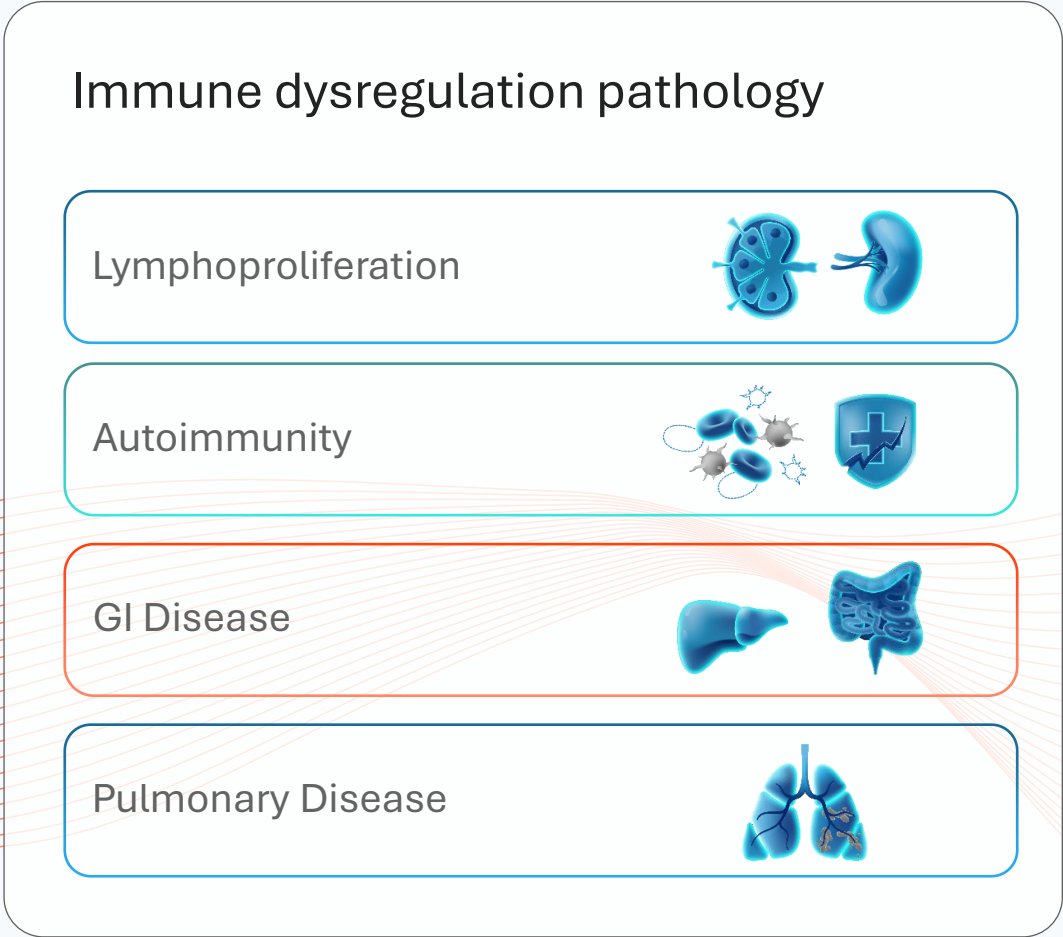
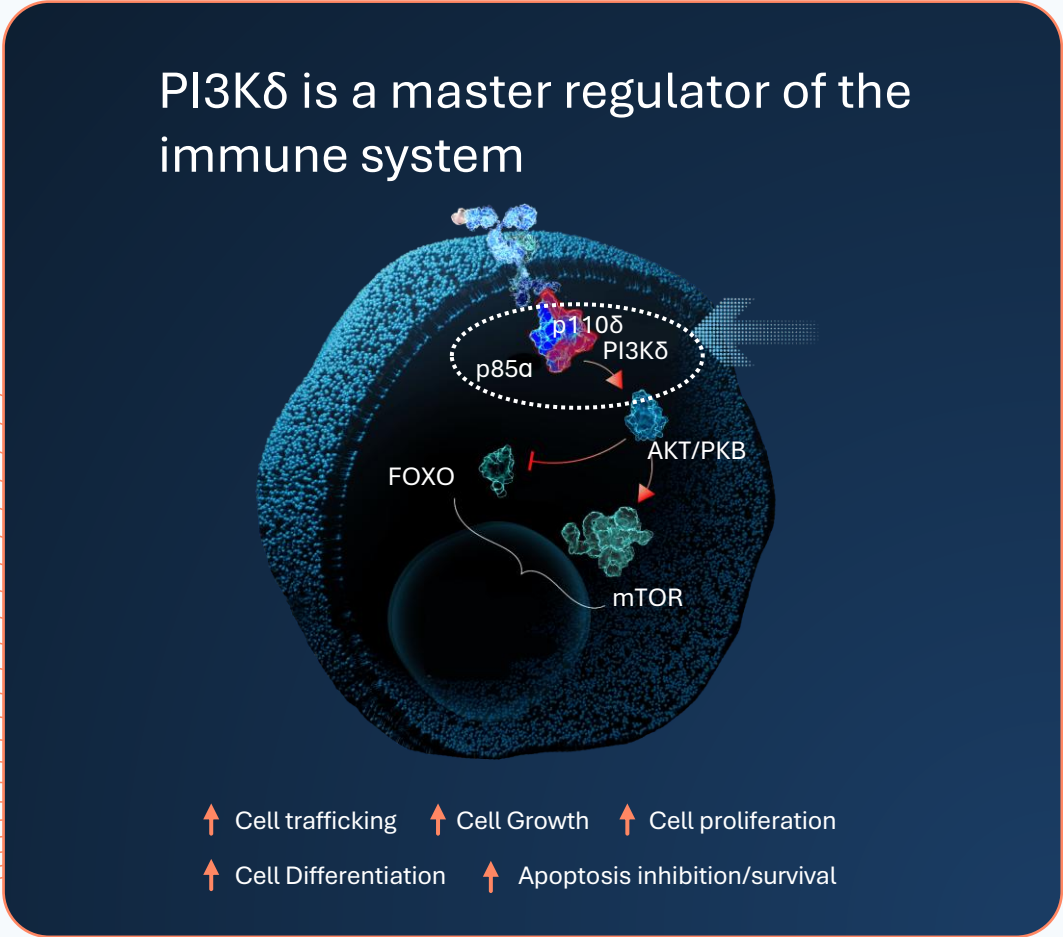
PhII trial readouts Q4'26

\*APDS prevalence est. ~1.5 patients / million in U.S. and Core 8 ex-US markets. Patients identified: 298 patients in the U.S. (198 eligible 12+, 60 eligible 4-11), 1042 globally (as of June 30, 2026).

\*\*Previously launched in U.K.

\*\*\*Prevalence overlap: CVID prevalence est. ~39 patients / million. Genetic PIDs prevalence est. ~7.5 patients / million (4.5 patients / million of which are included in CVID prevalence)

# PI3K $\delta$ is a master regulator of the immune system and imbalance contributes to immune dysregulation



# PI3K $\delta$ inhibition validated in APDS

## Joenia (leniolisib)

 APPROVED for APDS



### **Sustained, durable efficacy**

Lymph-node and spleen volume reduced, sustained through multi-year OLE<sup>†</sup>



### **Established safety and tolerability\***

Primarily mild-to-moderate adverse events; no treatment-related SAEs with up to 7 years of therapy



### **Clinically meaningful improvements\*\***

Reduced infections, fewer hospitalizations, and lower treatment burden

\*Based on Phase III clinical trial and open label extension

\*\*Based on post-hoc analysis and real-world evidence

†OLE: Open Label Extension

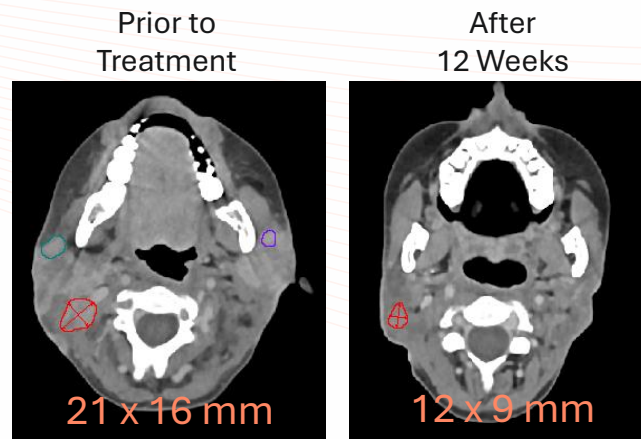
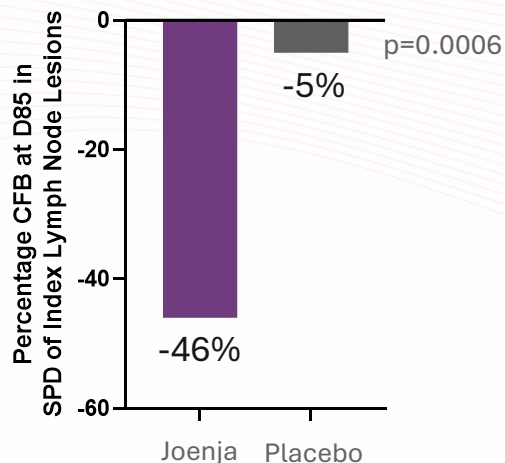
# Joenia<sup>®</sup> addresses the underlying cause of APDS to help restore immune balance – Phase III co-primary endpoints

At 12 weeks Joenia<sup>®</sup> decreased lymphadenopathy and increased naïve B cells

## Immune Dysregulation

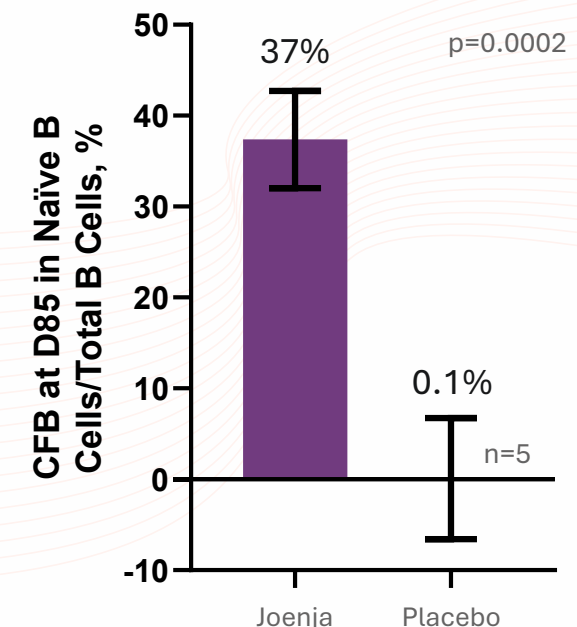
Change from baseline in index nodes\*

| Log <sub>10</sub> -transformed SPD of index lesions | Joenia (n=18) | Placebo (n=8)        |
|-----------------------------------------------------|---------------|----------------------|
| Baseline mean (SD)                                  | 3.03 (0.42)   | 3.05 (0.39)          |
| Change from baseline, LS mean (SE)                  | -0.27 (0.04)  | -0.02 (0.05)         |
| Difference vs placebo (95% CI)                      |               | -0.25 (-0.38, -0.12) |



## Immune Deficiency

Change from baseline in naïve B cells<sup>†</sup>



Data were analyzed using an ANCOVA model with treatment as a fixed effect and baseline as a covariate. Use of glucocorticoids and IRT at baseline were both included as categorical (Yes/No) covariates. Baseline is defined as the arithmetic mean of the baseline and D1 values when both are available, and if either baseline or the D1 value is missing, the existing value is used. P-value is 2-sided. Least square means are graphed. Error bars are standard error of the mean.

\*The analysis excluded 2 patients from each treatment group due to protocol deviations and 1 Joenia patient having complete resolution of the index lesion identified at baseline.

<sup>†</sup>Out of 27 patients in the PD analysis set, 13 patients met the analysis requirements, including having a percentage of <48% of naïve B cells at baseline, to form the B-PD analysis set.

Joenia [package insert]. Leiden, The Netherlands: Pharming Technologies B.V.; 2023.

Please see Important Safety Information and full Prescribing Information available at [joenia.com](https://joenia.com)

# Joenia<sup>®</sup> significantly reduced splenomegaly

Secondary endpoint: Significant reductions in spleen size by 2D and 3D analysis compared to placebo

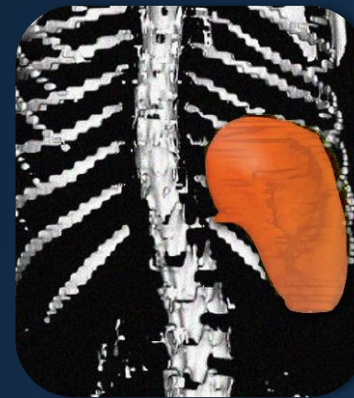
- The adjusted mean difference in bidimensional spleen size between Joenia<sup>®</sup> (n=19) and placebo (n=9) was  $-13.5 \text{ cm}^2$  (95% CI:  $-24.1, -2.91$ ),  $P=0.0148$
- The adjusted mean difference in 3D spleen volume between Joenia<sup>®</sup> (n=19) and placebo (n=9) was  $-186 \text{ cm}^3$  (95% CI:  $-297, -76.2$ ),  $P=0.0020$

At week 12

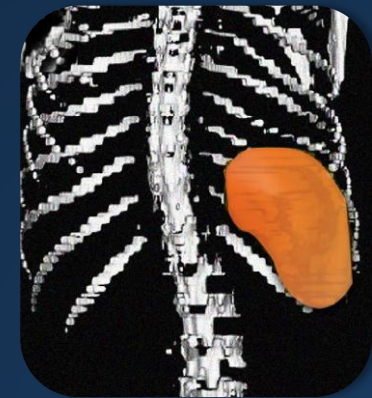
**27%**

reduction in 3D spleen volume\*

Secondary measure: spleen volume scan results of actual patient illustrate average improvement documented for patients taking Joenia<sup>®</sup>



**Prior to treatment: 491 mL**



**At week 12: 314 mL**

Actual patient images of a 17-year-old male. As individual results vary, images may not be representative of all patients.

Rao VK, et al. Blood. 2023;141(9):971-983.

\*In the PD analysis set, the mean (SD) percentage change from baseline to week 12 in 3D spleen volume ( $\text{mm}^3$ ) was  $-26.68\%$  (12.137) with Joenia<sup>®</sup> (n=19) and  $-1.37\%$  (24.238) with placebo (n=9). The ANCOVA model was used with treatment as a fixed effect and  $\log_{10}$ -transformed baseline as a covariate for index and non-index lesions. The use of both glucocorticoids and IV Ig at baseline was included as categorical (yes/no) covariates. This analysis excluded 2 patients in each treatment group. In the Joenia<sup>®</sup> group, 1 patient with a complete index lesion response was excluded, and 3 patients were excluded for no non-index lesion at baseline. PD, pharmacodynamics.

# Reports of Joenja® changing patients' lives

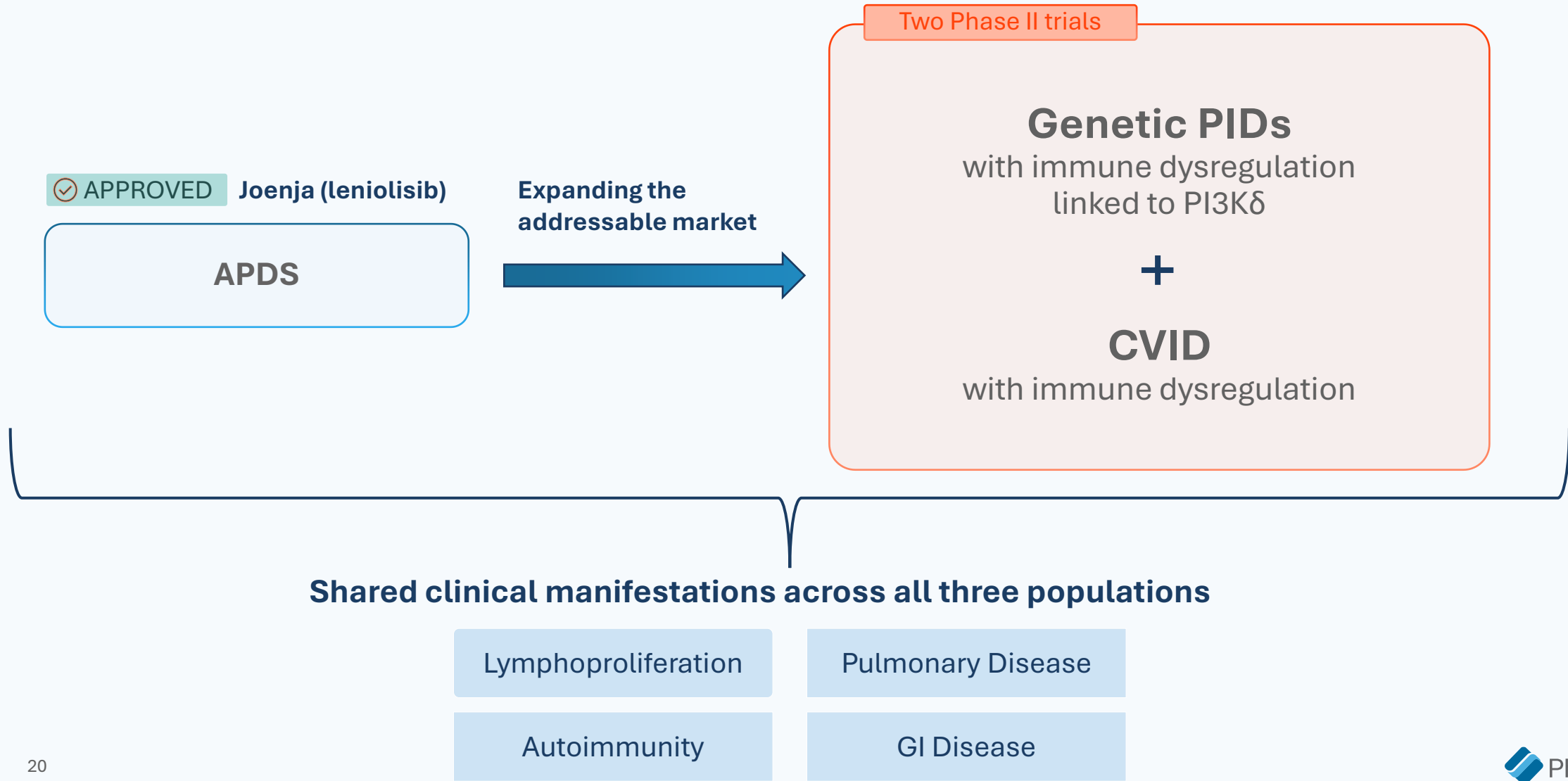
24-year-old male with APDS whose progress was followed in the Joenja® open-label extension study for 6 years



|                                 | Before study enrollment                                                                                                                                                                                                           | Since starting Joenja treatment                                                                                                                                                                                                          |
|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Infections and treatment burden | <ul style="list-style-type: none"><li>Experienced fatigue from IRT infusions, anxiety, and difficulty coping with treatment burden</li><li>Hospitalized yearly for infections</li><li>Frequently prescribed antibiotics</li></ul> | <ul style="list-style-type: none"><li>Stopped IRT infusions and fatigue got better</li><li>No hospitalizations</li><li>He had 7 infections, none of which returned</li><li>Only doctor he visits regularly is his immunologist</li></ul> |
| Clinical manifestations         | <ul style="list-style-type: none"><li>Low blood platelet counts</li><li>Damaged lung airways</li><li>Gastrointestinal issues and migraines</li></ul>                                                                              | <ul style="list-style-type: none"><li>Blood platelet count increased</li><li>Damaged lung airways did not get worse</li></ul>                                                                                                            |

Rao VK, et al. Blood Adv. 2024;8(12):3092-3108. doi:10.1182/bloodadvances.2023011000.

# Leniolisib opportunity: Targeting shared PI3K $\delta$ -driven immune dysregulation across primary immunodeficiencies (PIDs)



# Leniolisib Phase II trials in CVID and PIDs: Fully enrolled, readouts 4Q 2026

## CVID with immune dysregulation

N = 20

Open-label, single-arm, multi-center

**NCT06897358**

## Genetic PIDs with immune dysregulation

N = 12

Open-label, single-arm basket trial at NIH (ALPS-FAS, CTLA4, NFKB1, PTEN, SOCS1, NRAS/KRAS RALD)

**NCT06549114**

Dose-ranging: **10 mg / 30 mg / 70 mg** twice daily · shared 3-year open-label extension

### ENDPOINTS

Lymph-node &  
spleen size

Blood cell counts

Lung & liver (end-organ)

Novel and indication-  
specific patient /  
clinician outcomes

Biomarkers  
(CXCL13, B cells)

### WHAT WE AIM TO DEMONSTRATE

Clinically meaningful reductions in lymphoproliferation and cytopenias, end-organ stabilization and supportive biomarker shifts — establishing proof of concept and confirming dose.

**Fully enrolled**  
Topline Q4 2026

# Leniolisib expanded access in CVID derisks upcoming Phase II readout

- Improvement from baseline to last treatment visit
- No change or no progression from baseline to last treatment visit
- Manifestation was not reported at baseline

**6**

Patients treated

**1.4 yrs**

Median exposure

**No reported  
disease  
progression**

- Immune profile improvements (reduced transitional & CD21lo B cells)
- Manageable safety consistent with disease severity

## Clinician-reported patient outcomes across key clinical manifestations

|                                       | P1             | P2             | P3 | P4              | P5 | P6 |
|---------------------------------------|----------------|----------------|----|-----------------|----|----|
| <b>Changes in Cytopenias*</b>         |                |                |    |                 |    |    |
| Neutrophils                           | ●              | ●              | ●  | ●               | —  | ●  |
| Lymphocytes                           | ●              | —              | ●  | ●               | —  | ●  |
| Platelets                             | ●              | —              | ●  | ●               | —  | ●  |
| <b>Changes in Lymphoproliferation</b> |                |                |    |                 |    |    |
| Splenomegaly                          | ●              | —              | ●  | ●               | —  | ●  |
| Lymphadenopathy                       | —              | ●              | ●  | ●               | ●  | ●  |
| <b>Changes in organ disease</b>       |                |                |    |                 |    |    |
| Liver disease                         | ● <sup>†</sup> | ●              | ●  | ● <sup>‡</sup>  | ●  | ●  |
| Lung disease                          | —              | ● <sup>§</sup> | ●  | ● <sup>  </sup> | ●  | ●  |

\*\*\*Information summarized here is clinician-reported on an individual patient basis in the absence of any prospectively defined data collection strategy\*\*\*

(Uzel et al. Clinical Immunology Society Annual Meeting Poster, May 6-9, 2026)

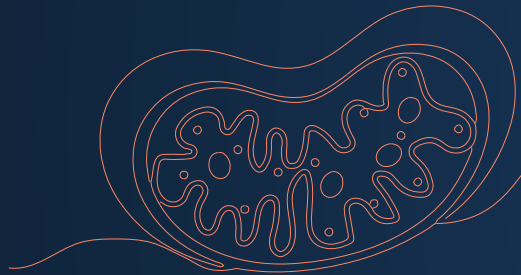
\* Increase in leukocytes was reported in P4.

† Mild improvement observed via magnetic resonance elastography.

‡ Improvement based on stabilized transaminitis.

§ Pulmonary nodules resolved and dyspnea improved.

|| Improvement based on findings from imaging, lung volume & diffusion capacity.



Napazimone (KL1333)  
mtDNA Mitochondrial Disease

# Napazimone (KL1333) for mtDNA-driven primary mitochondrial disease

## Aiming for the first disease-modifying treatment

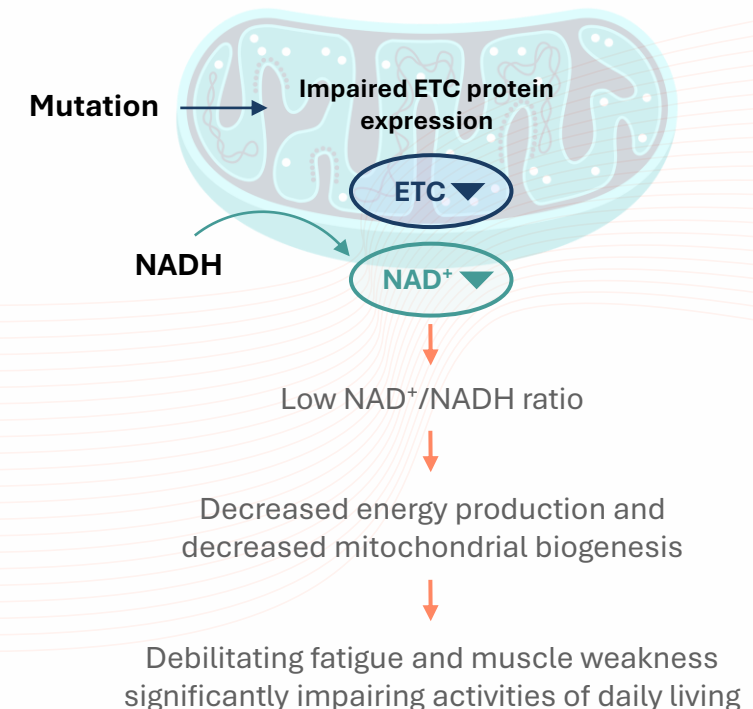
### Napazimone (KL1333) targets underlying pathology

- Normalizes NAD<sup>+</sup>/NADH ratio and mitochondrial function, with evidence from in vitro data, animal models, and in patients treated with KL1333
- >30,000 diagnosed patients with mtDNA disorders<sup>1</sup>

### Registrational clinical study underway

- Clinically-relevant Fatigue, Sit-to-Stand endpoints supported by FDA
- Positive interim analysis – both endpoints cleared futility
- Over 45 sites actively recruiting
- On track to complete enrollment in 2026 and for trial readout in late 2027

### DYSFUNCTIONAL MITOCHONDRIA

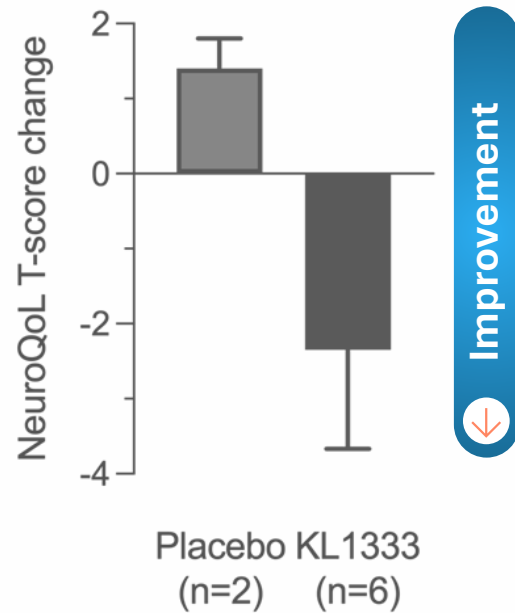


1. In US, EU4 and UK. Diagnoses can include MELAS-MIDD and KSS-CPEO spectrum disorders as well as MERRF syndrome.

# In a Phase Ia/b study, napazimone (KL1333) demonstrated positive changes in outcome measures

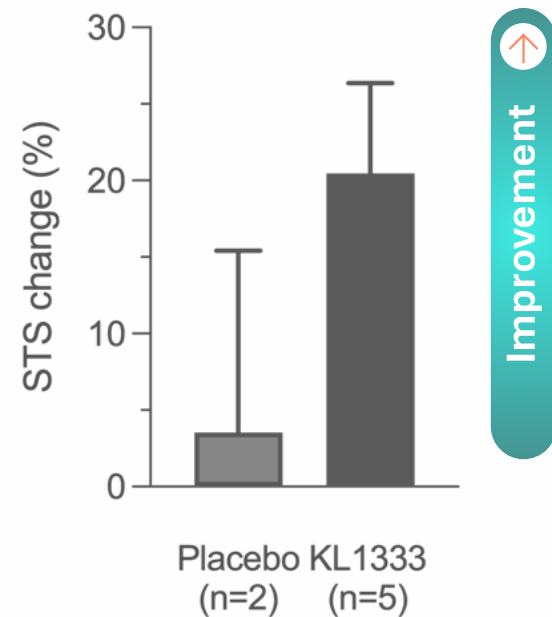
## Reduction of fatigue

Changes from baseline to day 10<sup>1</sup>



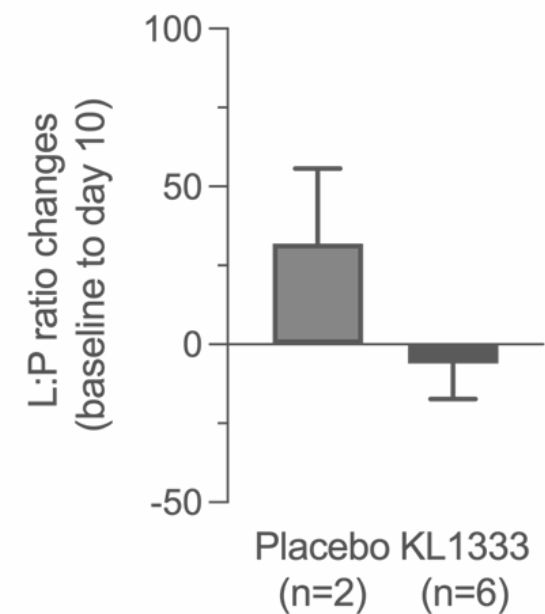
## Improvement in muscle function

Changes from baseline to day 10<sup>1</sup>



## Biomarker changes

Lactate: Pyruvate ratio<sup>1</sup>



1. Pizzamiglio C et al., Optimizing rare disorder trials: a phase 1a/1b randomized study of KL1333 in adults with mitochondrial disease, Brain 2025;148(1):39-46 <https://pmc.ncbi.nlm.nih.gov/articles/pmid/39657714/>

# Napazimone (KL1333) – FALCON study positive interim analysis

## Pivotal FALCON Study

### WAVE 1 – Fully enrolled

- 40 patients recruited across six countries (U.S., UK, France, Spain, Belgium, Denmark)
- Interim analysis at 24 weeks

### WAVE 2 – Enrolling

- 180 total patients treated for 48 weeks
- Over 45 active sites, with significant expansion in US
- Readout anticipated 2027



## Interim Futility Analysis

### Positive outcome achieved, with both primary endpoints passing futility

Promising differences favoring the active arm vs. placebo for both primary efficacy endpoints; if trends continue consistently, we expect a successful result at the completion of this trial

Data monitoring committee (DMC) concluded:

- Safety and tolerability profile acceptable
- No changes to study design
- 180 total patients confirmed in the study

An abstract graphic consisting of several concentric orange circles on the left side of the slide. A single orange line starts from the bottom right of these circles and extends downwards and to the left, ending in a small loop.

## Financials and Outlook

# 2026 financial guidance and long-term capital outlook

## Revenue and operating expenses (in constant currency):

|                    | FY 2026 Guidance      | Notes                                                                                                                                                                                                                 |
|--------------------|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Total Revenues     | US\$375 - 395 million | <ul style="list-style-type: none"><li>• 0 - 5% growth</li><li>• COGS: ~11%</li></ul>                                                                                                                                  |
| Operating Expenses | US\$315 - 320 million | <ul style="list-style-type: none"><li>• 1 – 3% growth</li><li>• +US\$40 million R&amp;D to advance pipeline</li><li>• -US\$9 million from G&amp;A structural cost reductions (as announced in October 2025)</li></ul> |

Significant and accelerating Joenja growth, and RUCONEST revenue stabilization and return to growth during 2H 2026.

Strong financial discipline, and prioritized investments to drive near- and long-term value creation.

Available cash (US\$159.5M) and future cash flows expected to cover current pipeline and pre-launch costs.

## Advancing Pharming as a leading global rare disease company

### Strong commercial foundation

- RUCONEST resilience – durable cash engine
- Joenja sales momentum

### Significant growth opportunities

#### Joenja - commercial

- Geographic, pediatric and prevalence expansion

#### Pipeline - blockbuster potential

**Q4 2026:** Two Phase II readouts with leniolisib for PIDs/CVID

**2027:** FALCON pivotal study readout with napazimone in mtDNA mitochondrial disease

### Building a leading rare disease company

- More disciplined operating model
- Scalable organization
- Value creation focus
- Aligning shareholder base + vision



WWW.PHARMING.COM

# Thank you!

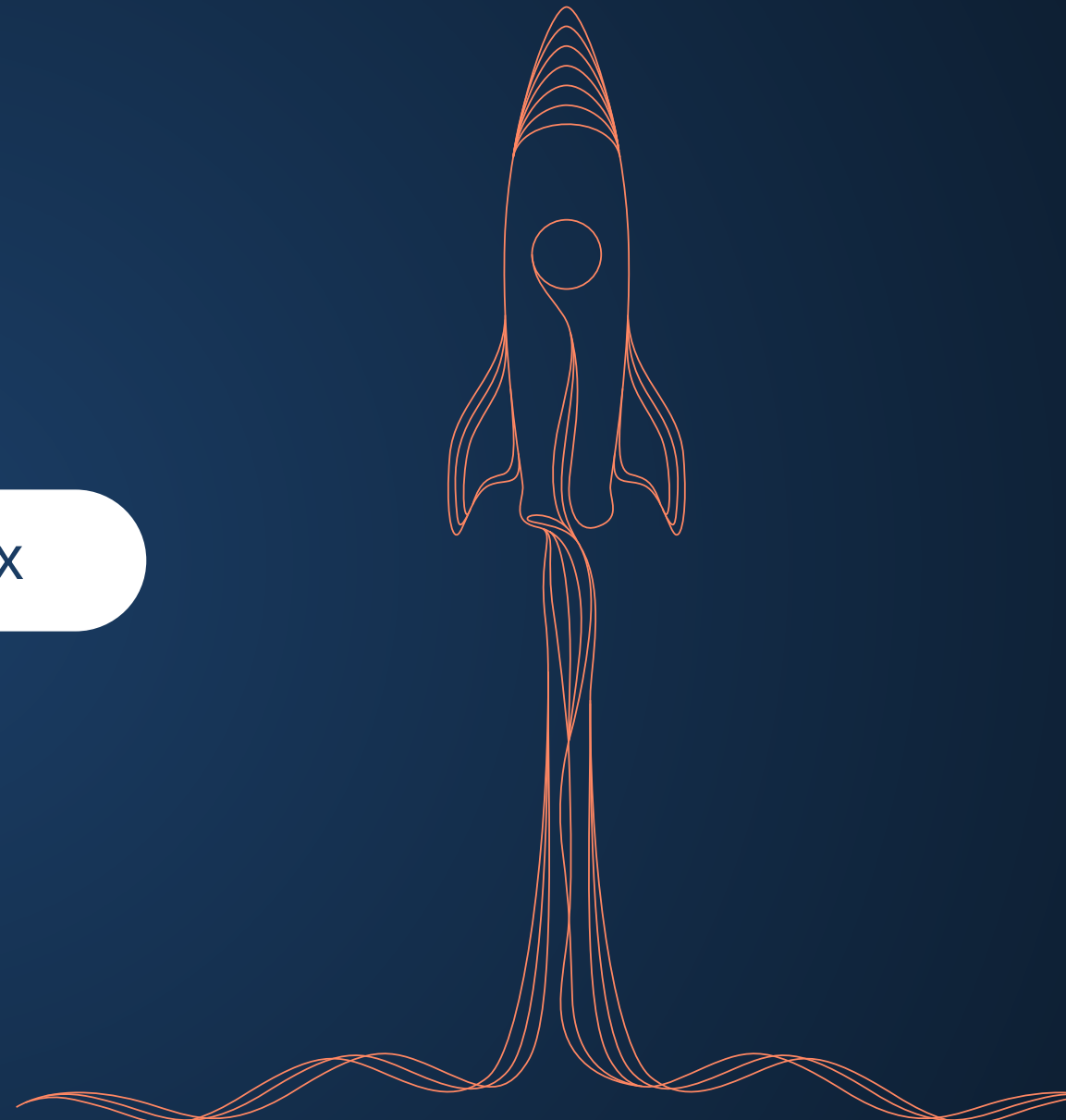
#### **The Netherlands**

Pharming Group  
Vondellaan 47  
2332 AA Leiden  
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10 Independence Blvd  
Suite 401,  
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# Appendix



# Joenia<sup>®</sup>: Targeting the root cause of APDS to help restore immune balance

Treatment with Jenja<sup>®</sup> in a randomized, controlled-trial led to:

- Significant improvements in immune dysregulation (e.g, lymph node and splenomegaly reductions)
- Significant improvements in immunophenotype

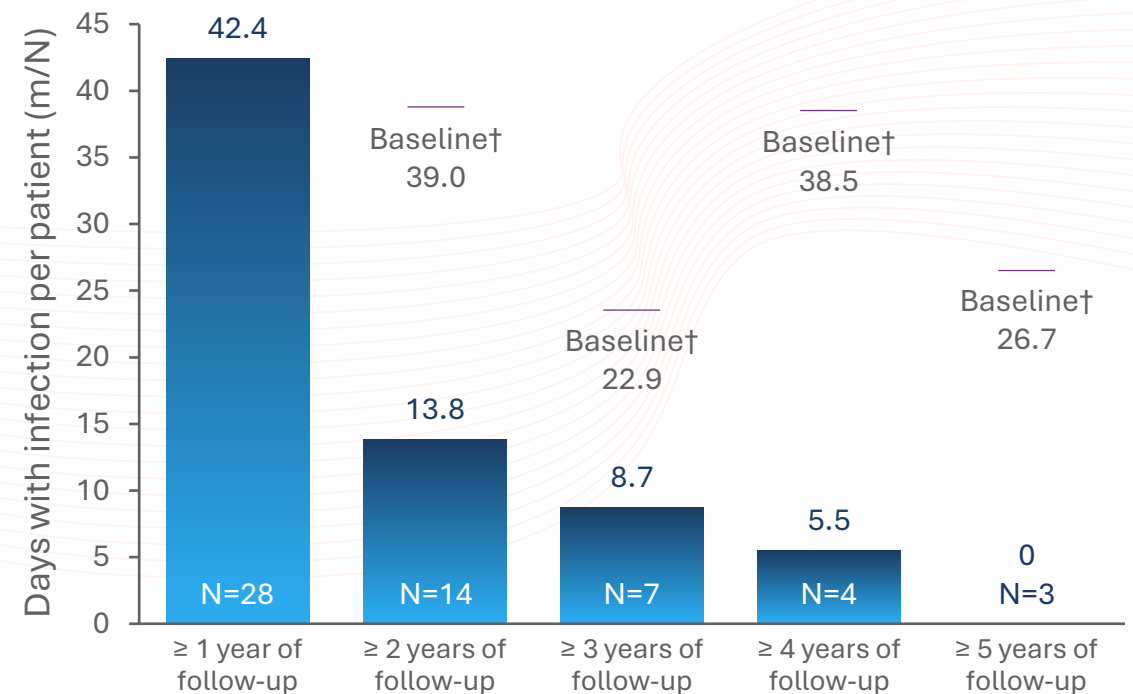
## Favorable Safety Profile

- No serious AEs were related to Jenja treatment
- No patients withdrew from the clinical trials due to an adverse drug reaction
- The most common adverse reactions (incidence >10%) in the Phase III trial were headache, sinusitis, and atopic dermatitis

## Long-term open-label study

- Median duration of Jenja<sup>®</sup> exposure was ~2 years
- Reduction in infections (see right)

## Patient-reported Annual Rate of Infection Days\*



# Joenja<sup>®</sup> clinical trial designs

## Pivotal Trial - Part 1: Dose-finding<sup>1,2</sup>



Nonrandomized, open-label,  
dose-escalating



6 patients with APDS



12 weeks



10 mg, 30 mg, 70 mg bid  
(4 weeks each dose)



70 mg bid selected for Part 2

## Pivotal Trial - Part 2: Efficacy & Safety Evaluation<sup>3</sup>



Randomized, triple-blinded,  
placebo-controlled



31 patients with APDS  
(21 Joenja<sup>®</sup>, 10 placebo)



12 weeks



70 mg bid



Co-primary efficacy end points

- Change from baseline in log<sup>10</sup>-transformed SPD of index lesions
  - Also assessed as % change
- Change from baseline in percentage of naïve B cells out of total B cells

Secondary and exploratory end  
points  
Safety

## Open-label extension study<sup>4,5</sup>



Nonrandomized, open-label, long-  
term study



- 35 patients with APDS from Parts 1 and 2
- 2 patients with APDS previously treated with investigational PI3Kδ inhibitors



Ongoing



70 mg bid



Long-term safety, tolerability,  
efficacy, and pharmacokinetics

bid, twice a day; PI3Kδ, phosphoinositide 3-kinase delta; SPD, sum of product diameters

1. Rao VK, et al. *Blood*. 2017;130(21):2307-2316. 2. NCT02435173. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT02435173>. Updated May 6, 2015. Accessed March 13, 2023. 3. Rao VK, et al. *Blood*. 2023;141(9):971-983.

4. NCT02859727. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT02859727>. Updated October 31, 2022. Accessed March 3, 2023. 5. Data on file. Pharming Healthcare Inc; 2022.

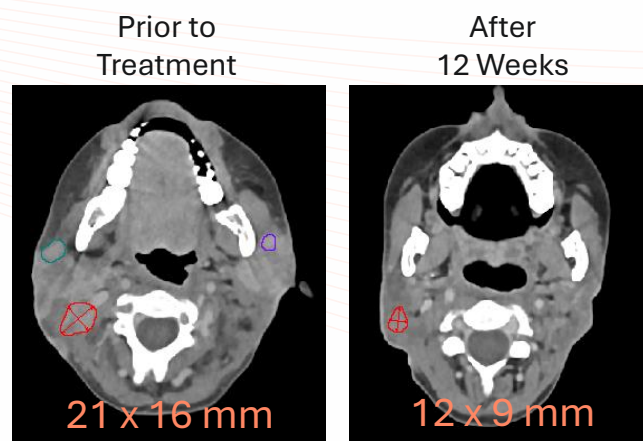
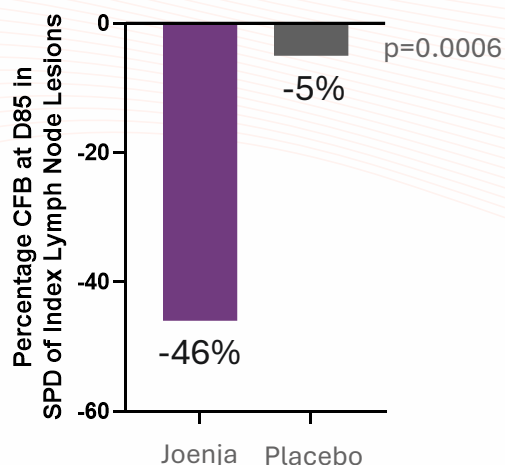
# Joenia<sup>®</sup> addresses the underlying cause of APDS to help restore immune balance – Phase III co-primary endpoints

At 12 weeks Joenia<sup>®</sup> decreased lymphadenopathy and increased naïve B cells

## Immune Dysregulation

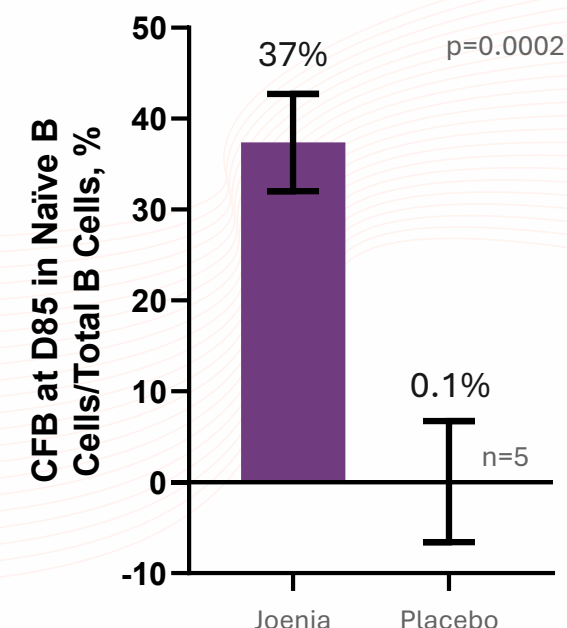
Change from baseline in index nodes\*

| Log <sub>10</sub> -transformed SPD of index lesions | Joenia (n=18) | Placebo (n=8)        |
|-----------------------------------------------------|---------------|----------------------|
| Baseline mean (SD)                                  | 3.03 (0.42)   | 3.05 (0.39)          |
| Change from baseline, LS mean (SE)                  | -0.27 (0.04)  | -0.02 (0.05)         |
| Difference vs placebo (95% CI)                      |               | -0.25 (-0.38, -0.12) |



## Immune Deficiency

Change from baseline in naïve B cells<sup>†</sup>



Data were analyzed using an ANCOVA model with treatment as a fixed effect and baseline as a covariate. Use of glucocorticoids and IRT at baseline were both included as categorical (Yes/No) covariates. Baseline is defined as the arithmetic mean of the baseline and D1 values when both are available, and if either baseline or the D1 value is missing, the existing value is used. P-value is 2-sided. Least square means are graphed. Error bars are standard error of the mean.

\*The analysis excluded 2 patients from each treatment group due to protocol deviations and 1 Joenia patient having complete resolution of the index lesion identified at baseline.

<sup>†</sup>Out of 27 patients in the PD analysis set, 13 patients met the analysis requirements, including having a percentage of <48% of naïve B cells at baseline, to form the B-PD analysis set.

Joenia [package insert]. Leiden, The Netherlands: Pharming Technologies B.V.; 2023.

Please see Important Safety Information and full Prescribing Information available at [joenia.com](https://joenia.com)

# Joenia<sup>®</sup> significantly reduced splenomegaly

Secondary endpoint: Significant reductions in spleen size by 2D and 3D analysis compared to placebo

- The adjusted mean difference in bidimensional spleen size between Joenia<sup>®</sup> (n=19) and placebo (n=9) was  $-13.5 \text{ cm}^2$  (95% CI:  $-24.1, -2.91$ ),  $P=0.0148$
- The adjusted mean difference in 3D spleen volume between Joenia<sup>®</sup> (n=19) and placebo (n=9) was  $-186 \text{ cm}^3$  (95% CI:  $-297, -76.2$ ),  $P=0.0020$

At week 12

**27%**

reduction in 3D spleen volume\*

Secondary measure: spleen volume scan results of actual patient illustrate average improvement documented for patients taking Joenia<sup>®</sup>



**Prior to treatment: 491 mL**



**At week 12: 314 mL**

Actual patient images of a 17-year-old male. As individual results vary, images may not be representative of all patients.

Rao VK, et al. Blood. 2023;141(9):971-983.

\*In the PD analysis set, the mean (SD) percentage change from baseline to week 12 in 3D spleen volume ( $\text{mm}^3$ ) was  $-26.68\%$  (12.137) with Joenia<sup>®</sup> (n=19) and  $-1.37\%$  (24.238) with placebo (n=9). The ANCOVA model was used with treatment as a fixed effect and  $\log_{10}$ -transformed baseline as a covariate for index and non-index lesions. The use of both glucocorticoids and IV Ig at baseline was included as categorical (yes/no) covariates. This analysis excluded 2 patients in each treatment group. In the Joenia<sup>®</sup> group, 1 patient with a complete index lesion response was excluded, and 3 patients were excluded for no non-index lesion at baseline. PD, pharmacodynamics.

# Joenna<sup>®</sup> safety profile

## Phase III Trial<sup>1,2</sup>

Adverse reactions reported by ≥2 patients treated with Joenna and more frequently than placebo

|                    | Joenna <sup>®</sup> (n=21)<br>n (%) | Placebo (n=10)<br>n (%) |
|--------------------|-------------------------------------|-------------------------|
| Headache           | 5 (24)                              | 2 (20)                  |
| Sinusitis          | 4 (19)                              | 0                       |
| Dermatitis atopic* | 3 (14)                              | 0                       |
| Tachycardia†       | 2 (10)                              | 0                       |
| Diarrhea           | 2 (10)                              | 0                       |
| Fatigue            | 2 (10)                              | 1 (10)                  |
| Pyrexia            | 2 (10)                              | 0                       |
| Back pain          | 2 (10)                              | 0                       |
| Neck pain          | 2 (10)                              | 0                       |
| Alopecia           | 2 (10)                              | 0                       |

- Study drug-related AEs occurred in 8 patients; the incidence was lower in the Joenna<sup>®</sup> arm (23.8%) than in the placebo arm (30.0%)
- No AEs led to discontinuation of study treatment

## Open-label Extension Study<sup>3</sup>

Data cutoff for interim analysis: December 13, 2021

- 32/37 patients reported ≥1 AE
- 78.4% of AEs were grade 1, 48.6% grade 2, 27.0% grade 3, 0% grade 4
- No SAEs related to Joenna<sup>®</sup>

| Most common AEs                   | n    |
|-----------------------------------|------|
| Upper respiratory tract infection | 8    |
| Headache                          | 6    |
| Pyrexia                           | 6    |
| Otitis externa                    | 5    |
| Weight increase                   | 5    |
| COVID-19, positive/negative       | 5/14 |

One patient with significant baseline cardiovascular comorbidities suffered cardiac arrest resulting in death at extension Day 879; determined by investigator not to be related to study drug

### Across all trials<sup>2</sup>

- 38 patients had a **median exposure of ~2 years**
- 4 patients had **>5 years of exposure**

A patient with multiple occurrences of an AE is counted only once in the AE category. Only AEs occurring at or after first drug intake are included.

\*Includes dermatitis atopic and eczema. †Includes tachycardia and sinus tachycardia.

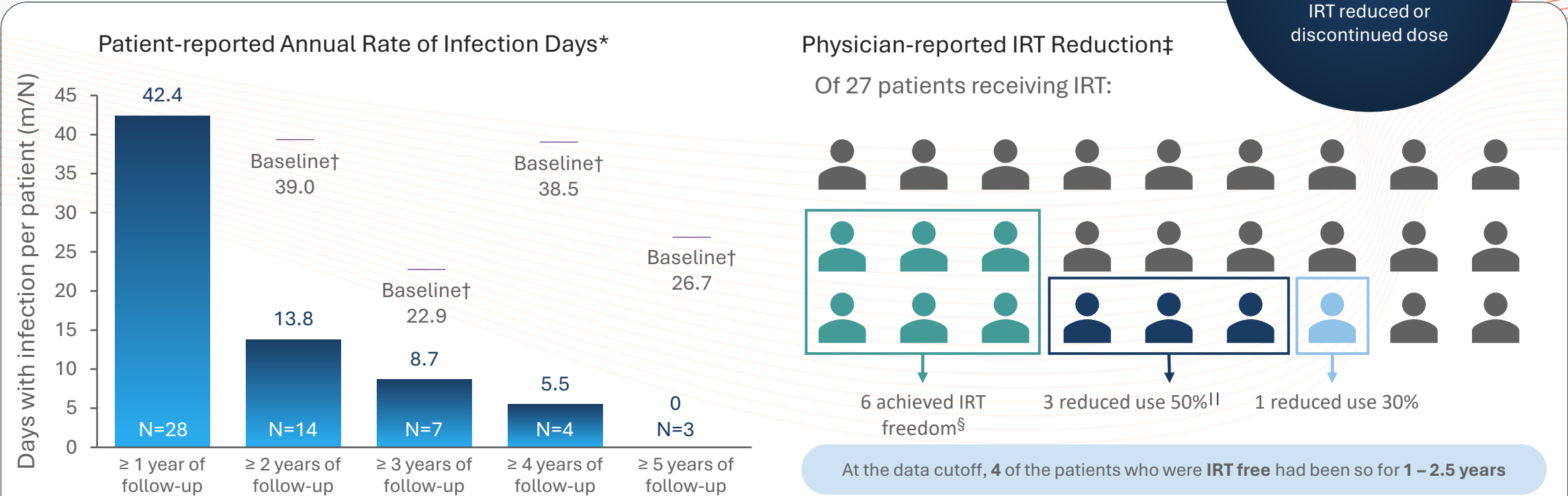
AEs, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SAE, serious adverse event.

1. Rao VK, et al. Blood. 2023;141(9):971-983. 2. Joenna [package insert]. Leiden, The Netherlands: Pharming Technologies B.V.; 2023. 3. Data on file. Pharming Healthcare Inc; 2022.

Please see Important Safety Information and full Prescribing Information available at joenna.com

# Open-label extension interim analysis of days spent with infections and IRT reduction

37%  
of patients receiving  
IRT reduced or  
discontinued dose



Although safety was the primary objective of the open-label study, this post hoc analysis from the open-label study was not powered to provide any statistical significance of efficacy and therefore no conclusions should be drawn.

\*Infections that developed during the study were reported as adverse events. Investigators were requested to inquire about signs and symptoms of infections at each visit, with a particular focus on bacterial enterocolitis. Patients were not provided an infection diary to document infections occurring between visits. One patient was excluded from the analysis due to an incorrect year that was recorded for an infection. †Baseline infections are each group's year 1 annual rate of infections. N values changed because patients were in the OLE for different lengths of time. ‡Data on concomitant medication usage was reported at each patient visit. §One patient had a subsequent one-time dose. ||One patient achieved IRT freedom for 3 months but subsequently restarted IRT.  
IRT, immunoglobulin replacement therapy; m, number of infection days; N, number of patients in follow-up category.  
Rao VK, et al. Poster presented at: 64<sup>th</sup> Annual American Society of Hematology Annual Meeting; December 10-13, 2022; New Orleans, LA.  
Please see Important Safety Information and full Prescribing Information available at joenja.com