Pharming Group N.V.

Oppenheimer Movers in Rare Disease Summit

December 11, 2025

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 2024 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2024, 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.

Combination of commercial and pipeline assets poised to deliver strong value creation

Pharming®

Commercial

Pipeline

HAE

RUCONEST®
Unique value proposition/positioning
Highly specific manufacturing process

PIDs
with immune dysregulation

Joenja® for APDS
Significant near-term catalysts
Up to 100x current prevalence

Leniolisib for PIDs / CVID
Phase II trials

> $1B revenue potential

PMD

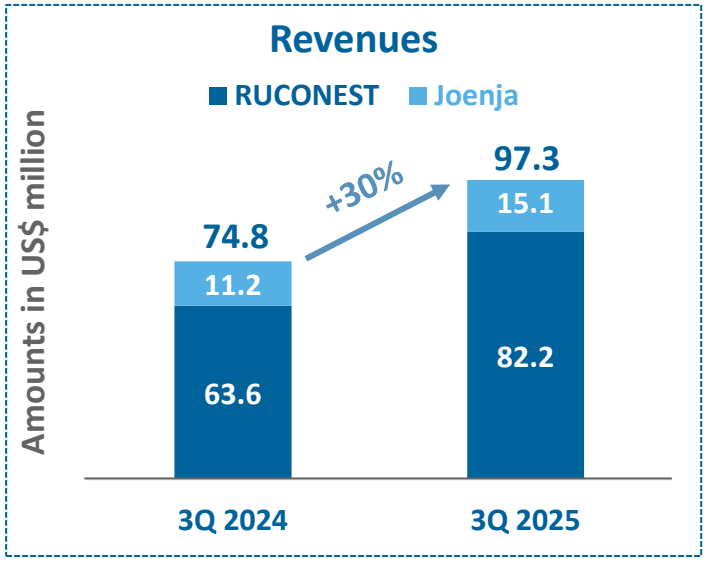
KL1333
Registrational Phase II trial
Positive interim analysis

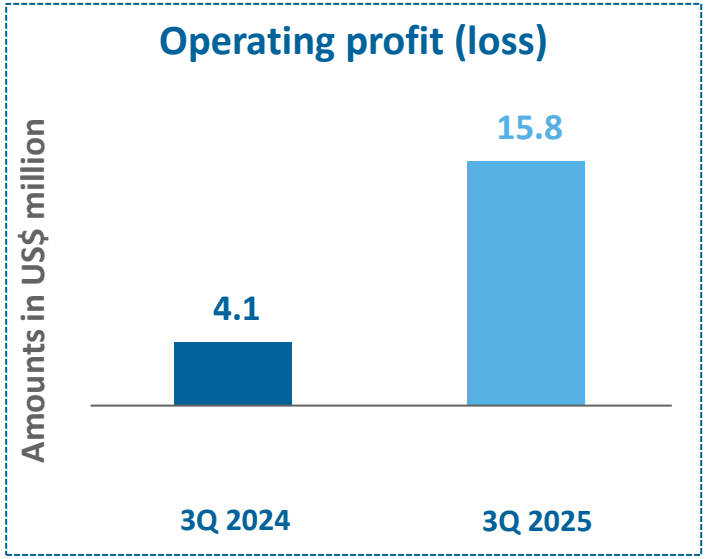
> $1B revenue potential

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

Strong third quarter 2025 performance





- Total revenues up 30%
- Significant growth in operating profit
- Significant cash flow from operations – US$32 million
- High double-digit Joenja® and RUCONEST® revenue growth driven by growth in patients
- **Raised 2025 revenue guidance to US$365-375 million due to strong RUCONEST® performance and outlook**
- Announced significant reduction in general and administrative headcount in October, to optimize capital deployment to high growth initiatives

Executing on high value rare disease pipeline

APDS

Leniolisib sNDA for 4-11 yo APDS patients – FDA Priority Review, Jan. 26 PDUFA

Japan, EMA and other regulatory reviews on track for 2026 approvals

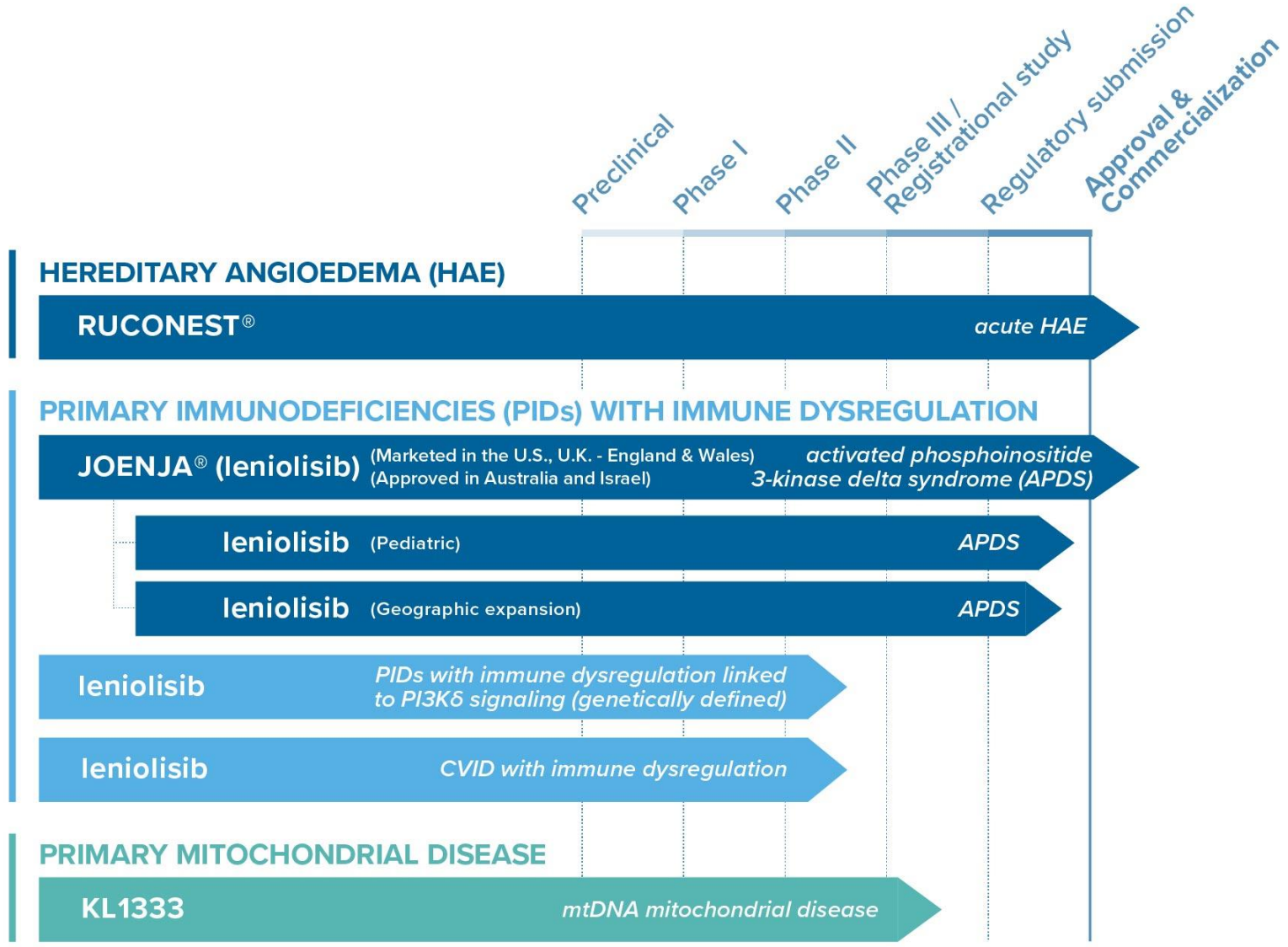
PIDs
with immune dysregulation

Genetic PID and CVID Phase II POC trials on track for 2H 2026 read-outs

PMD

KL1333 pivotal trial – 20+ sites actively enrolling with additional 20+ being opened, on track for late 2027 read-out

Diverse rare disease portfolio and pipeline

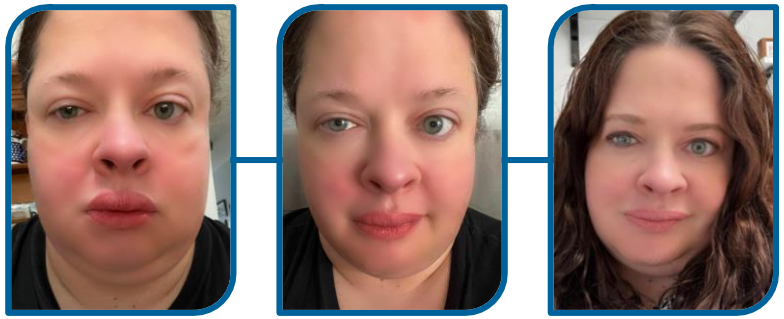


Pharming®

RUCONEST® for HAE

RUCONEST® unique value proposition and positioning

- Type 1, Type 2, and Normal C1-INH HAE patients rely on RUCONEST®
  - Only recombinant C1-INH protein replacement therapy
  - Targets the root cause of HAE across all pathways
  - IV administration – rapid onset, high dose
- 97% attacks treated with just 1 dose[1]
- 93% acute attacks stopped for at least 3 days[2]
- RUCONEST® mostly used by patients experiencing more severe/frequent attacks

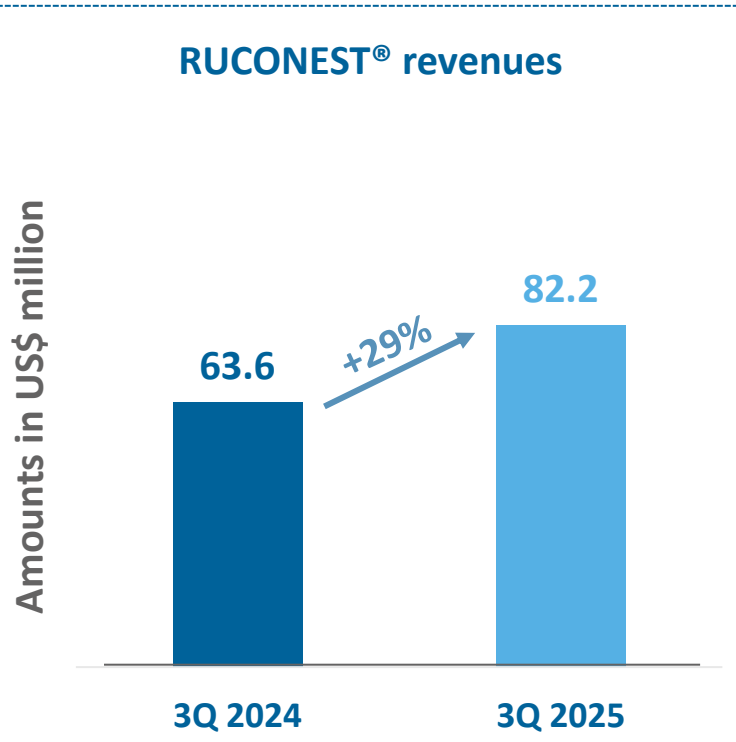


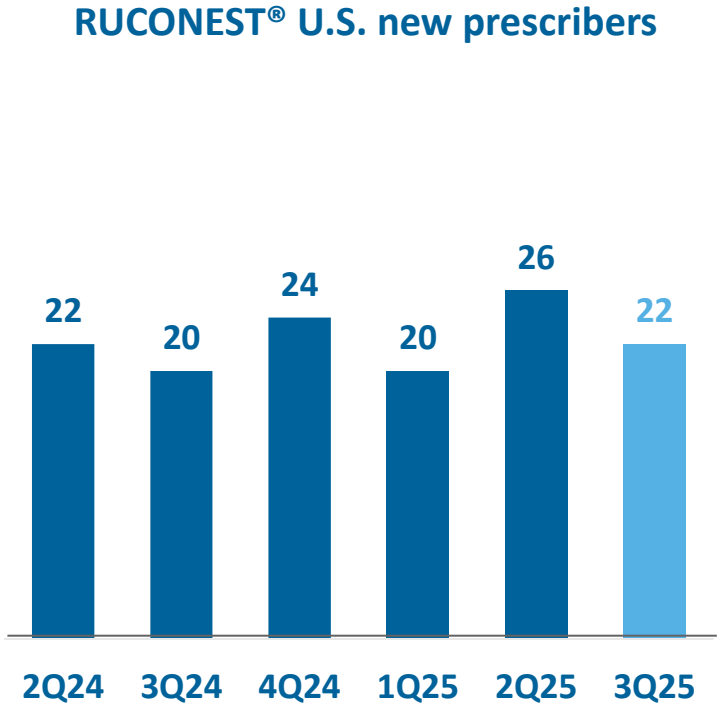
Time of taking RUCONEST | 4 hours after | 24 hours after

Building Trust
10+ YEARS
Supporting Patients With HAE

References: 1. RUCONEST®. Prescribing information. Pharming Healthcare Inc; 2020. 2. Bernstein JA, et al. *Ann Allergy Asthma Immunol.* 2017;118(4):452-453. 3. Data on file. Pharming Healthcare Inc; 2019
The most common adverse reactions (incidence ≥2%) were headache, nausea and diarrhea. The most serious adverse reaction reported in clinical trials was anaphylaxis.

RUCONEST® strong growth continues in acute HAE market





- **Strong U.S. in-market demand**
  - Continuing to add prescribers and patients
  - New patient enrollments remain high (~60)
  - Increase in more severe / frequent attack patients
- **Continued robust U.S. volume growth**
  - +24% in 3Q25
  - +28% in 9M25

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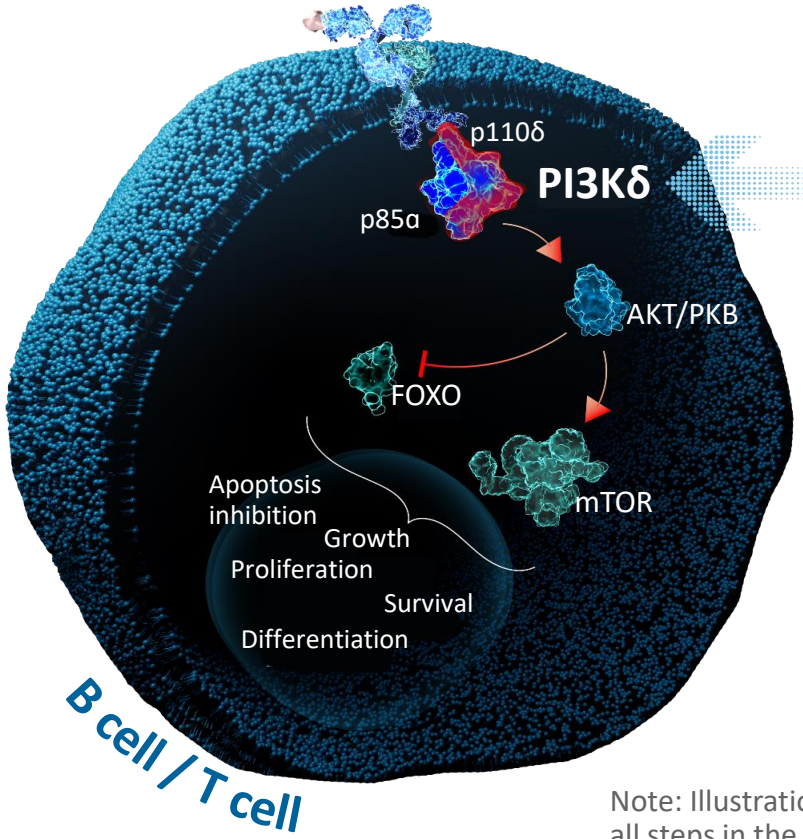
Joenja® (leniolisib)
APDS & PID indications

APDS is a rare primary immunodeficiency (PID)
Genetic defect leads to PI3Kδ hyperactivity

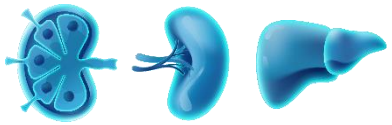
Hyperactive PI3Kδ results in dysregulated B and T cell development[1-3]



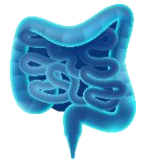
Note: Illustration does not include all steps in the signaling pathway.

Immune imbalance leads to diverse signs and symptoms[1,4-6]

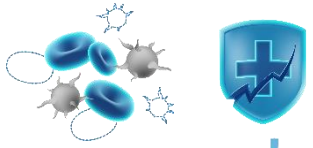
Severe, recurrent, persistent infections
- Sinopulmonary
- Herpesvirus (especially EBV and CMV)



Lymphoproliferation
- Lymphadenopathy
- Splenomegaly/hepatomegaly
- Nodular lymphoid hyperplasia



Enteropathy



Autoimmunity
- Cytopenias
- Autoimmune disorders
- Autoinflammatory disorders

Bronchiectasis

Lymphoma

FOXO, forkhead box O; mTOR, mammalian target of rapamycin; PI3Kδ, phosphoinositide 3-kinase delta; PKB, protein kinase B.

1. Lucas CL, et al. *Nat Immunol*. 2014;15(1):88-97. 2. Fruman DA, et al. *Cell*. 2017;170(4):605-635. 3. Okkenhaug K, Vanhaesebroeck B. *Nat Rev Immunol*. 2003;3(4):317-330. 4. Coulter TI, et al. *J Allergy Clin Immunol*. 2017;139(2):597-606. 5. Elkaim E, et al. *J Allergy Clin Immunol*. 2016;138(1):210-218. 6. Jamee M, et al. *Clin Rev Allergy Immunol*. 2020;59(3):323-333.

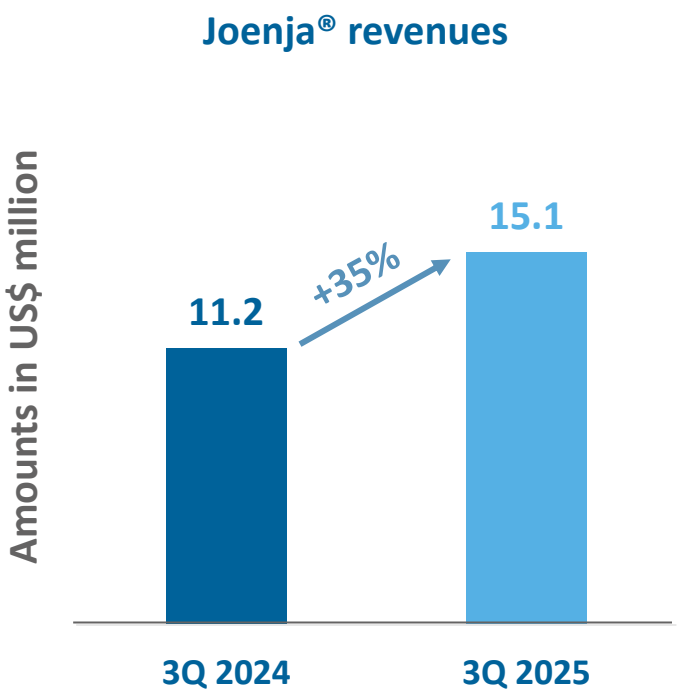
Reports of Joenja® changing patients' lives

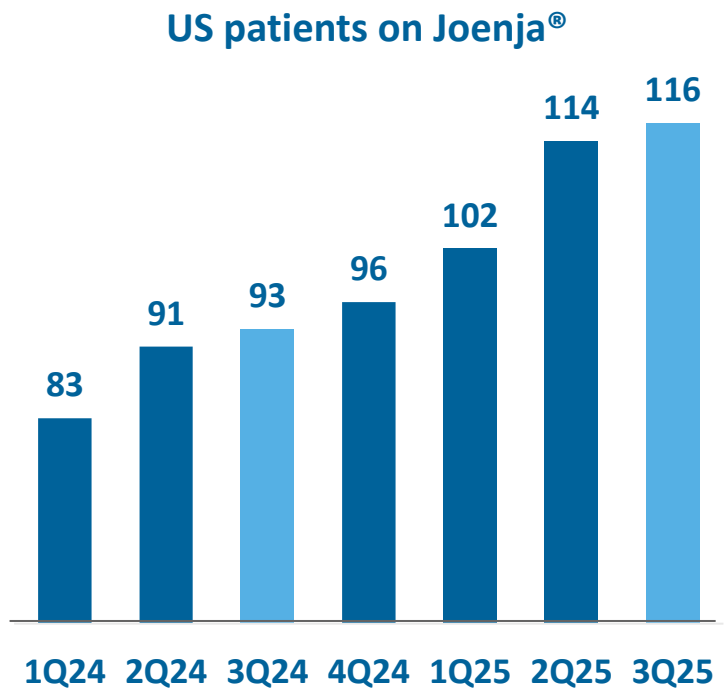
24-year-old male with APDS whose progress was followed in the Joenja® open-label extension study for 6 years

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

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

Joenja® strong double-digit growth in 12y+ APDS segment

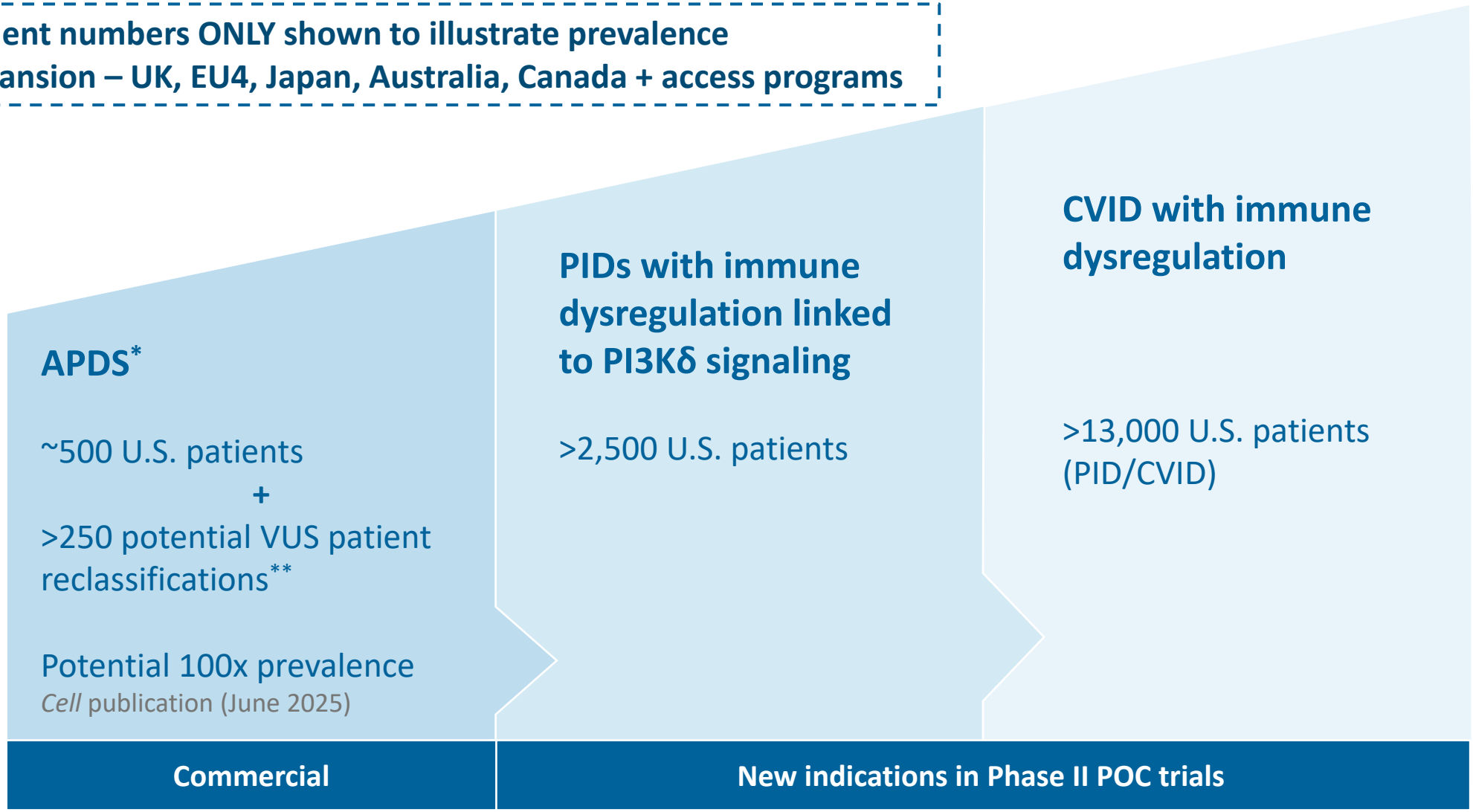




- **Strong YoY increase in APDS patients on therapy in the US**
  - ➢ 116 patients (+25% vs 3Q24)
- **Acceleration of U.S. APDS patient identification**
  - ➢+13 in Q3, +36 YTD
- **Additional 180 APDS patients in access programs and clinical studies globally**

Joenja® (leniolisib) lifecycle to realize $1Bn+ sales potential

U.S. patient numbers ONLY shown to illustrate prevalence
Geo expansion – UK, EU4, Japan, Australia, Canada + access programs



*Initial APDS prevalence estimate ~1.5 patients / million. 270 patients currently identified in the U.S. (73 pediatric), 990 identified globally. (Data as of September 30, 2025)
**Estimate: 20% of >1,400 U.S. patients with a variant of uncertain significance, or VUS, in the PIK3CD and PIK3R1 genes implicated in APDS could ultimately be diagnosed with APDS.

Joenja® APDS pediatric label expansion – go to market strategy

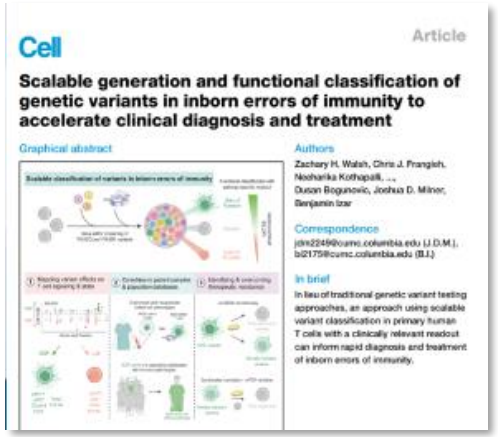
Children 4-11 years old with APDS

- FDA Priority Review with PDUFA date of Jan 31, 2026*
- FDA filing based on Phase III data consistent with the improvements and safety seen in the previously reported randomized controlled trial in adolescent and adult APDS patients
- Identified 54 patients in the U.S., many already on drug
- Launch readiness of track

*Previously 1H26. Assuming a positive FDA decision

Activities surrounding expanded APDS prevalence

Findings


Cell

Article

Scalable generation and functional classification of genetic variants in inborn errors of immunity to accelerate clinical diagnosis and treatment

Graphical abstract

Authors

Zachary H. Walsh, Chris J. Frangieh, Nooharika Kothapalli, ..., Duson Bogunovic, Joshua D. Milner, Benjamin Izar

Correspondence

In brief

In lieu of traditional genetic variant testing approaches, an approach using scalable variant classification in primary human T cells with a clinically relevant readout can inform rapid diagnosis and treatment of inborn errors of immunity.

- **>100 new PI3Kδ gain of function (GOF) variants identified in Cell paper**
- **Carriers of these variants were found in population databases with prevalence up to 100X higher than current APDS estimates**
- **Associated patient phenotypes more diverse than “classic” APDS**

Next steps

- **Global advisory board to discuss how these variants may cause disease (Nov. 2025)**
- **Identify individuals who may benefit from PI3Kδ inhibition – build predictive, AI-driven model**
  - Apply AI-based clustering and PheWAS* to link GOF variants to patient phenotypes in large biobanks
  - Generate data supporting expansion of APDS clinical definition
  - Apply predictive model to identify patients in large health system EMRs
- **Identify additional GOF variants**

*PheWAS – Phenome Wide Association Study

Leniolisib development in PIDs with immune dysregulation: Significant expansion of addressable patient population

Patient Population

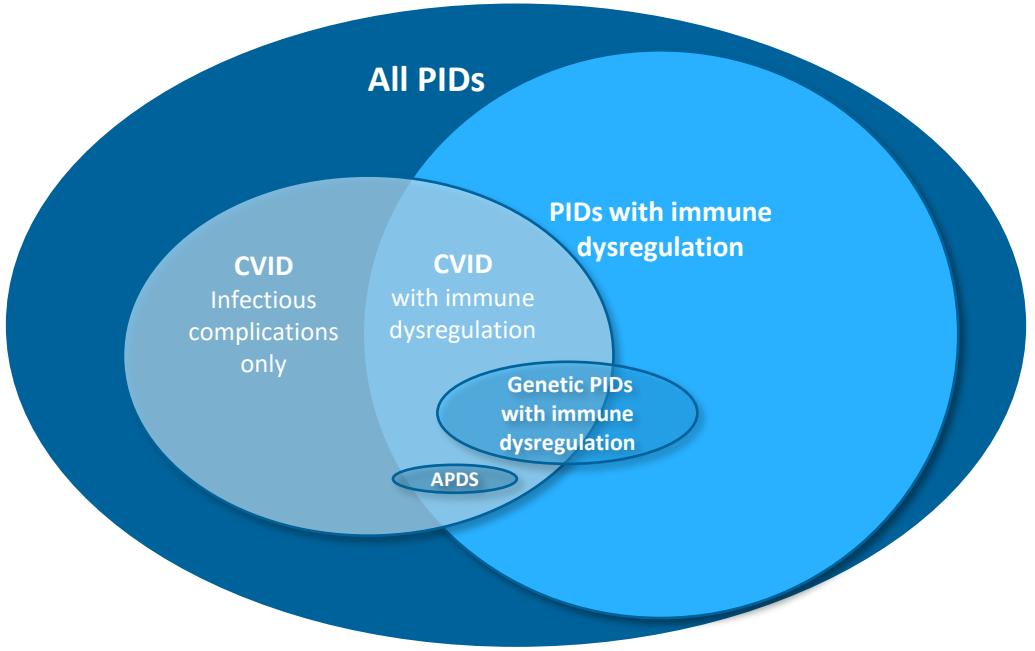
- PID patients with clinical manifestations similar to APDS
- Significant unmet clinical need, no approved therapies
- Prevalence 5-26x APDS

Rationale

- Critical role of PI3Kδ in lymphocyte regulation, driving lymphoproliferation and autoimmunity
- Positive experience in compassionate use patients

Two Phase II studies underway

- Genetically defined PIDs with immune dysregulation[1]
- Common variable immunodeficiency (CVID) with immune dysregulation[2]
- On track for 2H 2026



1. PIDs include ALPS-FAS, CTLA4 haploinsufficiency, NFKB1 haploinsufficiency and PTEN deficiency, amongst others. Prevalence 7.5 patients / million
2. Prevalence 39 patients/million

Three primary immunodeficiency with immune dysregulation indications driven by dysfunctional B and T cells under the influence of the PI3Kδ pathway

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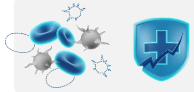
	APDS	Additional PIDs linked to PI3Kδ	CVID w/immune dysregulation
Prevalence per million population	1.5	7.5	39
Genetic Diagnosis	Yes (PIK3CD, PIK3R1)	Yes (6 different mutations in study)	No. Clinical Dx (75% no genetic drivers)
Link to PI3Kδ pathway	PI3Kδ Lock & KEY	mutation linked to PI3Kδ hyperactivity	Cluster of clinical manifestations driven by B & T Cell dysfunction

Recurrent viral and bacterial infections



Autoantibodies: Autoimmune cytopaenias

Lymphoproliferation: lymphadenopathy splenomegaly

Lymphocytes infiltrate end-organs: lung, GI tract, liver,

Malignancy: Lymphomas

Joenja controls B and T cell dysregulation via PI3Kδ pathway, correcting the abnormal immunophenotype

Generally well controlled with Ig, antibiotics

Current SoC
Poor disease control
(Steroids, immunosuppressants, and immunomodulators)

Current SoC
Poor disease control
(Steroids, immunosuppressants, and immunomodulators)

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KL1333 for mtDNA Mitochondrial Disease

KL1333 for mtDNA-driven primary mitochondrial disease
Aiming for the first disease-modifying treatment

KL1333 targets underlying pathology

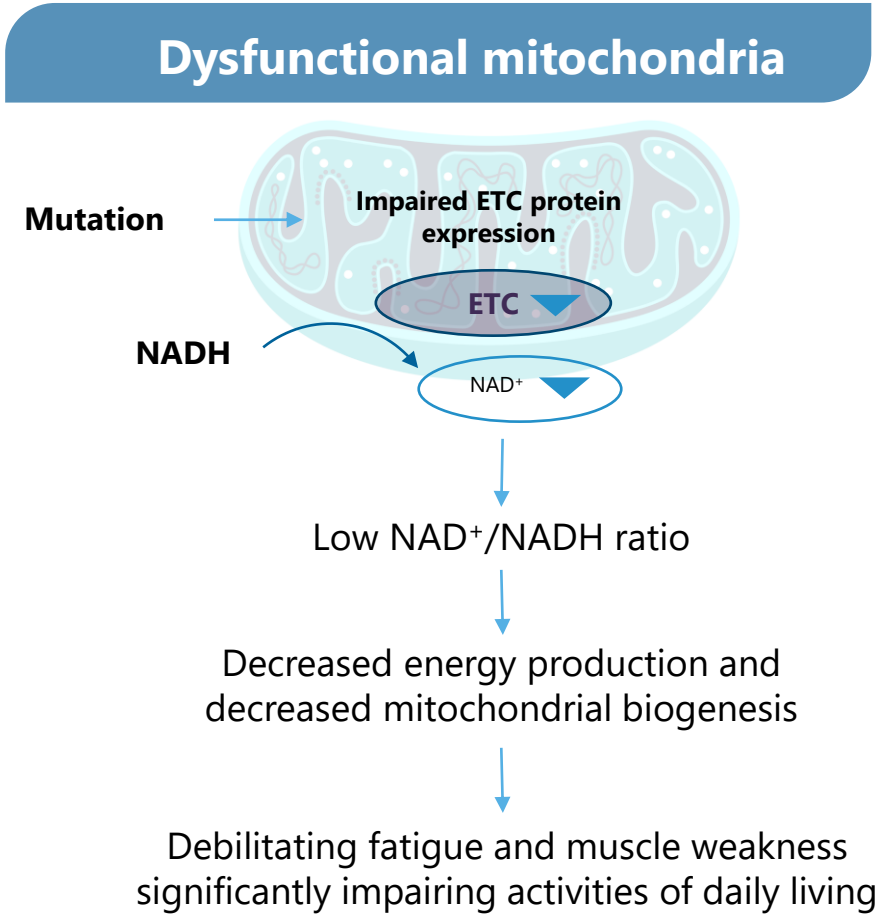
- Normalizes NAD+/NADH ratio and mitochondrial function, with evidence from in vitro data, animal models, and in patients treated with KL1333

Significant patient population

- >30,000 diagnosed patients with mtDNA disorders[1]
- Majority of patients treated in centers of excellence[2]

Registrational clinical study underway

- Clinically-relevant endpoints, supported by FDA
- Positive interim analysis in pivotal study
- Expect readout in 2027 and FDA approval end of 2028

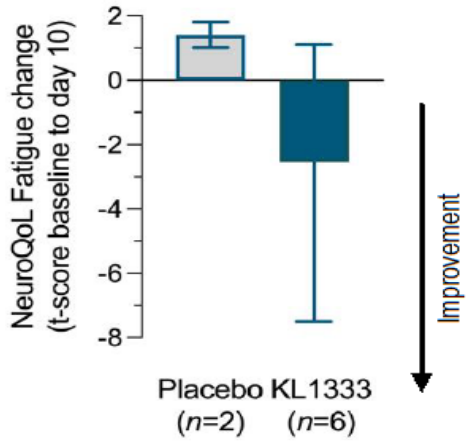


1. In US, EU4 and UK. Diagnoses can include MELAS-MIDD and KSS-CPEO spectrum disorders as well as MERRF syndrome.
2. UNITED MITOCHONDRIAL DISEASE FOUNDATION, Voice of the Patient Report, 2019.

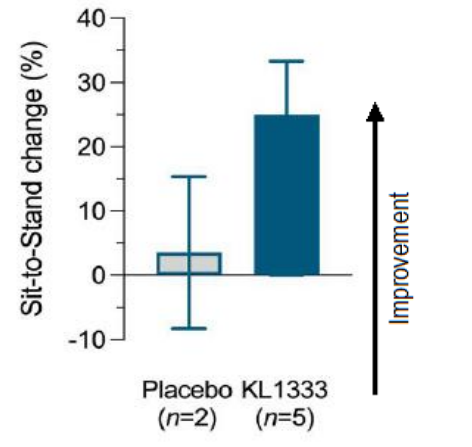
KL1333 Phase 1b demonstrated significant activity vs. placebo

- KL1333 showed efficacy in patients diagnosed with mtDNA PMD after 10 days using 50 mg/day
  - Fatigue reduction (NeuroQoL fatigue change)
  - Muscle function improvement (30 seconds sit-to-stand)
- Improved lactate/pyruvate ratio, reflecting target engagement
- No serious adverse events reported

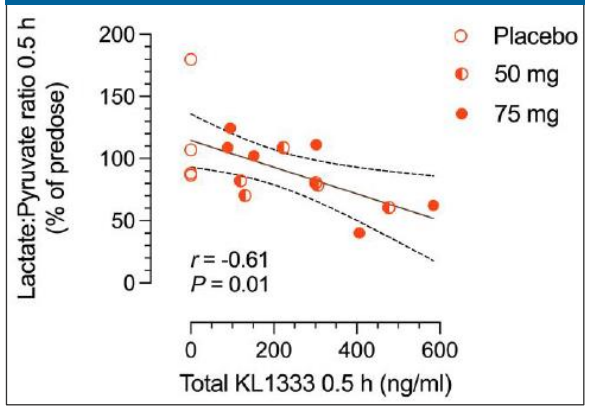
Fatigue Reduction
Changes from baseline to day 10



Muscle Function Improvement
Changes from baseline to day 10



Lactate:Pyruvate Ratio
Changes from baseline to day 10



Source: Pizzamiglio C et al., Optimizing rare disorder trials: a phase 1a/1b randomized study of KL1333 in adults with mitochondrial disease, Brain, 2024.

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
- All Wave 1 sites + three new sites active (n=20)
- Planning 40+ total sites, with significant expansion in the 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
- Data monitoring committee (DMC) concluded:
  - Safety and tolerability profile acceptable
  - No changes to study design
  - 180 total patients confirmed in the study

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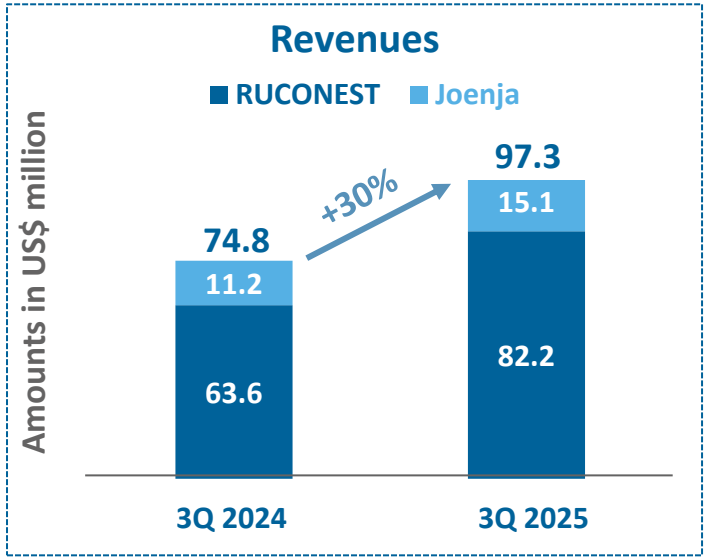
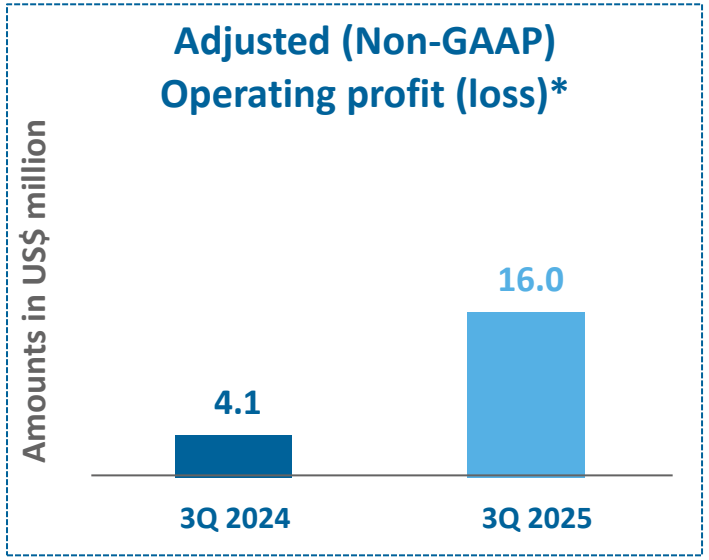
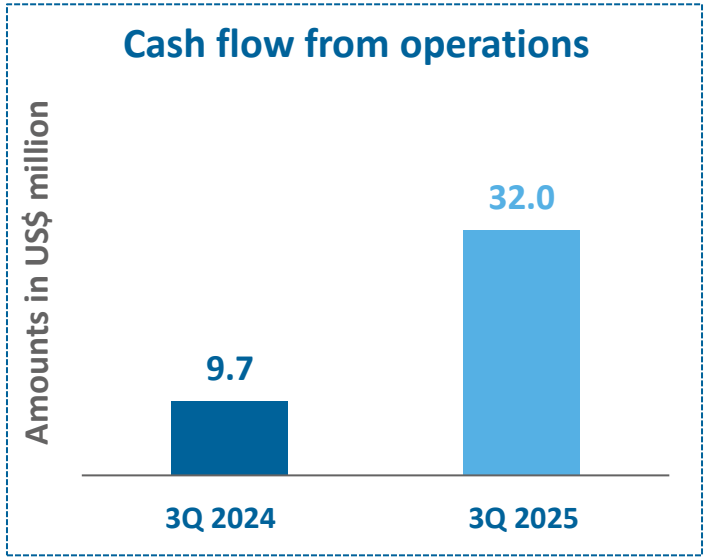
Financials and Outlook

Financial highlights: 3Q 2025 vs 3Q 2024



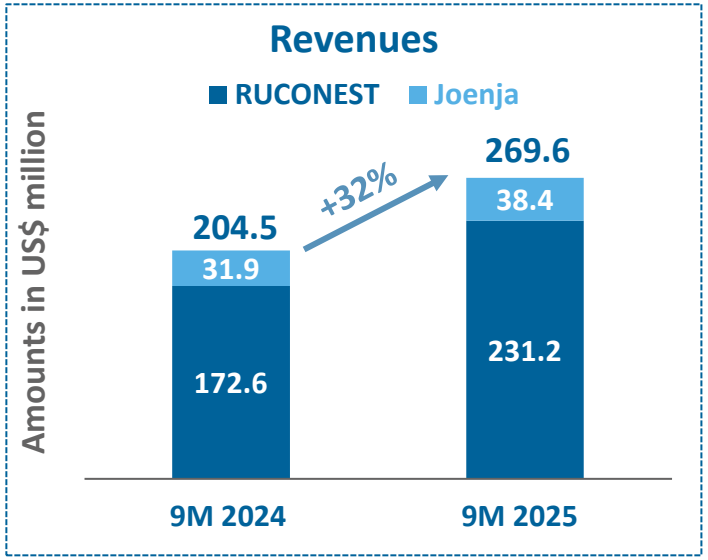


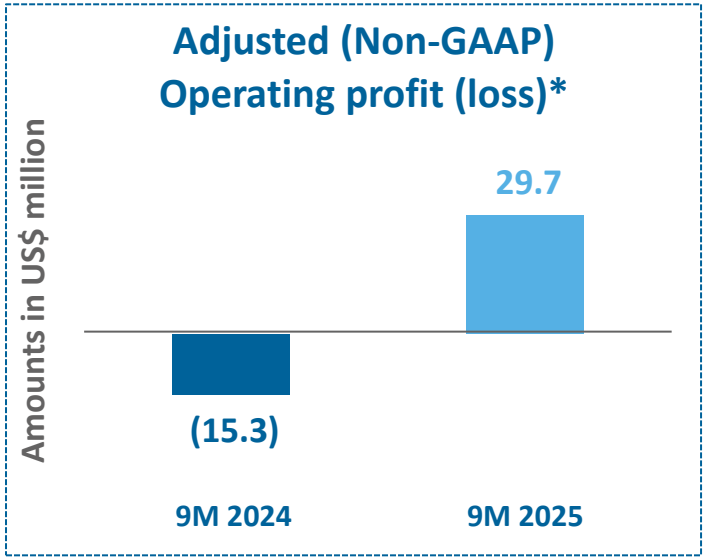


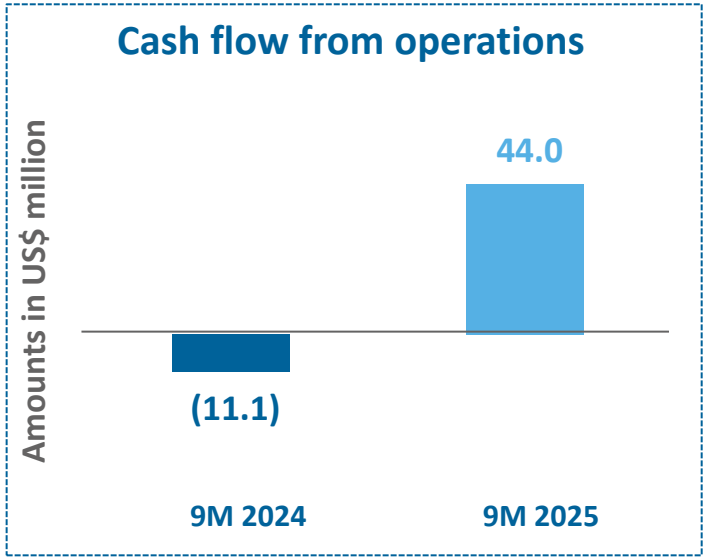
- Total revenues grew 30% to US$97.3 million, driven by high double-digit growth for both products
- Significant growth in Operating Profit to US$16.0 million, almost 4X prior year
- Significant increase in cash flow from operations – US$32 million
- Cash and marketable securities increased by US$38 million to US$168.9 million at end of quarter

* Adjusted operating profit for 3Q 2025 excludes US$0.2 million of non-recurring Abliva acquisition-related expenses.

Financial highlights: 9M 2025 vs 9M 2024







- Total revenues grew 33% to US$269.6 million, driven by strong double-digit growth for both products
- Significant growth in Operating Profit to US$29.7 million, compared to a loss in prior year
- Strong cash flow from operations – US$44.0 million
- Cash and marketable securities US$168.9 million at end of quarter, back to year-end 2024 level

* Adjusted operating profit for 9M 2025 excludes US$10.1 million of non-recurring Abliva acquisition-related expenses (US$8.0 million in G&A, $2.1 million in R&D).

2025 financial guidance and long-term capital outlook

Revenue and operating expenses:

	FY 2025 Guidance	Notes
Total Revenues	**US$365 - 375 million**	23 - 26% growth
Operating Expenses	**US$304 - 308 million**	• Assumes constant currency • Includes $10.2 million non-recurring Abliva-related transaction and integration expenses • Excludes ~$7M restructuring costs in Q4

RUCONEST® well positioned to provide continued strong cash flows

Available cash and future cash flows expected to cover current pipeline and pre-launch costs

Driving strong commercial, financial and pipeline momentum

Strong Q3 growth momentum

High dbl-digit growth for RUCONEST® and Joenja®

Strong operating profit growth

US$32M cash flow from operations

Promoted to AMX® (MidCap) index

Upgraded financial outlook

Raised 2025 revenue guidance to $365-375M

Strong RUCONEST® performance and outlook

Significant Joenja® APDS growth catalysts:

- Pediatric label, VUSs, targeted geo expansion, prevalence expansion

High value pipeline

Joenja® (leniolisib) for PIDs/CVID with immune dysregulation

- PhII readouts (2026)

KL1333 for mtDNA mitochondrial disease

- Pivotal study readout (2027)

Building a leading rare disease co.

Proven commercial and development capabilities

Scalable organization

Growth-oriented leadership team

Pharming®

www.pharming.com

NASDAQ: **PHAR** | EURONEXT Amsterdam: **PHARM**

Pharming®

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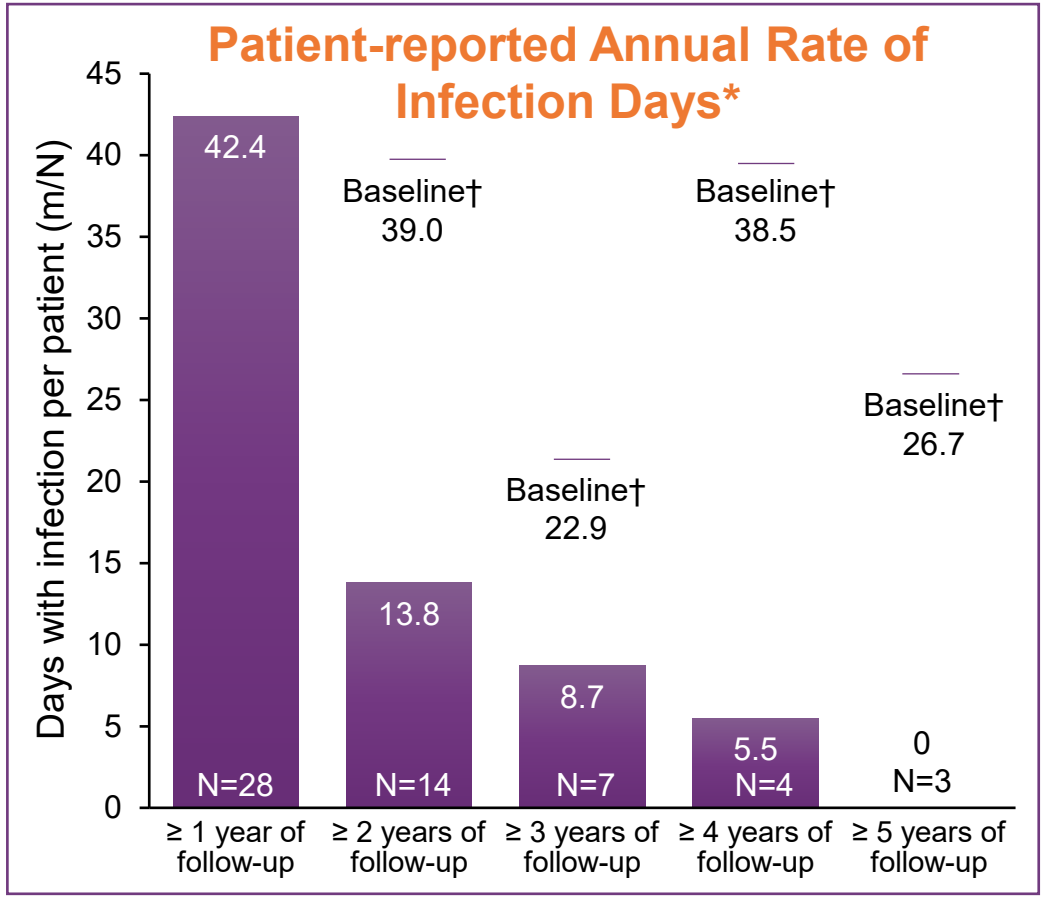
Appendix

Joenja: Targeting the root cause of APDS to help restore immune balance

Pharming®

- Treatment with Joenja 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 Joenja treatment
  - No patients withdrew from the clinical trials due to an adverse drug reaction
  - The most common adverse reactions (incidence >10%) in the phase 3 trial were headache, sinusitis, and atopic dermatitis
- Long-term open-label study
  - Median duration of Joenja exposure was ~2 years
  - Reduction in infections (see right)



Joenja® clinical trial designs

Pharming®

Pivotal Trial - Part 1: Dose-finding[1,2]

- 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[3]

- Randomized, triple-blinded, placebo-controlled
- 31 patients with APDS (21 Joenja®, 10 placebo)
- 12 weeks
- 70 mg bid
- Co-primary efficacy end points
  - Change from baseline in log^{10}-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[4,5]

- 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.

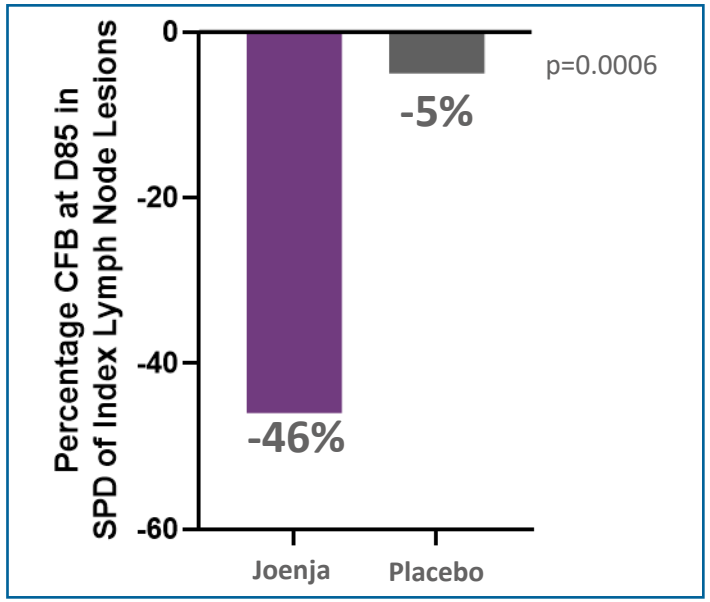
Joenja® addresses the underlying cause of APDS to help restore immune balance – Phase 3 co-primary endpoints

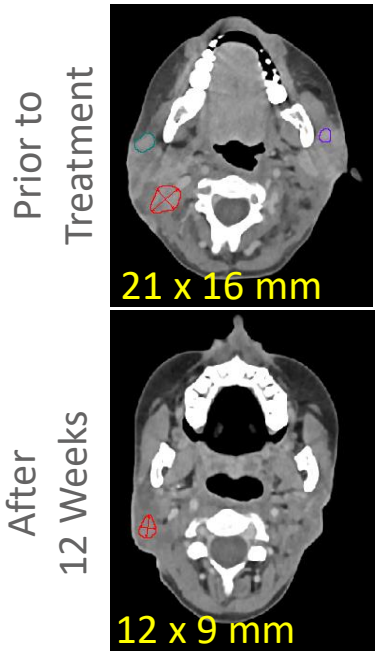
At 12 weeks Joenja® decreased lymphadenopathy and increased naïve B cells

Immune Dysregulation

Change from baseline in index nodes*

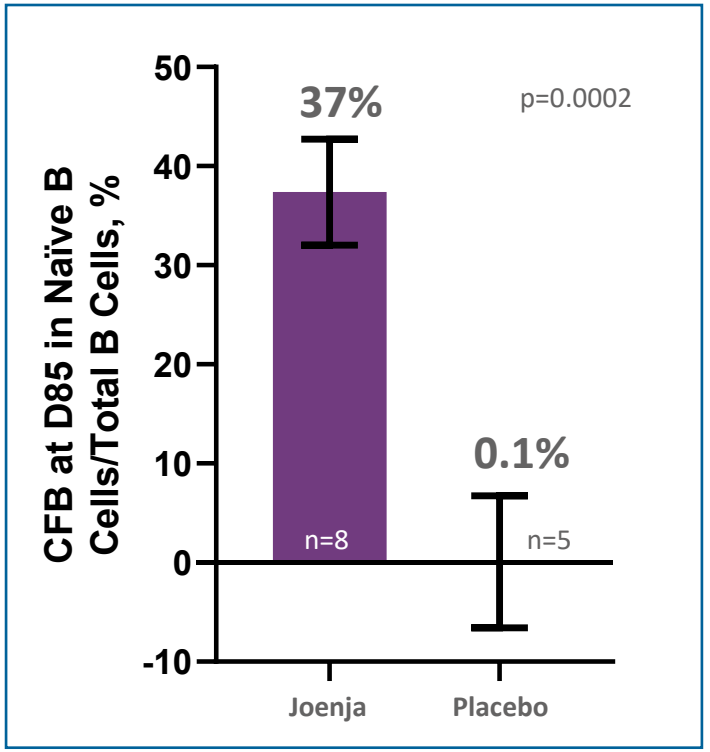
Log_{10}-transformed SPD of index lesions	Joenja (n=18)	Placebo (n=8)
Baseline mean (SD)	3.03 (0.42)	3.05 (0.39)
Change from baseline, LS mean (SE)	-0.27 (0.04)	-0.02 (0.05)
Difference vs placebo (95% CI)		-0.25 (-0.38, -0.12)





Immune Deficiency

Change from baseline in naïve B cells†



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 Joenja patient having complete resolution of the index lesion identified at baseline.

†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.

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

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

Joenja® 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 Joenja® (n=19) and placebo (n=9) was -13.5 cm^2 (95% CI: -24.1, -2.91), *P*=0.0148
- The adjusted mean difference in 3D spleen volume between Joenja® (n=19) and placebo (n=9) was -186 cm^3 (95% CI: -297, -76.2), *P*=0.0020

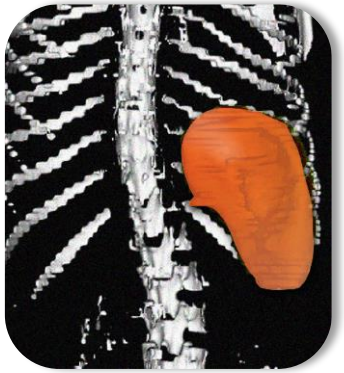
at week 12

27%

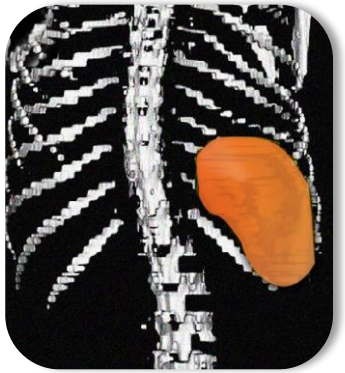
reduction in 3D spleen volume*

Secondary measure: spleen volume scan results of actual patient illustrate average improvement documented for patients taking Joenja®

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 (mm^3) was -26.68% (12.137) with Joenja® (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 Joenja® 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.

Joenja® safety profile

Phase 3 Trial[1,2]

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

	Joenja (n=21) n (%)	Placebo (n=10) 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 Joenja arm (23.8%) than in the placebo arm (30.0%)
- No AEs led to discontinuation of study treatment

Open-label Extension Study[3]

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 Joenja

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

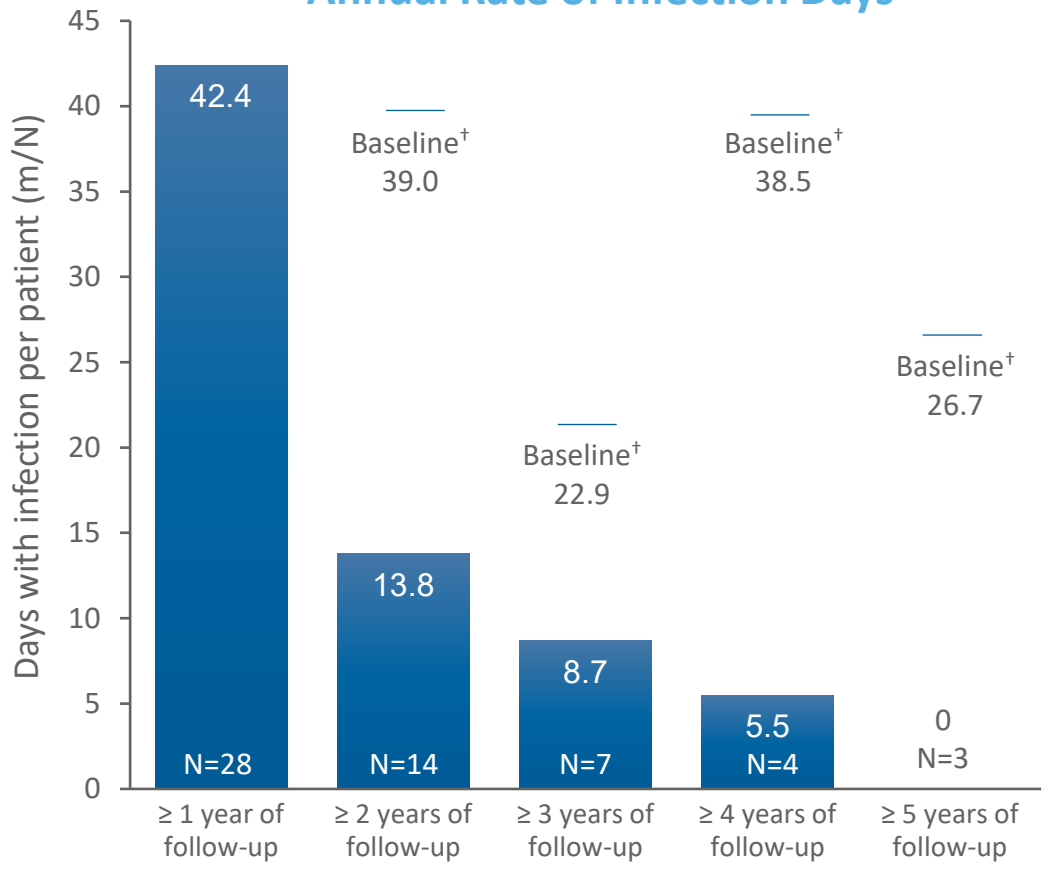
Across all trials[2]

- 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.** Joenja [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 joenja.com

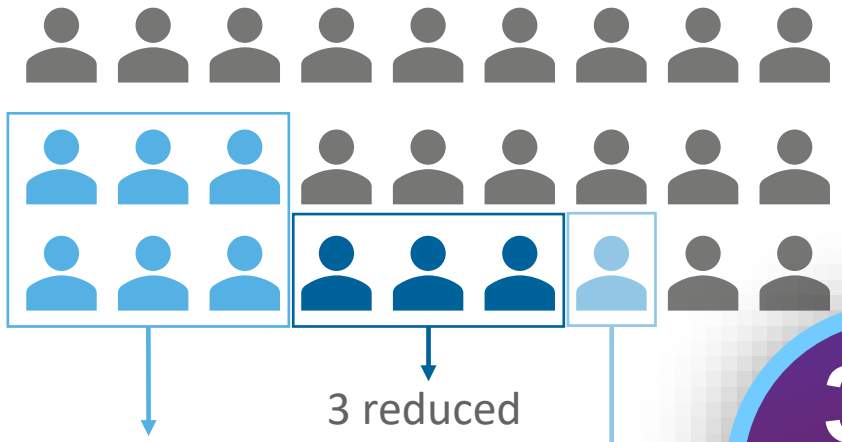
Open-label extension interim analysis of days spent with infections and IRT reduction

Annual Rate of Infection Days*



Physician-reported IRT Reduction‡

Of 27 patients receiving IRT:



6 achieved IRT freedom§

3 reduced use 50%‖

1 reduced use 30%

37% OF PATIENTS RECEIVING IRT REDUCED OR DISCONTINUED DOSE

At the data cutoff, **4** of the patients who were **IRT free** had been so for **1 – 2.5 years**

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: *64th 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

Pediatric APDS clinical trial results support regulatory filings

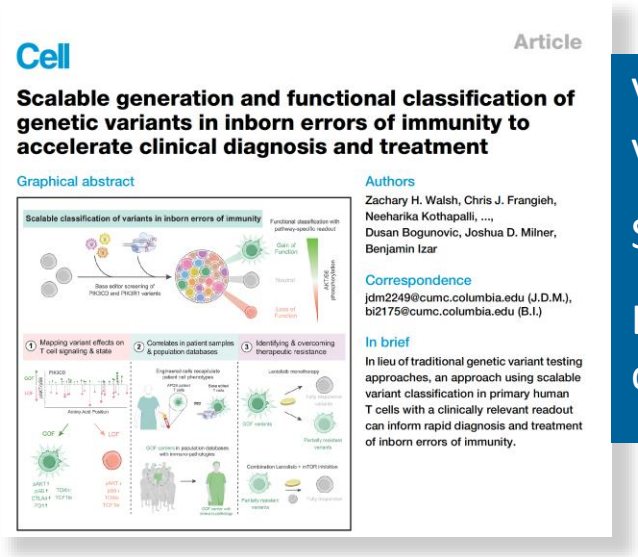
Pediatric

Phase III trial for children 4-11 years old with APDS

Positive topline data announced December 2024

- 21 patients enrolled in U.S., Europe, and Japan
- Both co-primary endpoints show improvement consistent with the RCT in adolescents and adults
- Benefits seen across the four tested dose levels
- No deaths/discontinuations due to AEs. No new safety findings
- Data presented at CIS conference in May
- Regulatory filings beginning with the U.S. in second half 2025

Newly published study expands characterization of APDS


Cell

Article

Scalable generation and functional classification of genetic variants in inborn errors of immunity to accelerate clinical diagnosis and treatment

Graphical abstract

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In brief

In lieu of traditional genetic variant testing approaches, an approach using scalable variant classification in primary human T cells with a clinically relevant readout can inform rapid diagnosis and treatment of inborn errors of immunity.

VUS patients: Inconclusive genetic test due to insufficient data to determine if variant is disease causing

Study uncovered >100 new variants leading to PI3Kδ hyperactivity (GOF variants)

Leniolisib restored / improved PI3Kδ signaling defects and immune abnormalities caused by GOF variants

Data suggests that VUS patients with these GOF variants should be reclassified as APDS

Genetic test labs will utilize data to independently re-assess VUSs and reclassify patients to APDS*

Expand studies to functionally evaluate the remainder of all possible variants in APDS genes

Frequency of new GOF variants in population databases is significantly higher than current understanding of APDS

Study concludes that APDS may be up to 100x more prevalent than previously estimated with broader clinical features

Population-based studies planned to refine the genetic prevalence and clinical manifestations of APDS using biobanks

* Over 1,400 known U.S. patients with a variant of uncertain significance, or VUS, in the PIK3CD and PIK3R1 genes implicated in APDS