Pharming Group N.V.

Canaccord Genuity

45th Annual Growth Conference

August 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.

Unique combination of commercial and pipeline assets poised to deliver strong value creation

Pharming®

Commercial

Pipeline

HAE

RUCONEST®
> $290 million TTM revenue

PIDs
with immune dysregulation

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

PID / CVID
Phase II trials

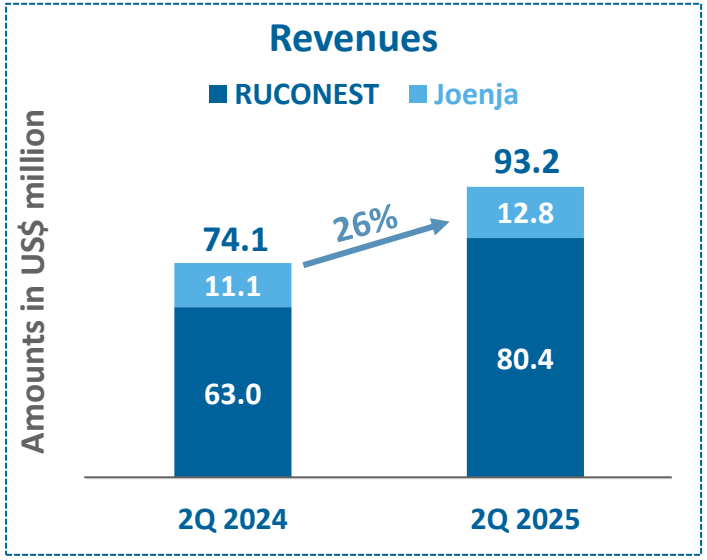
> $1B revenue potential

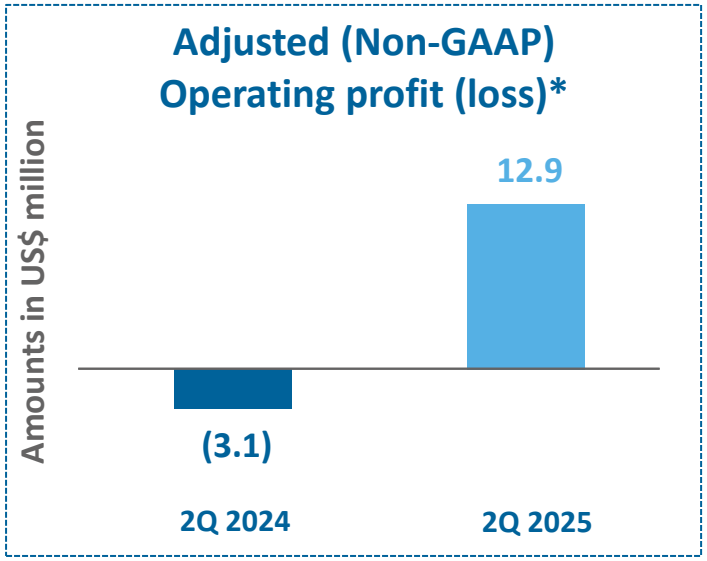
PMD

KL1333
Registrational Phase II trial

> $1B revenue potential

Strong second quarter 2025 performance





- Total revenues up 26%
- Meaningful operating profit and cash generated from operations
- Continued double-digit RUCONEST® revenue growth
- Double-digit Joenja® revenue growth with accelerating patient uptake
- Raised 2025 revenue guidance to US$335-350 million

* Adjusted operating profit for 2Q 2025 excludes US$2.1 million of non-recurring Abliva acquisition-related expenses.

Ongoing regulatory progress and pipeline execution

APDS

Japan NDA filed for adult and pediatric patients 4 years of age and older (June)

FDA filing for pediatric label expansion for children aged 4 to 11 years (3Q)

PIDs
with immune dysregulation

Genetic PID/CVID Phase II POC trials on track for 2026 read-outs

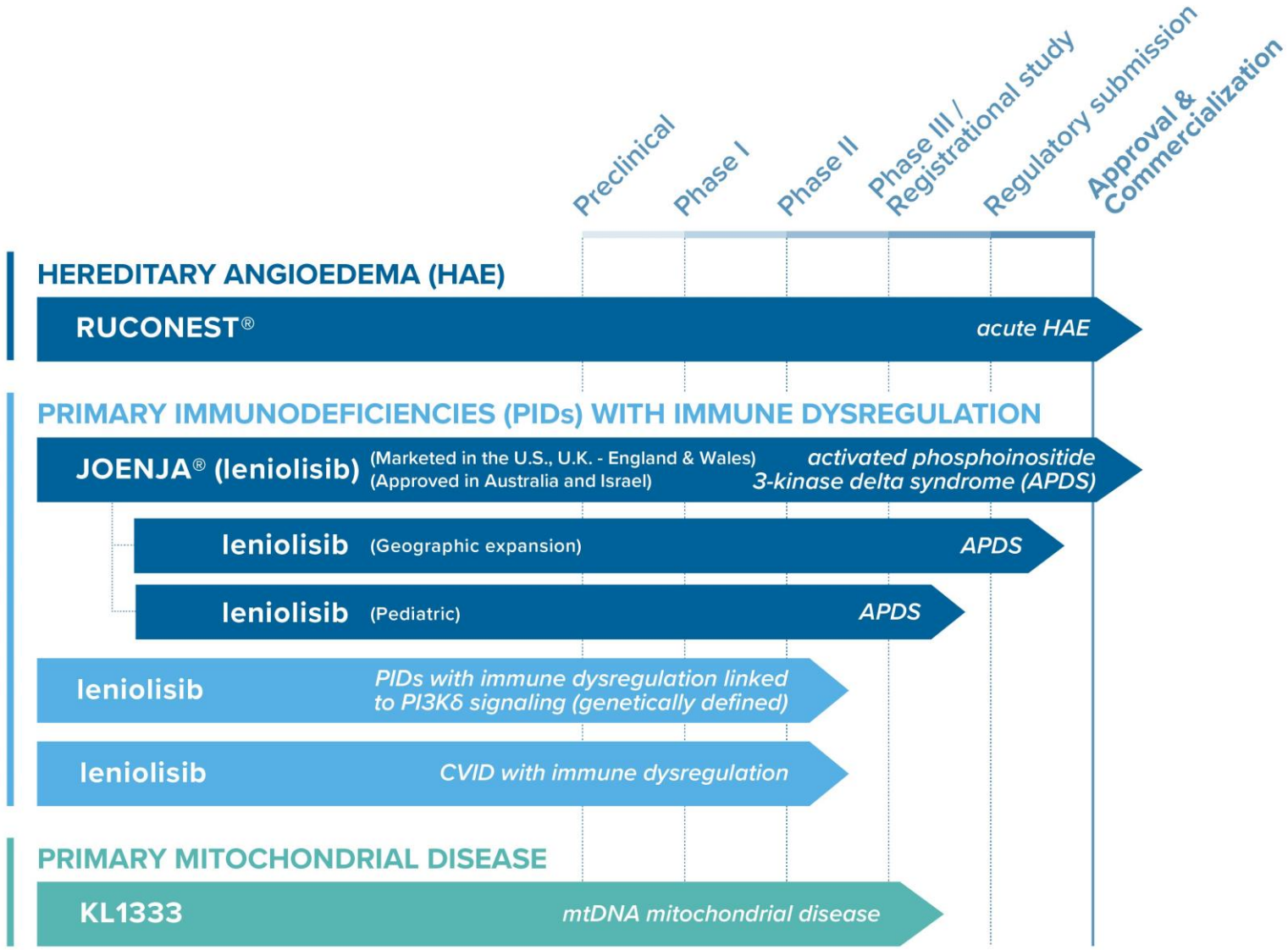
PMD

KL1333 pivotal trial – new sites activated, first patients dosed, on track for 2027 read-out

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

Diverse rare disease portfolio and pipeline



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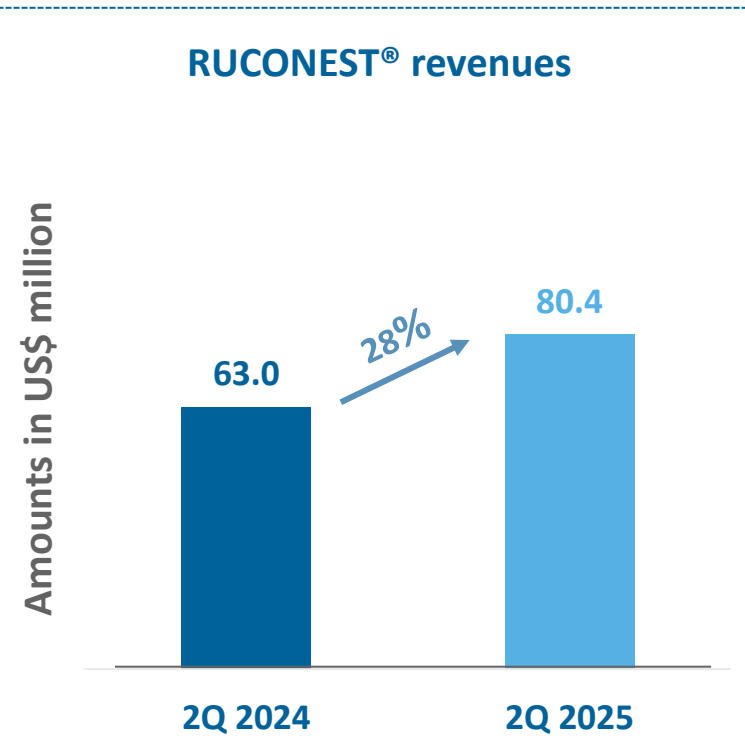
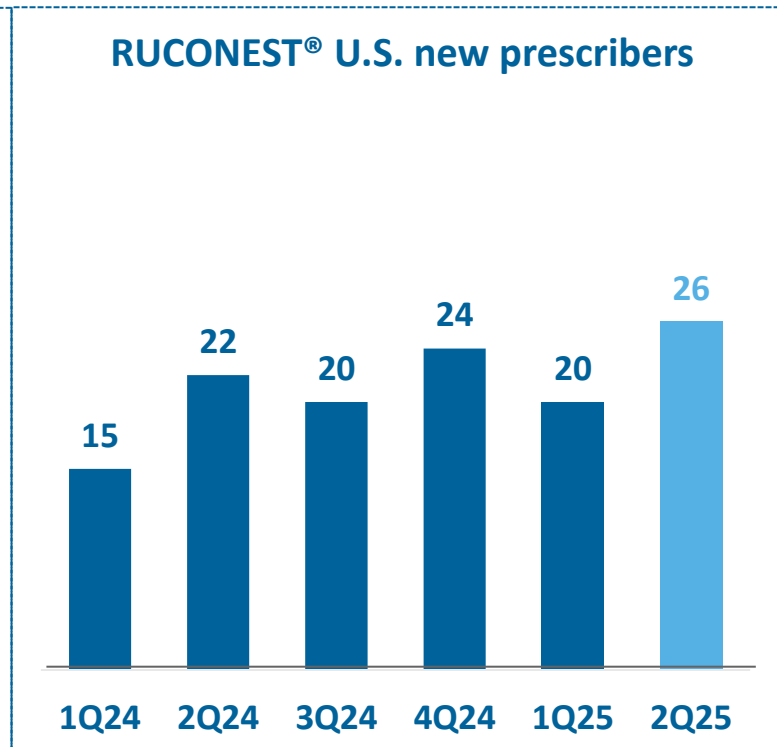
RUCONEST® for HAE

RUCONEST® strong growth continues in acute HAE market





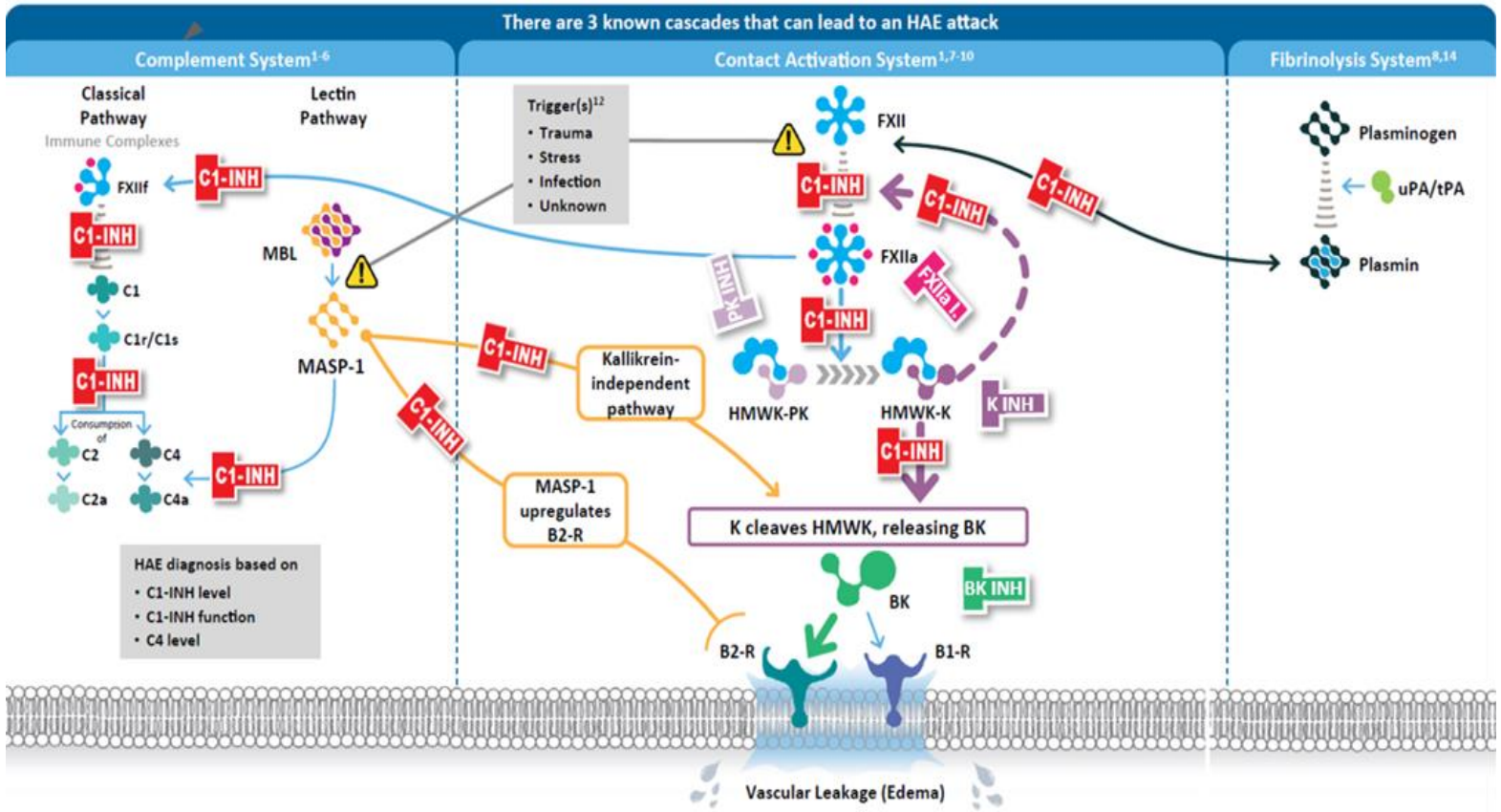
- **Strong U.S. in-market demand in 2Q 2025**
  - Continuing to add prescribers and patients
  - New patient enrollments remain high (~90)
- **Continued robust U.S. volume growth**
  - +27% in 2Q25
  - +31% in 1H25

RUCONEST® (rhC1INH)
Targets the root cause of HAE across all pathways

Pharming®

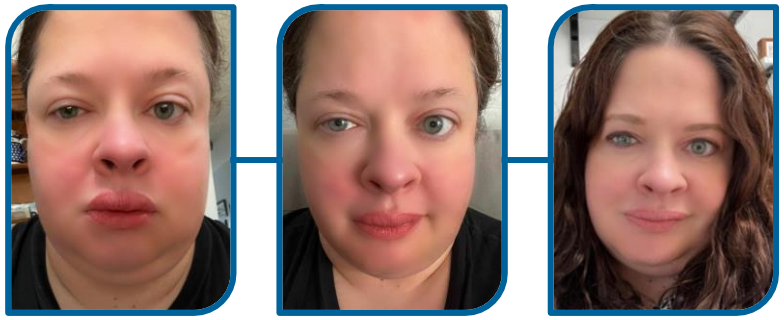
Only recombinant treatment that targets the root cause of HAE by replacing C1-INH

Only recombinant treatment that acts at multiple points in the cascades leading to HAE attacks



RUCONEST® unique value proposition and positioning

- Type 1, Type 2, and Normal C1-INH HAE patients rely on RUCONEST
- 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.

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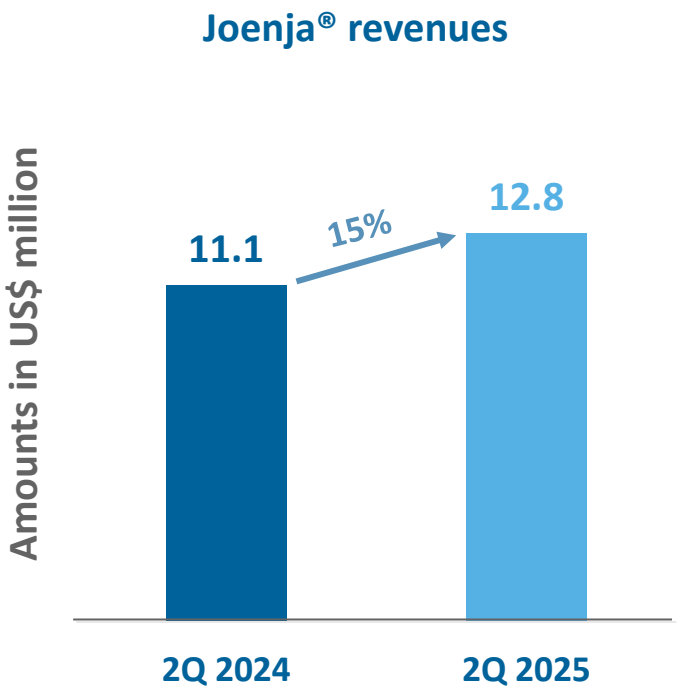
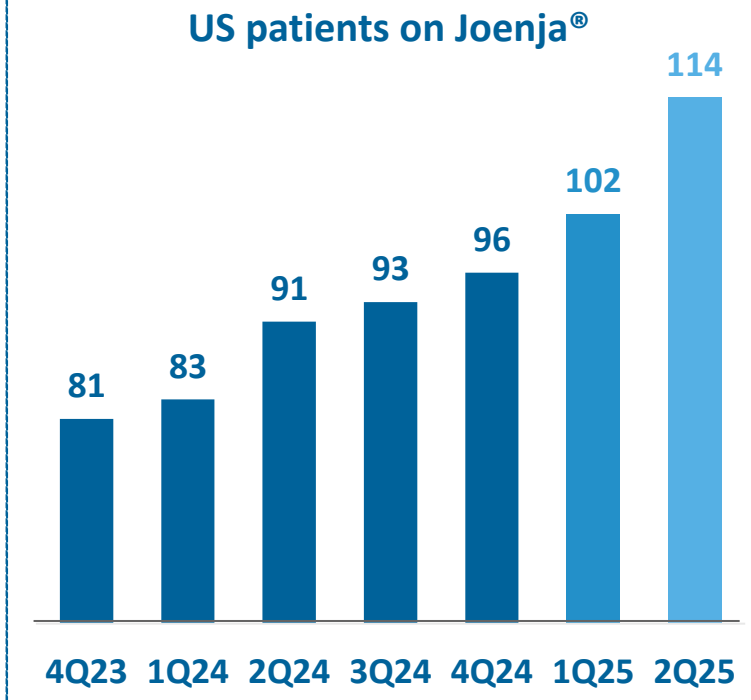
Joenja® (leniolisib)
APDS & PID indications

Joenja® acceleration in patient growth in 12y+ APDS

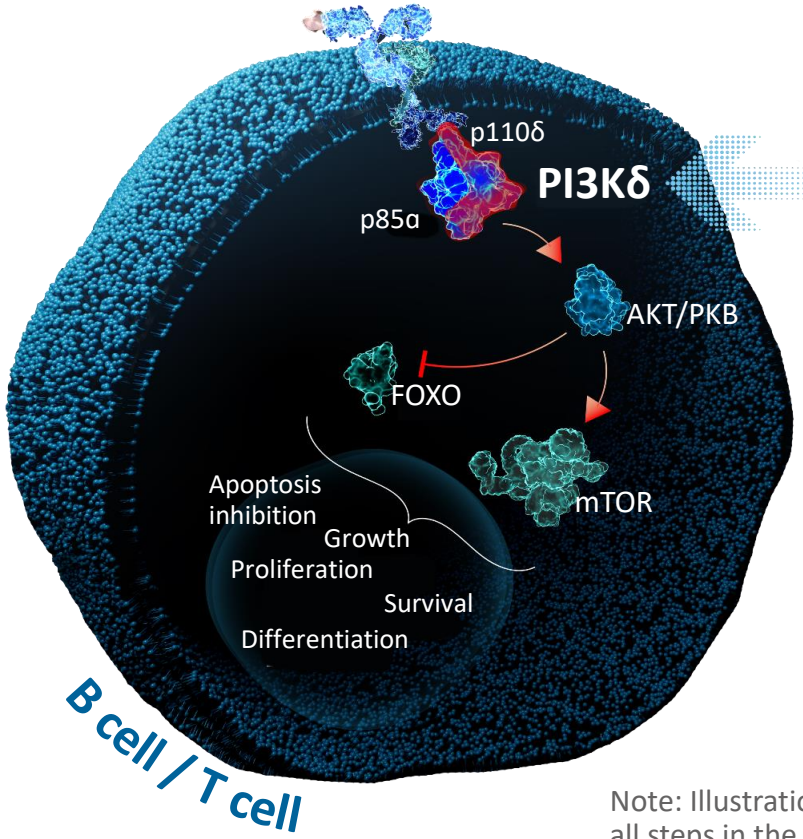




- **Acceleration in APDS patients on therapy**
  - 114 U.S. patients (+25% vs 2Q24)
  - 1H25 increase exceeded total for 2024
- **Launched in the U.K. in April**
- **Additional 185 APDS patients globally in access programs and clinical studies**

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.

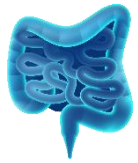
Immune imbalance leads to diverse signs and symptoms[1,4-6]

Severe, recurrent, persistent infections

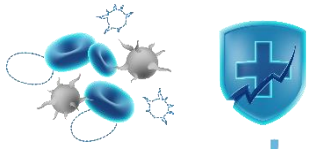
- Sinopulmonary
- Herpesvirus (especially EBV and CMV)

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

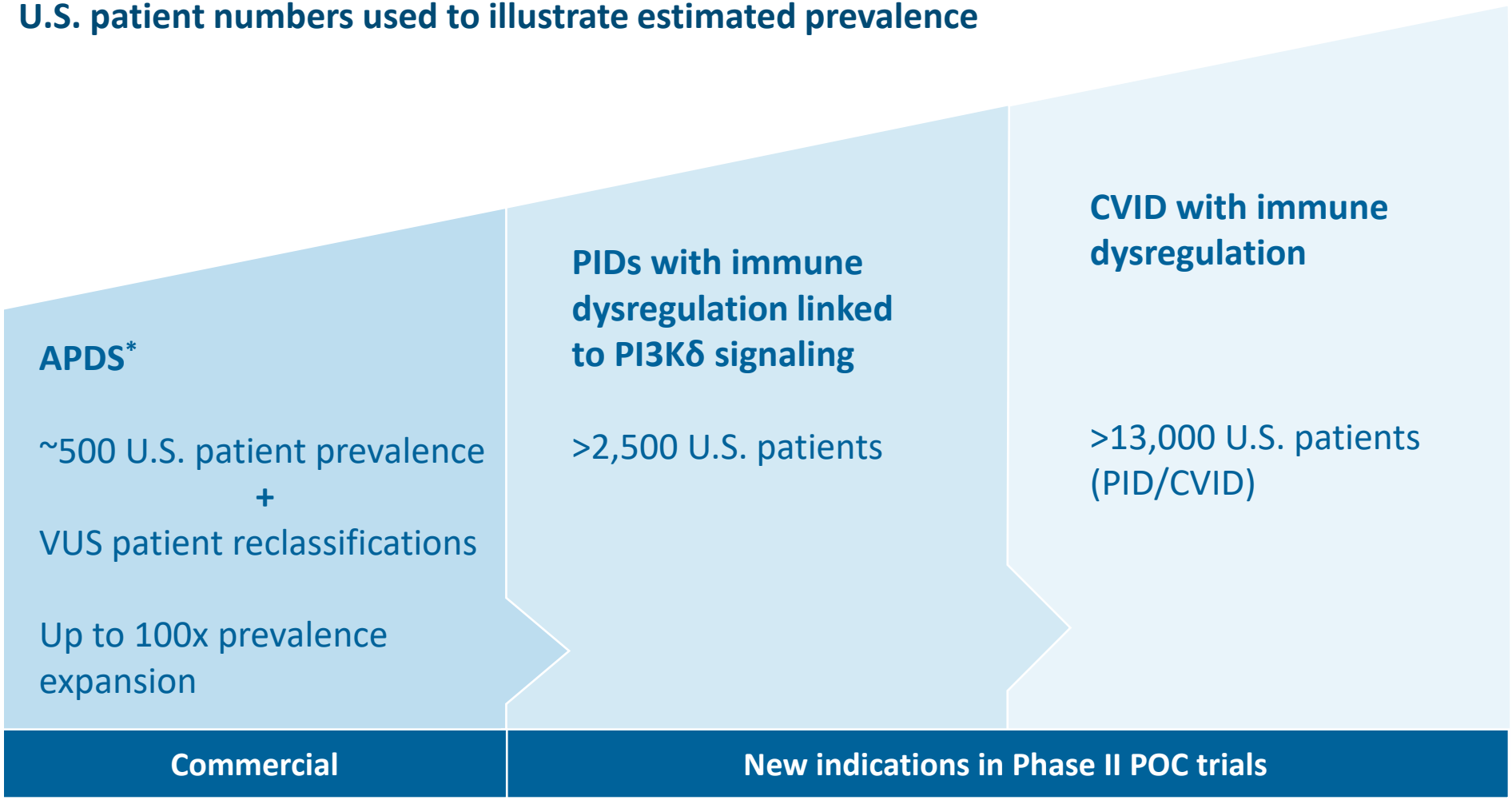
24-year-old male with APDS whose progress was followed in the Joenja® open-label extension study for 6 years

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

U.S. patient numbers used to illustrate estimated prevalence



*Initial estimate of APDS prevalence is ~1.5 patients / million. 257 patients, approximately 25% of whom are pediatric, currently identified in the U.S. out of ~500 total. 971 patients, approximately 33% of whom are pediatric, currently identified globally. (Data as of June 30, 2025)

Joenja® near-term growth catalysts – APDS

Reclassification of VUS* patients *2H25*

- >1400 patients in the US with VUS results
- June 2025 publication in *Cell* supports functional classification of >100 variants
- 20% patients could ultimately be diagnosed with APDS

Pediatric label expansion *1H26*

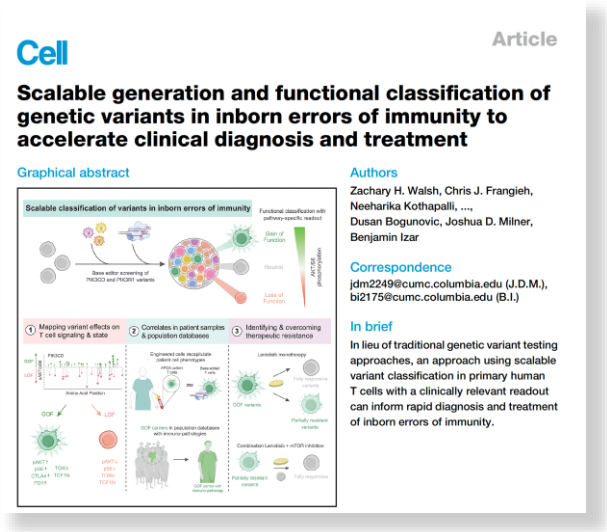
- 4-11 years pediatric filing in the US (3Q25)
- Approval expected in 1H26
- > 50 US pediatric patients, many already on drug

Geographic Expansion *ongoing*

- Launched and reimbursed in the UK
- Japan NDA filing for ages 4+ in June 2025
- Japan, EU and Canada approvals expected in 2026
- 150 APDS patients in access programs and clinical studies

*Variant of Uncertain Significance (VUS): Inconclusive results due to limited data on variant pathogenicity

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

Authors

Zachary H. Walsh, Chris J. Frangieh, Neeharika Kothapalli, ..., Dusan Bogunovic, Joshua D. Milner, Benjamin Izar

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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.

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

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

Patient Population

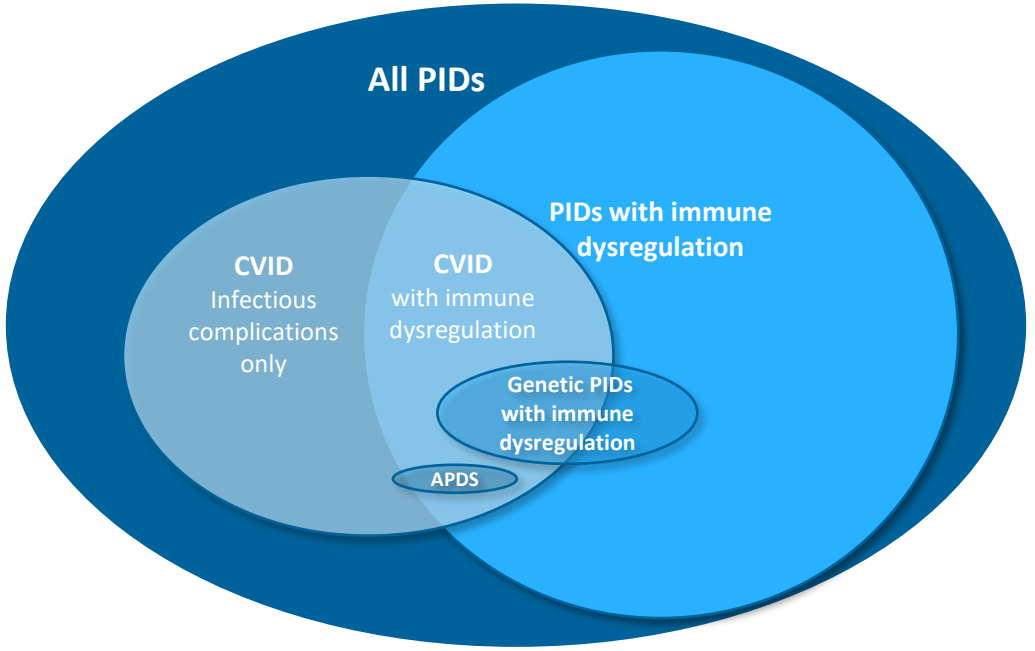
- PID patients with clinical manifestations similar to APDS
- Significant unmet clinical need, no approved therapies
- Prevalence 5-26x APDS

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]



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

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KL1333 for mtDNA Mitochondrial Disease

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

KL1333 targets underlying pathology

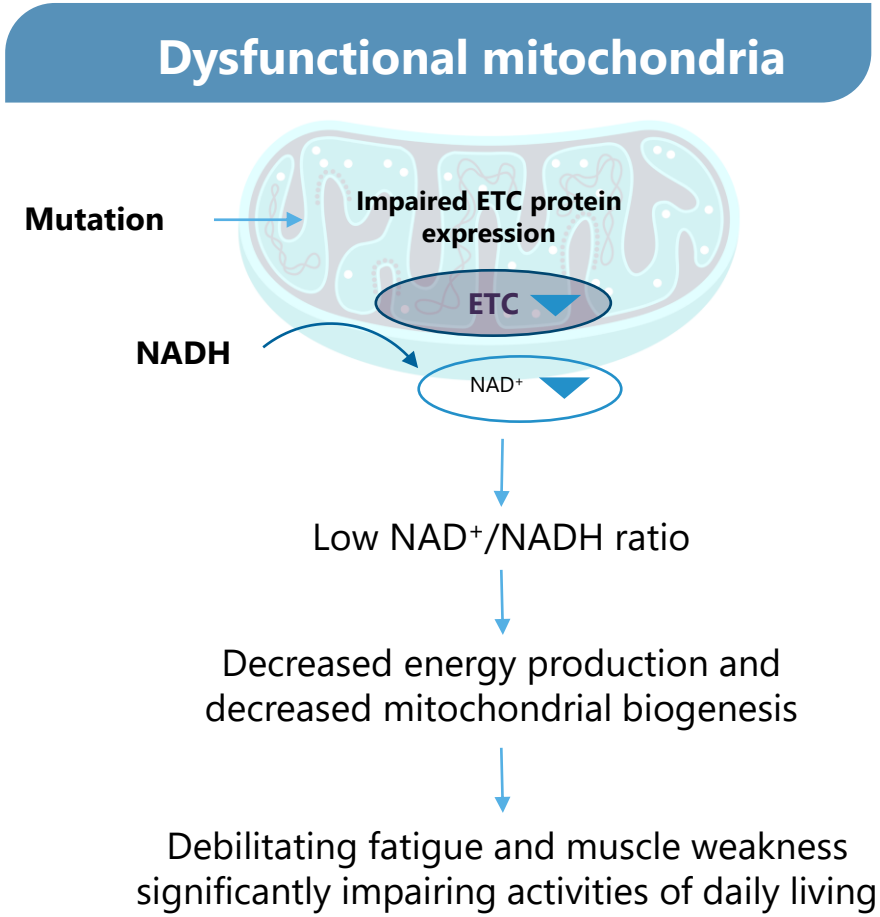
- Normalizes NAD+/NADH ratio and mitochondrial function, with evidence from in vitro data, animal models, and in patients treated with KL1333

Significant patient population

- >30,000 diagnosed patients
- Majority of patients treated in centers of excellence

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 – 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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Outlook

2025 financial guidance and long-term capital outlook

Revenue and operating expenses:

	FY 2025 Guidance	Notes
Total Revenues	**US$335 - 350 million**	13 - 18% growth
Operating Expenses	**US$304 - 308 million**	Assumes constant currency, Includes $10.2 million non-recurring Abliva-related transaction and integration expenses

RUCONEST® well positioned to provide continued strong cash flows

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

Building a leading global rare disease biopharma company

Strong start to 2025

Strong RUCONEST® growth and acceleration of Joenja® patient uptake.

2Q25 revenues +26%
1H25 revenues +33%

Achieved operating profit

Updated 2025 guidance

Raised revenue guidance to US$335 - 350M

High value pipeline

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

KL1333 for mtDNA mitochondrial disease

Significant catalysts

Joenja® for APDS: VUSs, pediatric label, geo expansion (2025-26)

Higher APDS prevalence

Leniolisib PIDs/CVID PhII readouts (2026)

KL1333 pivotal study readout (2027)

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Appendix

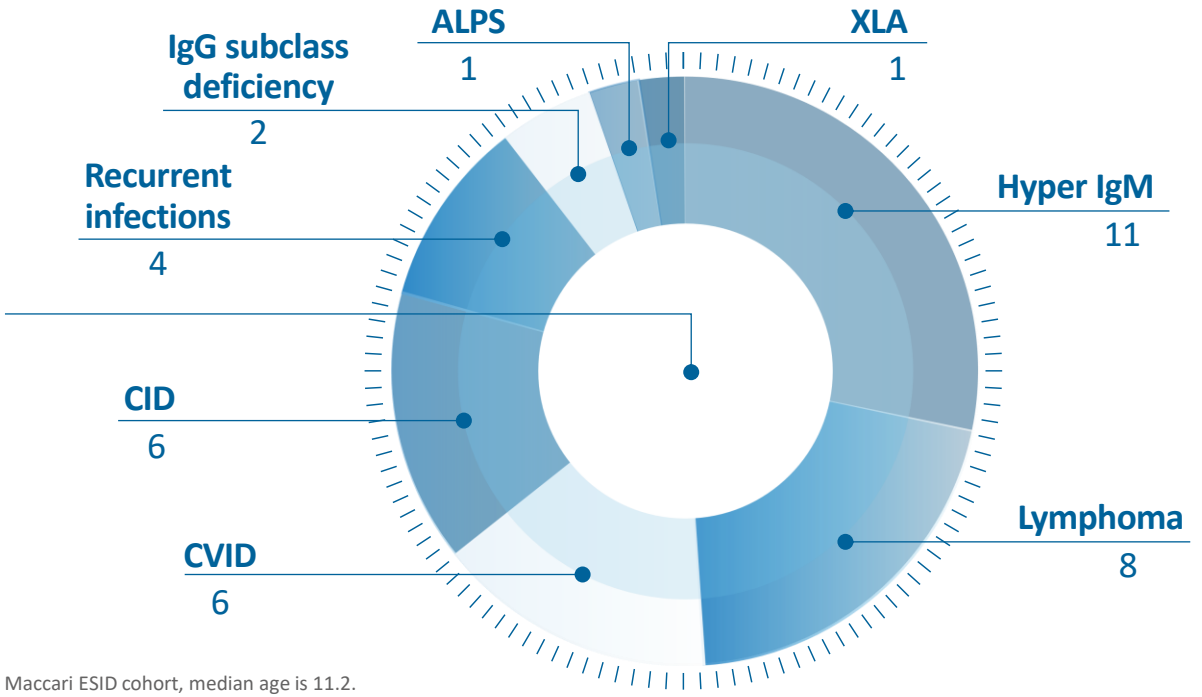
APDS: Heterogeneous, evolving symptomology can often lead to missed diagnoses

Timeline of the most common pathologies* seen in APDS[1-4]

Median age at diagnosis:
12 years (7-year median diagnosis delay)

<1 year (range, 1 month-10 years)	3 years (range, 1-6 years)	5 years (range, 1-18 years)	10.5 years (range, 6-15 years)	11.2 years† (range, 18 months-39 years)	18 years (range, 1.5-40 years)
Sinopulmonary infections	Benign lymphoproliferation	Enteropathy	Autoimmunity	Bronchiectasis	Malignancy
			Cytopenias, arthritis, or other dysregulation‡		

APDS has often been diagnosed as another PI or condition, causing delays in diagnosis[1]

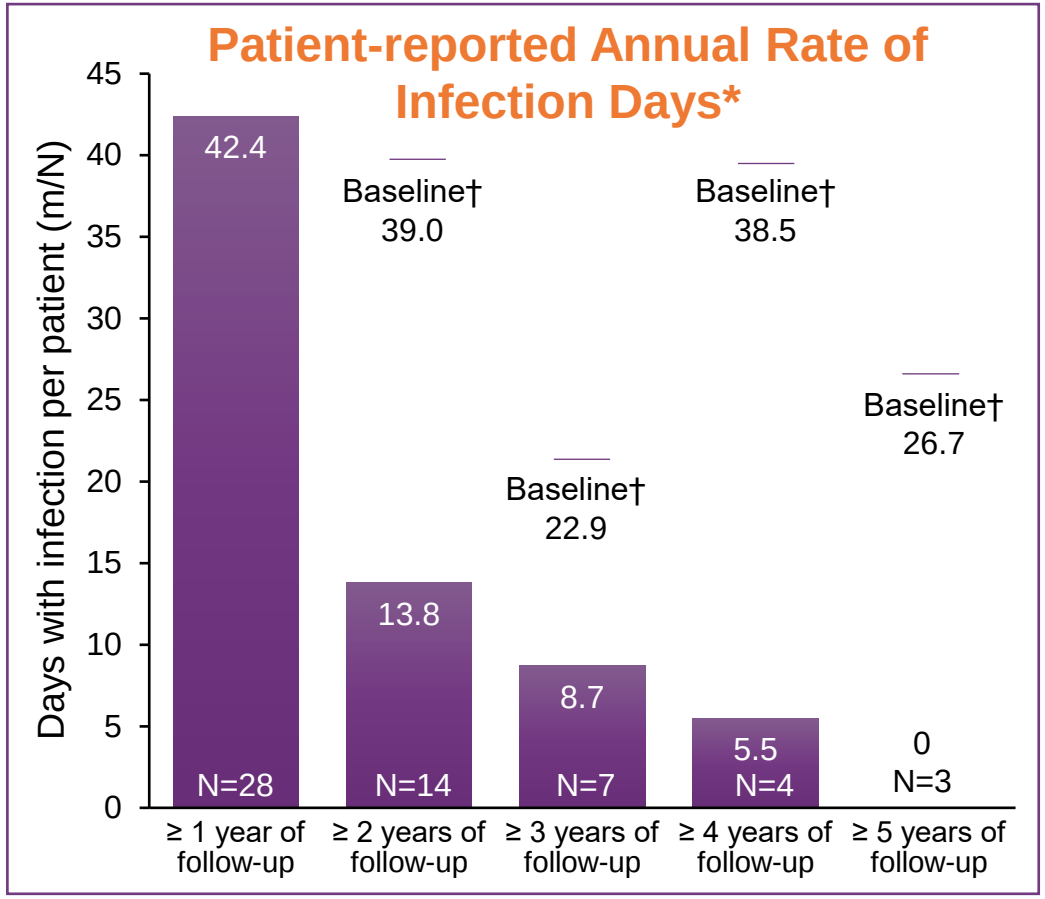


Improved identification of symptoms, increased genetic testing, and earlier diagnosis are needed

*Pathologies can occur at any time.
†In Elkaim APDS2 cohort, median age of bronchiectasis is 13; in Maccari ESID cohort, median age is 11.2.
‡No median ages are available for these manifestations.
ALPS, autoimmune lymphoproliferative syndrome; CID, combined immunodeficiency; CVID, common variable immune deficiency; ESID, European Society for Immunodeficiencies; HIGM, hyper immunoglobulin M syndrome; IgG, immunoglobulin G; PI3Kδ, phosphoinositide 3-kinase delta; XLA, X-linked agammaglobulinemia.
1. Jamee M, et al. *Clin Rev Allergy Immunol*. 2020;59(3):323-333. 2. Maccari ME, et al. *Front Immunol*. 2018;9:543. 3. Elkaim E, et al. *J Allergy Clin Immunol*. 2016;138(1):210-218.e9. 4. Coulter TI, et al. *J Allergy Clin Immunol*. 2017;139(2):597-606.

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

- 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

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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.

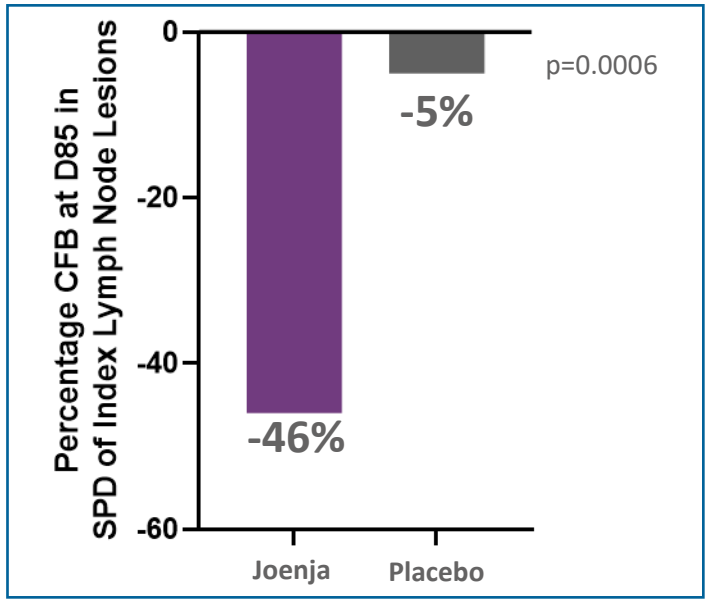
Joenja® addresses the underlying cause of APDS to help restore immune balance – Phase 3 co-primary endpoints

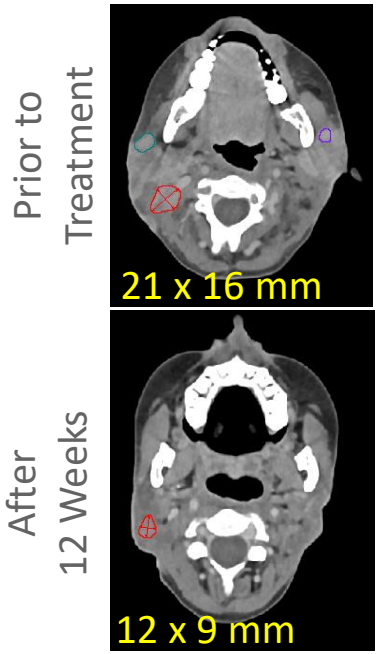
At 12 weeks Joenja® decreased lymphadenopathy and increased naïve B cells

Immune Dysregulation

Change from baseline in index nodes*

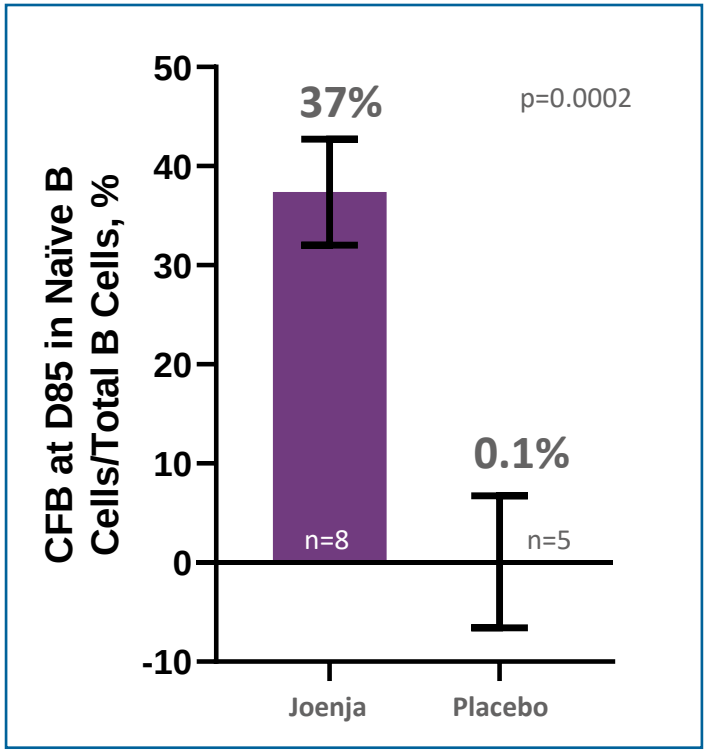
Log_{10}-transformed SPD of index lesions	Joenja (n=18)	Placebo (n=8)
Baseline mean (SD)	3.03 (0.42)	3.05 (0.39)
Change from baseline, LS mean (SE)	-0.27 (0.04)	-0.02 (0.05)
Difference vs placebo (95% CI)		-0.25 (-0.38, -0.12)





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

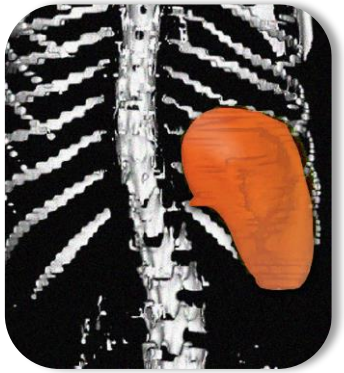
at week 12

27%

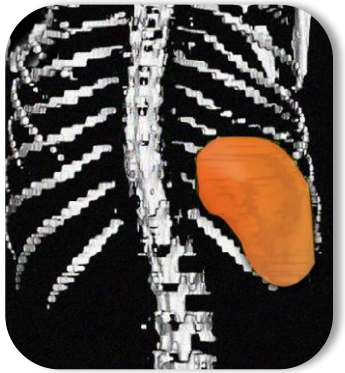
reduction in 3D spleen volume*

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

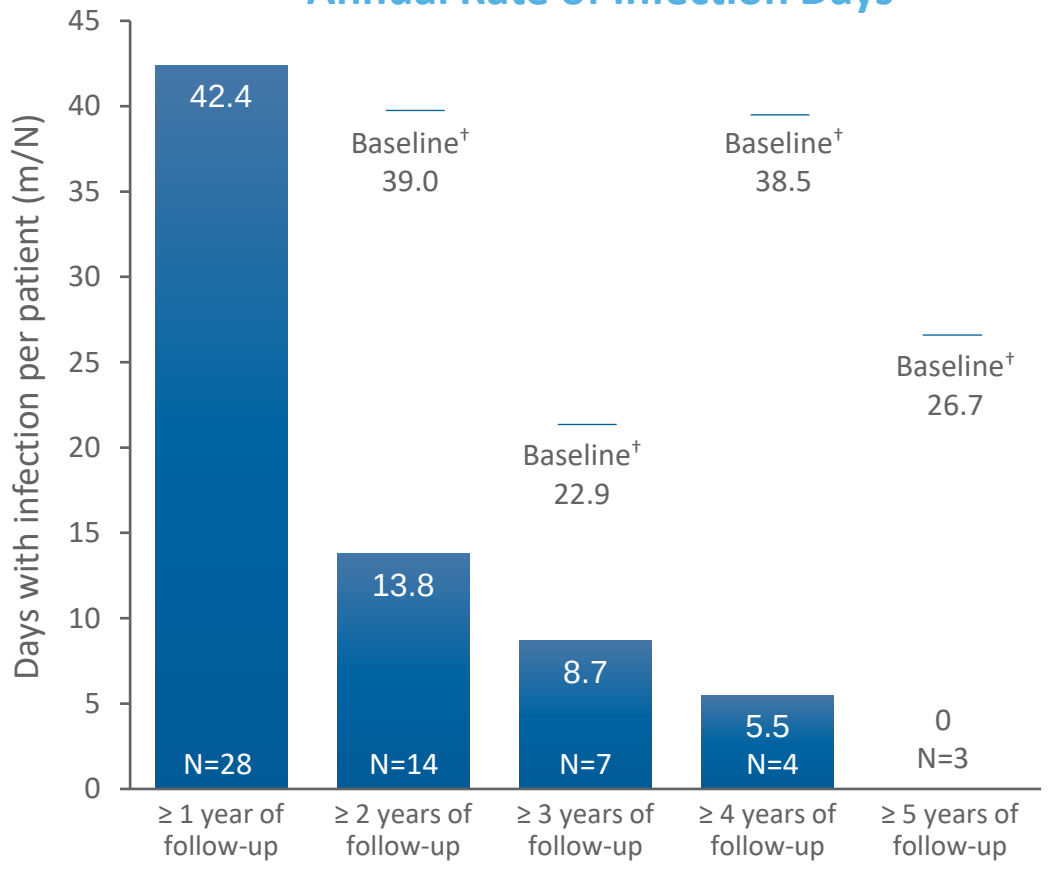
Across all trials[2]

- 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

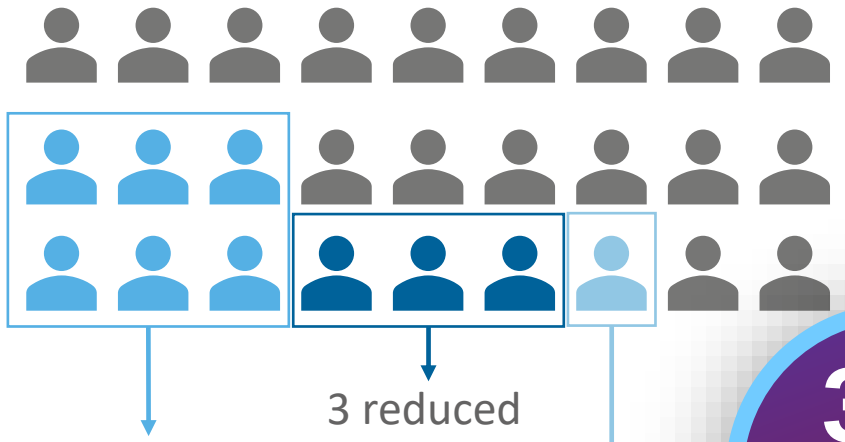
Open-label extension interim analysis of days spent with infections and IRT reduction

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 to be presented at CIS conference in May
- Regulatory filings beginning with the U.S. in second half 2025

Joenja® development status
Expanding the addressable patient population

Geographic expansion (APDS)

Europe – review extended to Jan. 2026
Single outstanding CMC request
Positive clinical benefit and safety concluded

U.K. – Marketing authorization 2024
Reimbursement: NICE positive final guidance and England / Wales launch April 2025

AUS approval, CAN regulatory review
Australia - approved March 2025
Canada decision in 2026*

Japan regulatory review
PMDA filing for adults/4+ pediatrics June 2025

Other country regulatory approvals /filings Access Programs

Pediatric expansion (APDS)

4 to 11 years – Positive data presented at CIS conference May 2025
U.S. FDA filing July 2025

1 to 6 years – Patient enrolment completed in April 2025

Indication expansion (additional PIDs)

PIDs with immune dysregulation linked to PI3Kδ signaling
Phase II trial ongoing

CVID with immune dysregulation
Phase II trial ongoing

* Anticipate regulatory action in 2026 for Canada

Leniolisib for PIDs with immune dysregulation – Phase II studies

Genetically defined PIDs with immune dysregulation linked to PI3Kδ

- Single arm, open-label, dose range-finding (N=12)
- Patients with PIDs linked to PI3Kδ signaling, e.g. ALPS-FAS[1], CTLA4 haploinsufficiency[2], NFKB1 haploinsufficiency[3], PTEN deficiency[4]
- Primary: Safety & Tolerability
- Secondary/Exploratory: PK/PD, efficacy measures
- 10/30/70 mg BID: 4/4/12 wks treatment, respectively
- Lead investigator: Gulbu Uzel, M.D., Senior Research Physician, Co-Investigator: V. Koneti Rao, M.D., FRCPA, Senior Research Physician, Primary Immune Deficiency Clinic (ALPS Clinic) (NIH)

Common variable immunodeficiency (CVID) with immune dysregulation

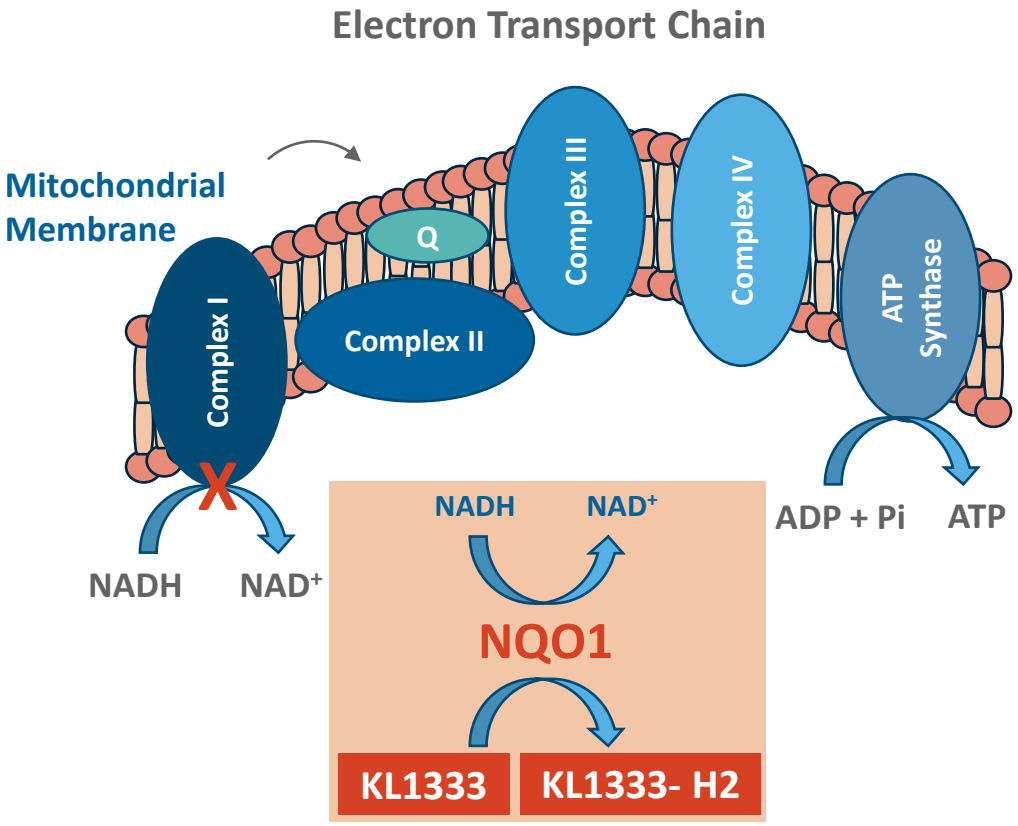
- Single arm, open-label, dose range-finding (N=20)
- Patients with a CVID diagnosis, evidence of lymphoproliferation, and at least one additional clinical manifestation of immune dysregulation
- Primary: Safety & Tolerability
- Secondary/Exploratory: PK/PD, efficacy measures
- 10/30/70 mg BID: 4/4/16 wks treatment, respectively
- Multi-center study (US, UK, EU)
- Lead investigator: Jocelyn Farmer, MD, PhD, Director of the Clinical Immunodeficiency Program (Beth Israel Lahey Health)

1. Bride K & Teachey D. F1000Res. 2017;6:1928. ; Rao VK & Oliveria JB. Blood 2011; 118(22):5741-51.
2. Kuehn HS, et al. Science 2014; 345:1623-27. ; Schwab C, et al. J Allergy Clin Immunol. 2018;142(6):1932-1946.
3. Lorenzini T, et al. J Allergy Clin Immunol. 2020:146:901-11.
4. Eissing M, et al. Transl Oncol. 2019;12(2):361-367. ; Tsujita, et al. J Allergy Clin Immunol. 2016;138(6):1872-80.

KL1333 corrects the underlying pathophysiology in PMD

KL1333 normalizes conversation of NADH to NAD+ via NQO1

Normalizes the NAD⁺/NADH Ratio



Restored Energy Metabolism

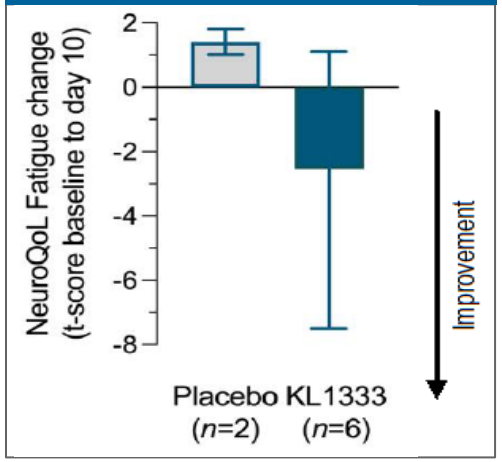
- Restored energy regulation and improved ETC function
- Stimulation of mitochondria biogenesis
- Overall resulting in symptom reduction and expected disease modification

KL1333: Phase 1b demonstrated significant activity vs. placebo

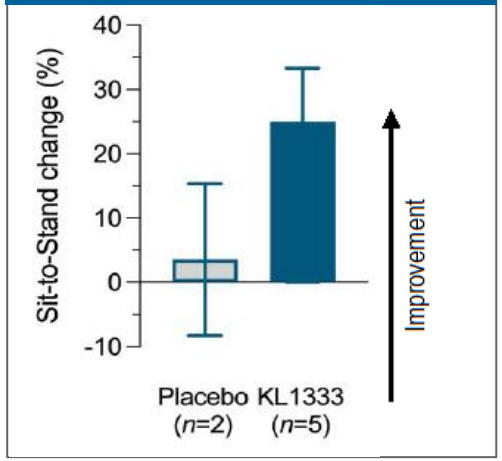
The placebo-controlled Phase 1b study demonstrated that KL1333 reduced patients' fatigue and myopathy after only 10 days, 50 mg/day

- KL1333 demonstrated efficacy in the phase 1b placebo-controlled portion with patients diagnosed with mtDNA mitochondrial disease
  - Fatigue reduction (NeuroQoL fatigue change)
  - Muscle function improvement (30 seconds sit-to-stand)
- KL1333 showed efficacy signals after 10 days using 50 mg/day
- Mitochondrial patients have increased lactate levels and increasing the concentration of KL1333 resulted in an improved lactate/pyruvate ratio, reflecting target engagement
- No serious adverse events reported

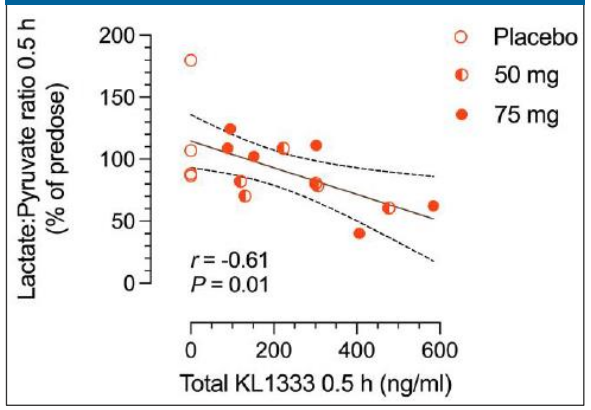
Fatigue Reduction
Changes from baseline to day 10



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.

Pivotal study design based on regulatory and patient advocacy input

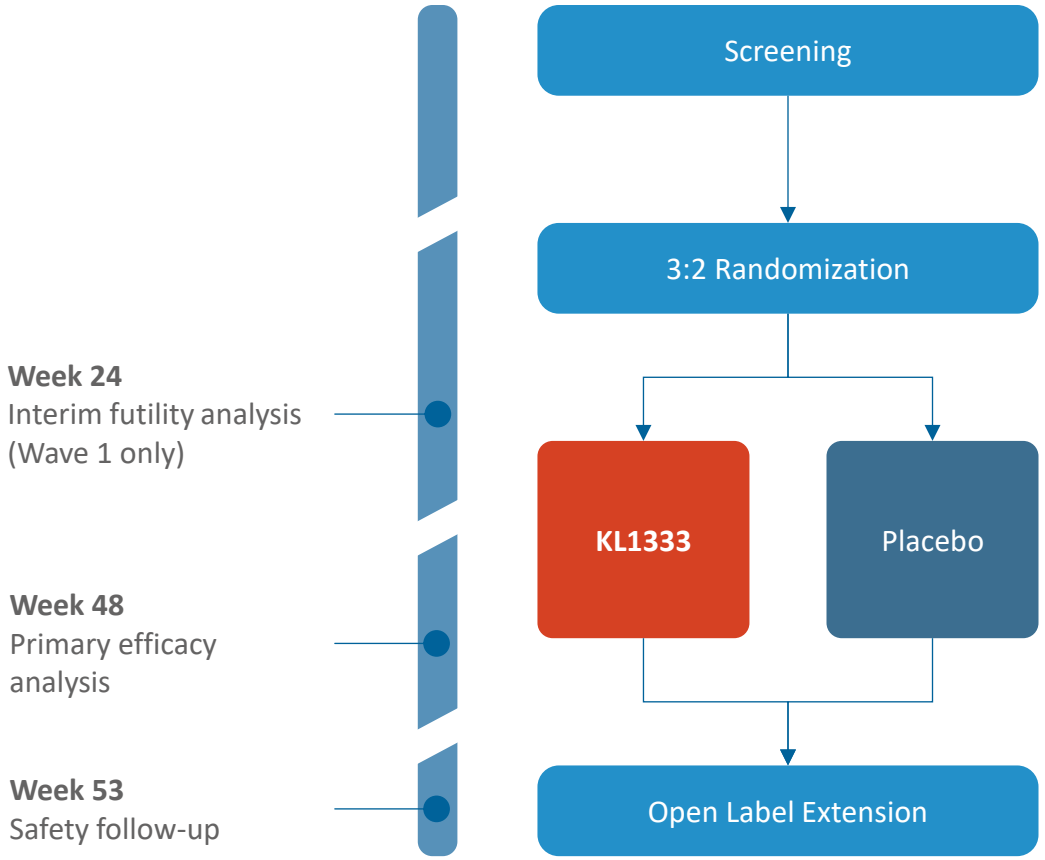
Regulatory Feedback

- Both FDA and EMA accepted study as registrational
- FDA said achieving one of the two endpoints would be sufficient for filing
- Conducted regular and detailed discussions with the FDA to facilitate alignment

Study Design

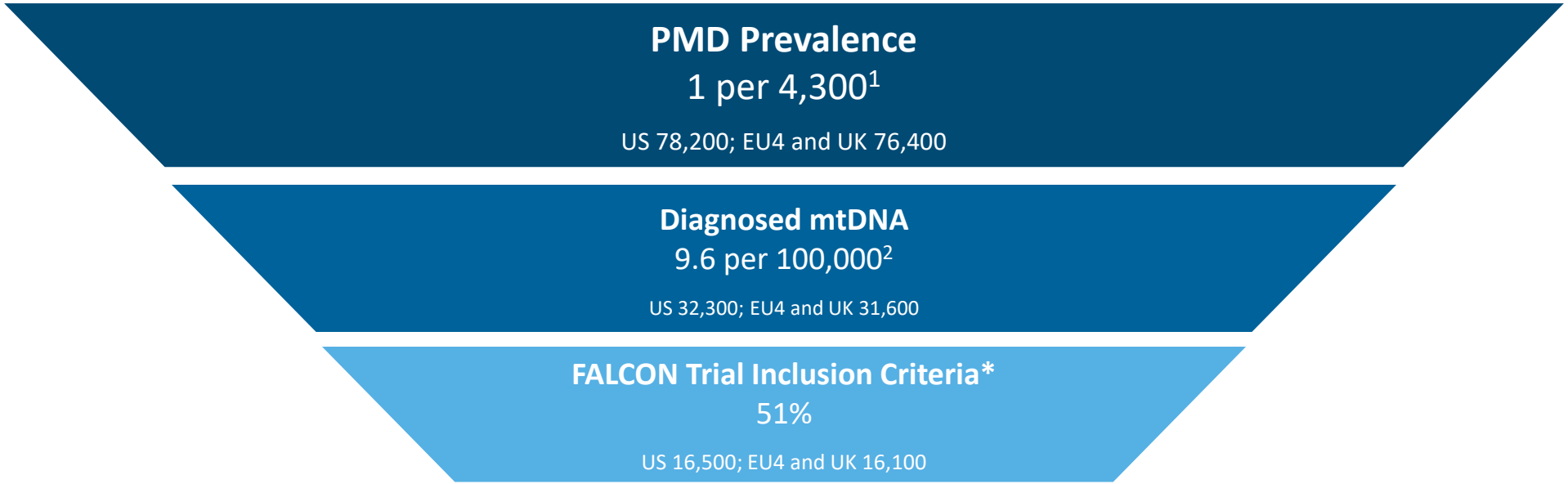
- **Methodology**
  - Randomized, double-blind, parallel-group, placebo-controlled pivotal study
- **Patients Included**
  - Adult PMD patients with mtDNA mutations* with fatigue and myopathy
- **Primary Endpoints**
  - Fatigue using the PROMIS Fatigue Mitochondrial Disease Short Form
  - Muscle weakness using the 30 second Sit-to-Stand test

Study Schematic



*Most prevalent mtDNA disorders include m.3243A>G associated MELAS-MIDD spectrum disorders, single large scale mtDNA deletion associated KSS-CPEO spectrum disorders, other multisystemic mtDNA-related disease (including MERRF)

Significant revenue opportunity for KL1333

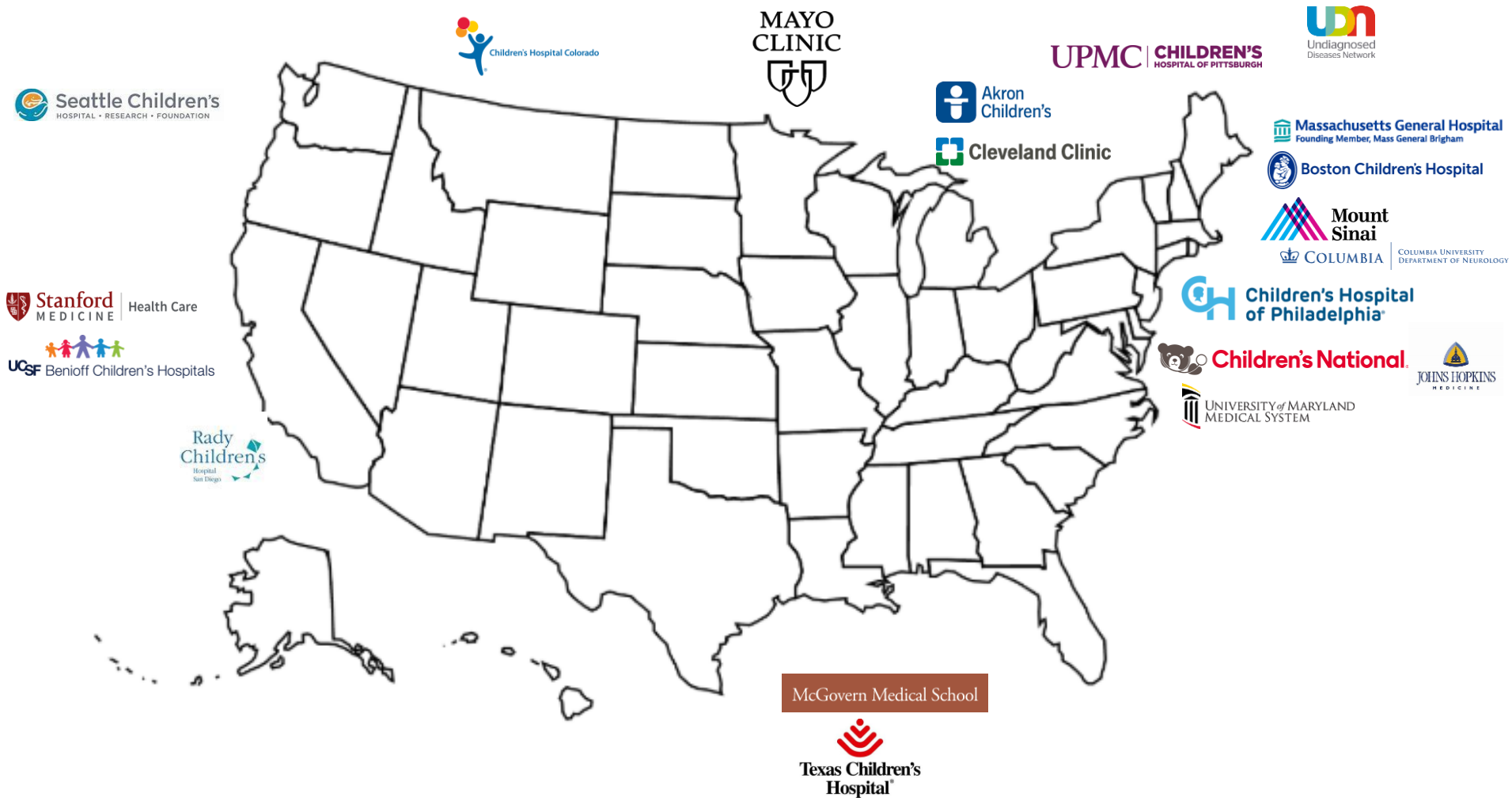


>30,000 diagnosed mtDNA mitochondrial disease patients addressable in the US, EU4 and UK

*mtDNA mutations including m.8344A>G MELAS-MIDD, MERRF, KSS-CEPO, large scale mtDNA deletions

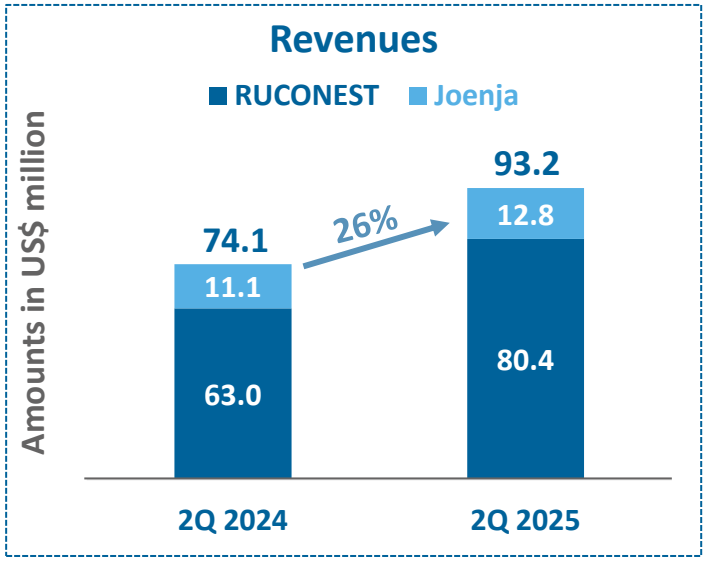
[1] Gorman, G.S. et al. Prevalence of nuclear and mitochondrial DNA mutations related to adult mitochondrial disease. Ann Neurol 2015 May;77(5):753-9.
[2] Gorman, G.S. et al. Mitochondrial Diseases. Nat. Rev. Vol 2, 1-22 (2016).

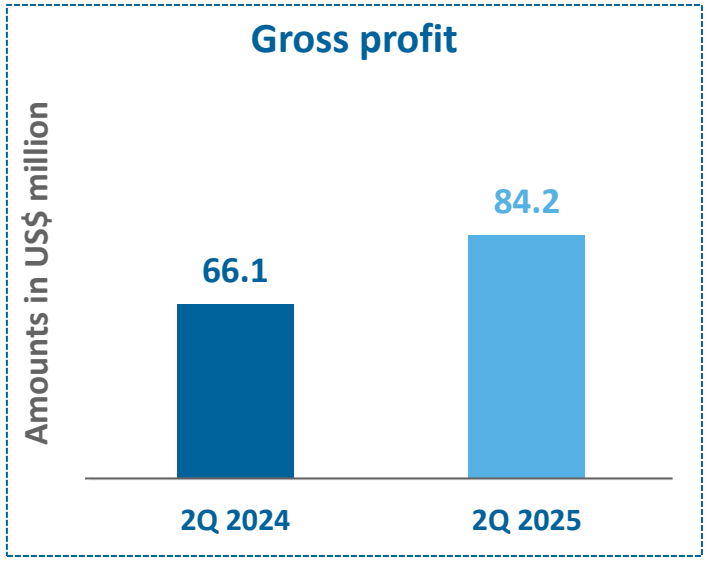
Majority of patients diagnosed and treated in US Centers of Excellence or academic institutions

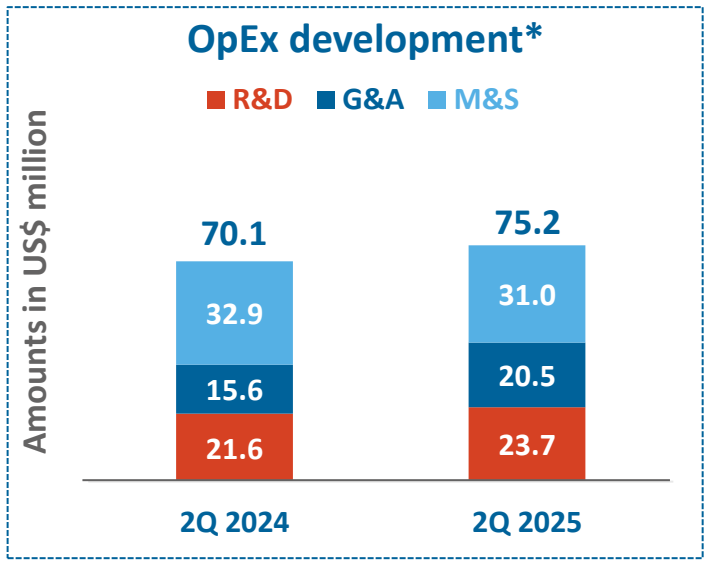


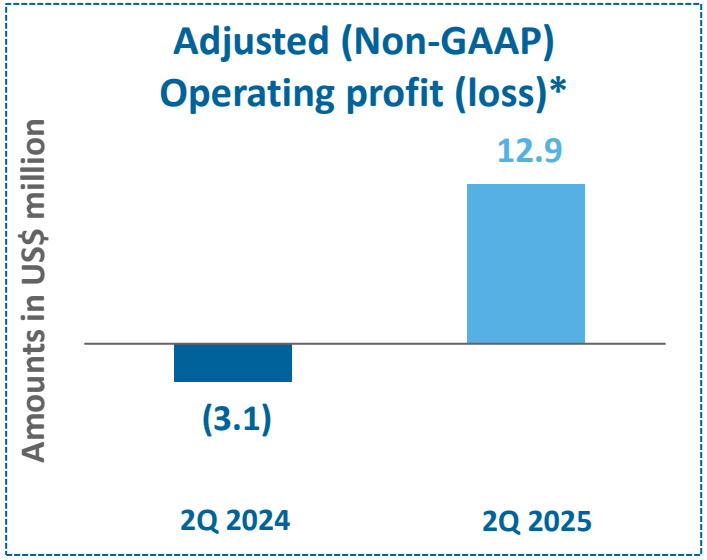
Mitochondrial Care Network – Centers: www.mitonetwork.org/centers

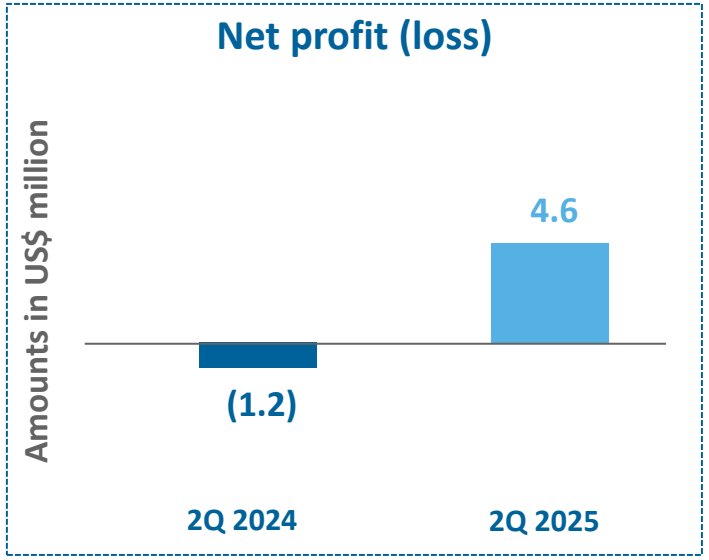
Financial highlights: 2Q 2025 vs 2Q 2024

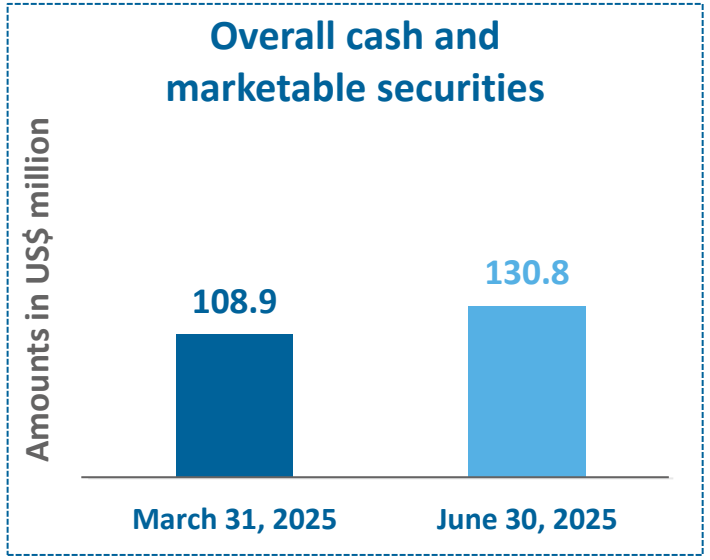






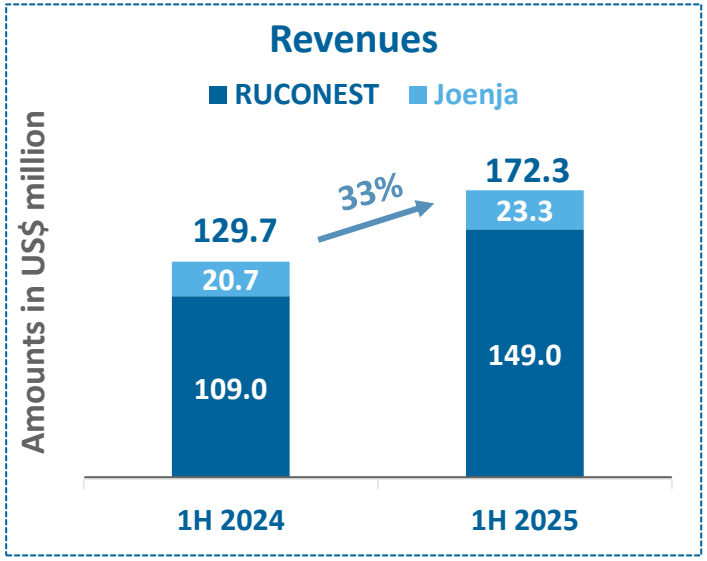


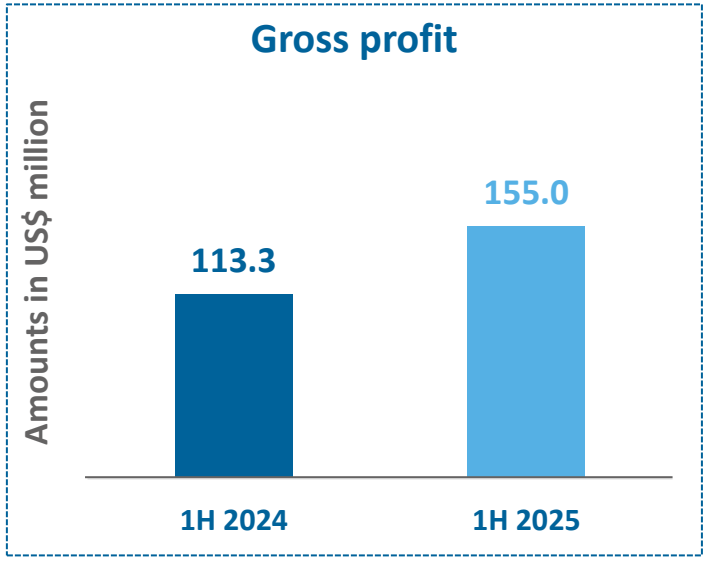


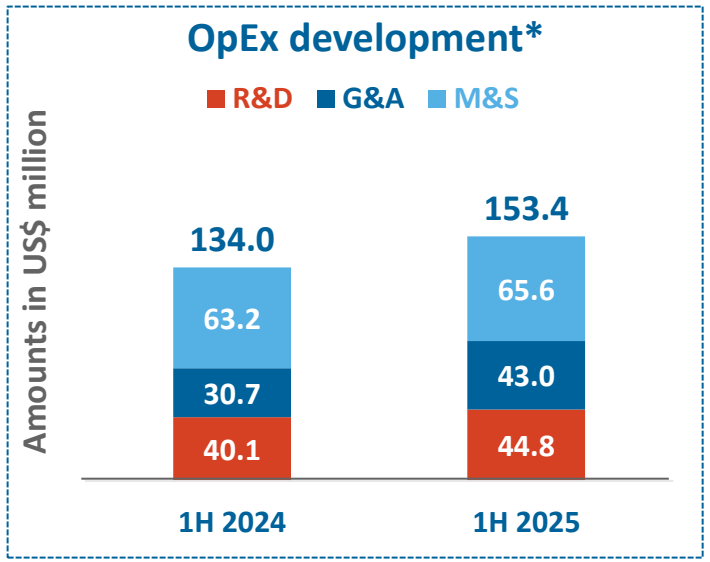


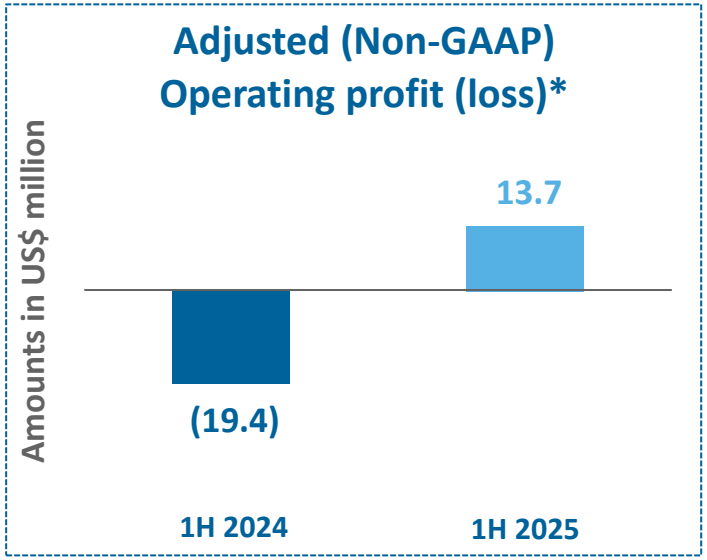
* Adjusted operating profit for 2Q 2025 excludes US$2.1 million of non-recurring Abliva acquisition-related expenses (US$1.9 million in G&A, $0.2 million in R&D).

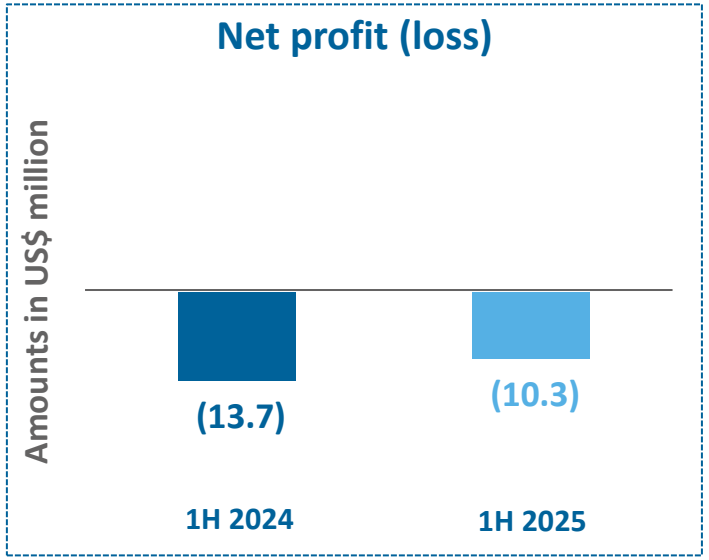
Financial highlights: 1H 2025 vs 1H 2024

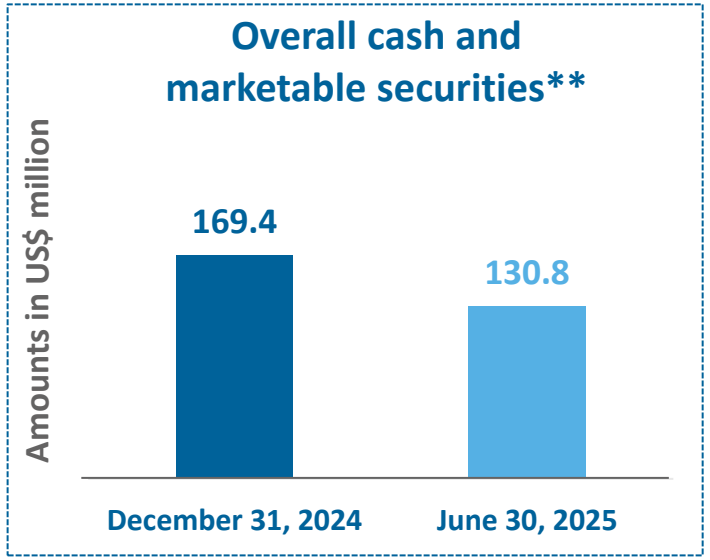








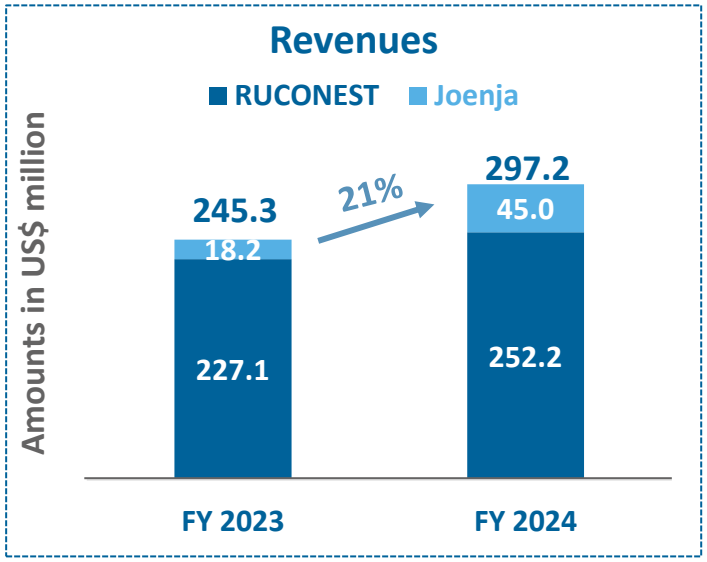


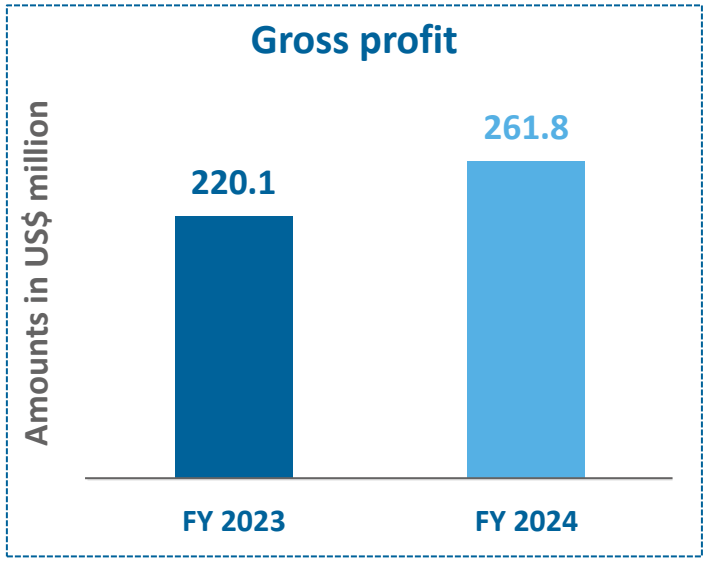


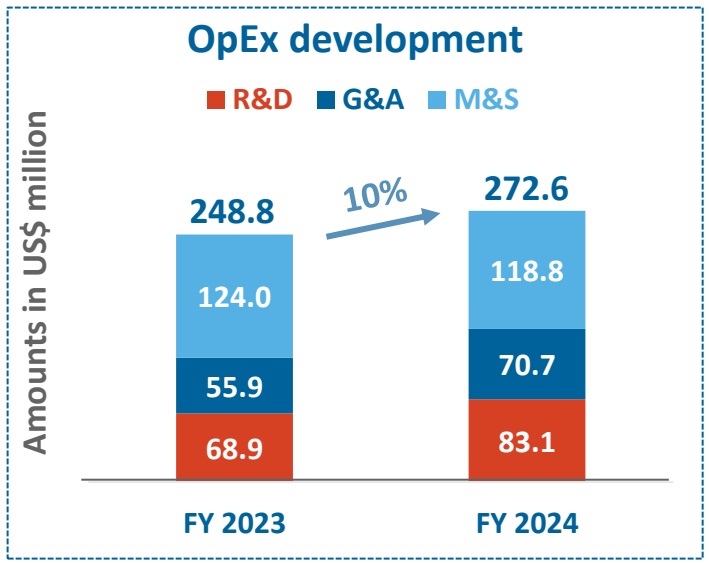
* Adjusted operating profit for 1H 2025 excludes US$9.9 million of non-recurring Abliva acquisition-related expenses (US$7.6 million in G&A, $2.3 million in R&D).

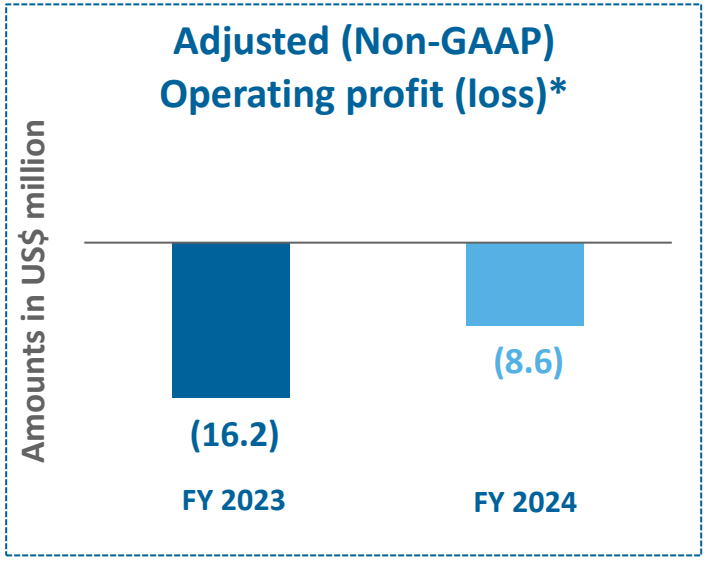
** Decrease in cash primarily driven by purchases of Abliva shares totaling US$66.1 million and non-recurring Abliva acquisition-related expenses totaling US$9.9 million.

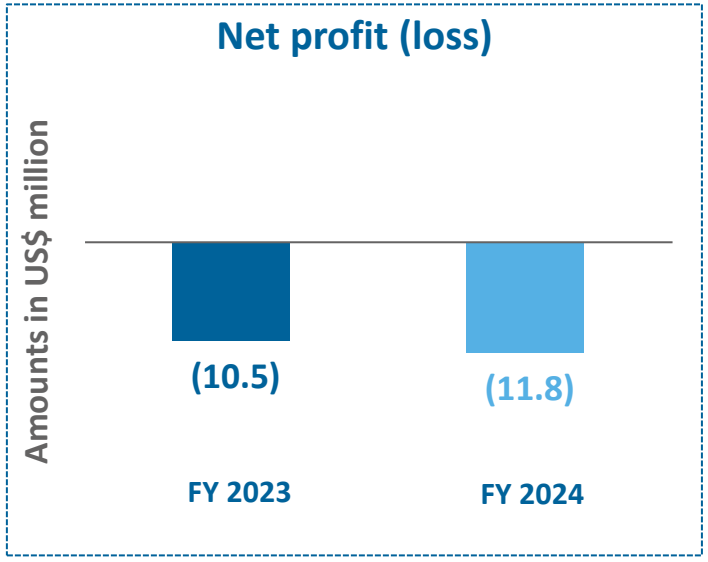
Financial highlights: FY 2024 vs FY 2023











* Operating profit (loss) for 2023 excludes milestone payments for Joenja® (US$10.5 million) and gain on sale of Priority Review Voucher to Novartis (US$21.3 million).
** US$30.4 million of the US$45.6 million decrease in overall cash and marketable securities is due to convertible bond refinancing.