



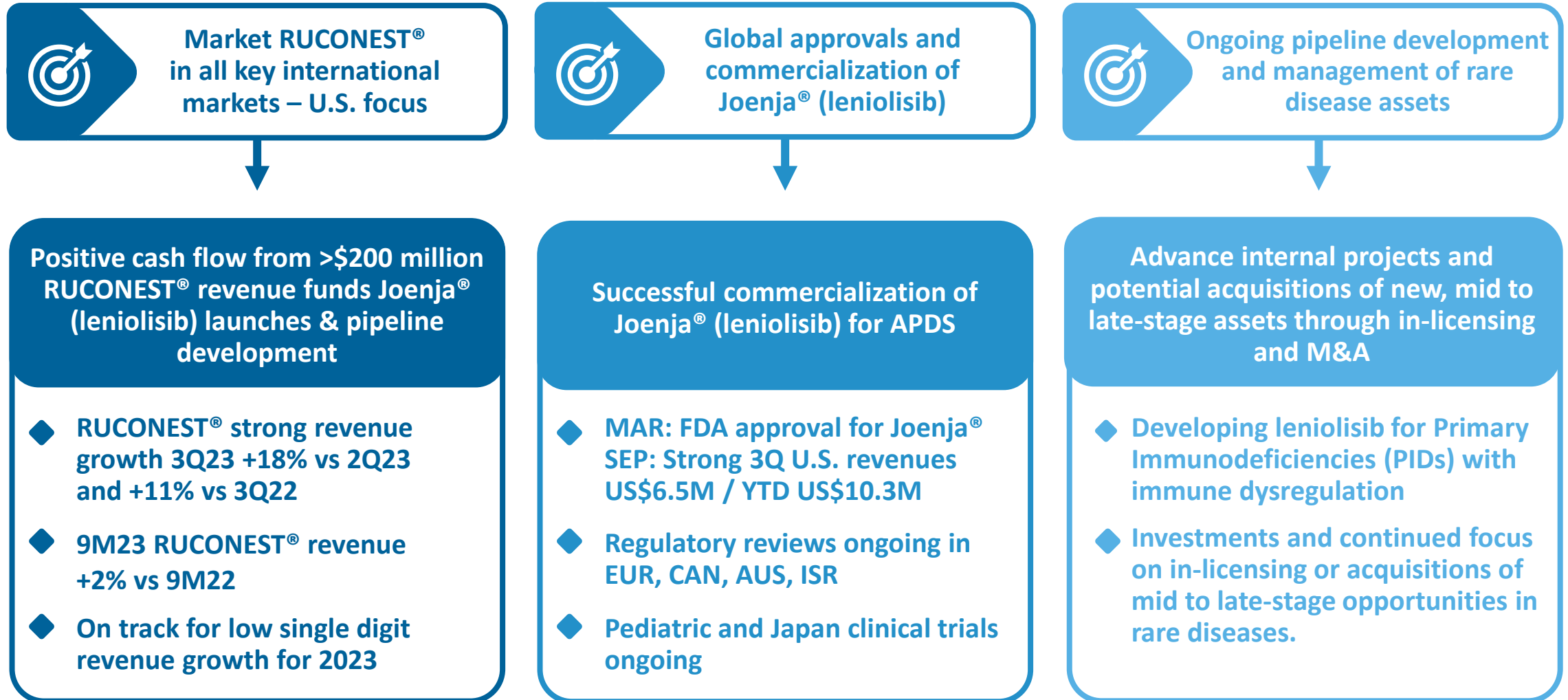
**Pharming Group N.V.**

Corporate Presentation

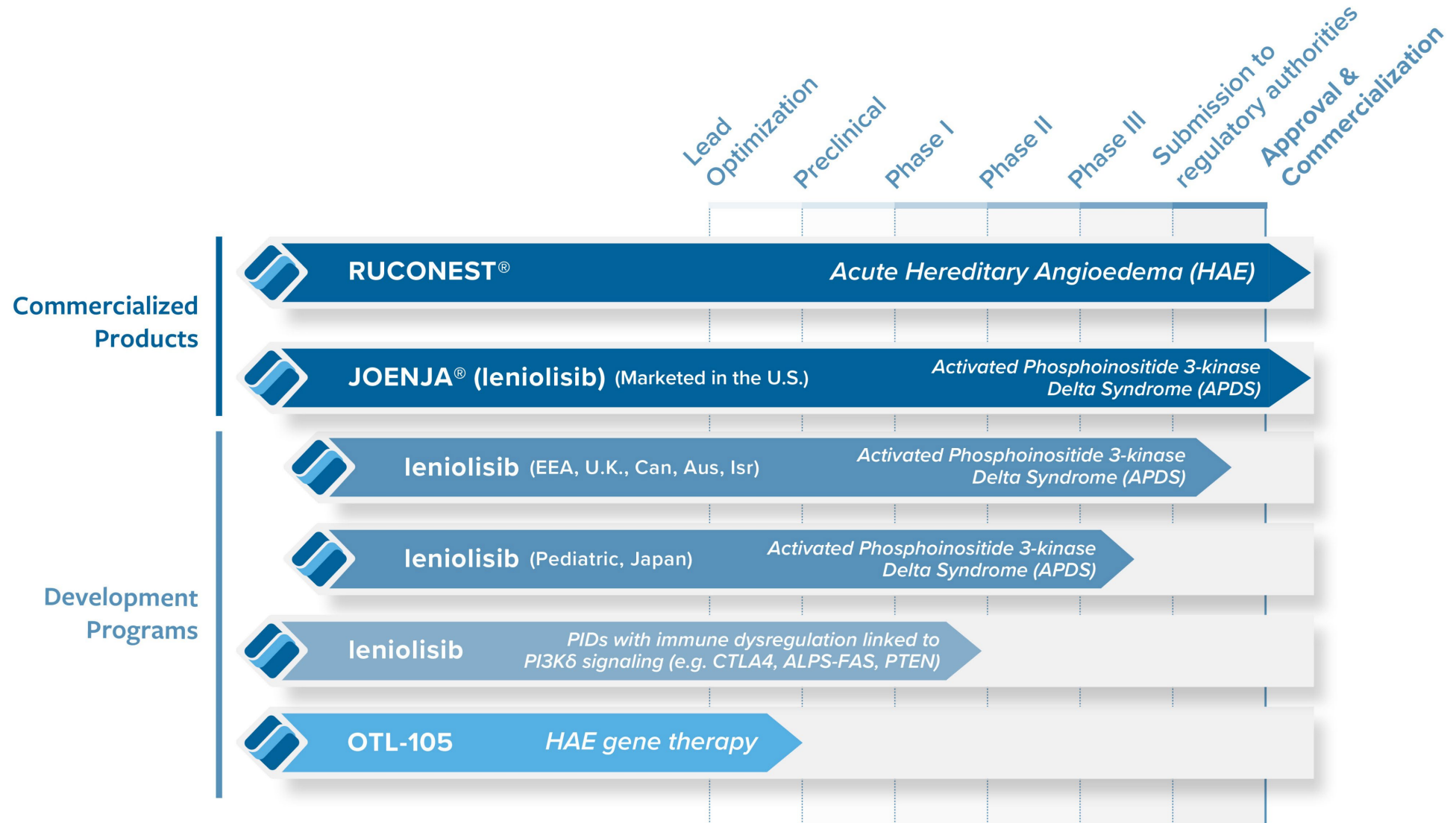
**December 2023**

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

*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 and technical developments. In light of these risks and uncertainties, and other risks and uncertainties that are described in Pharming's 2022 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2022, 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.*



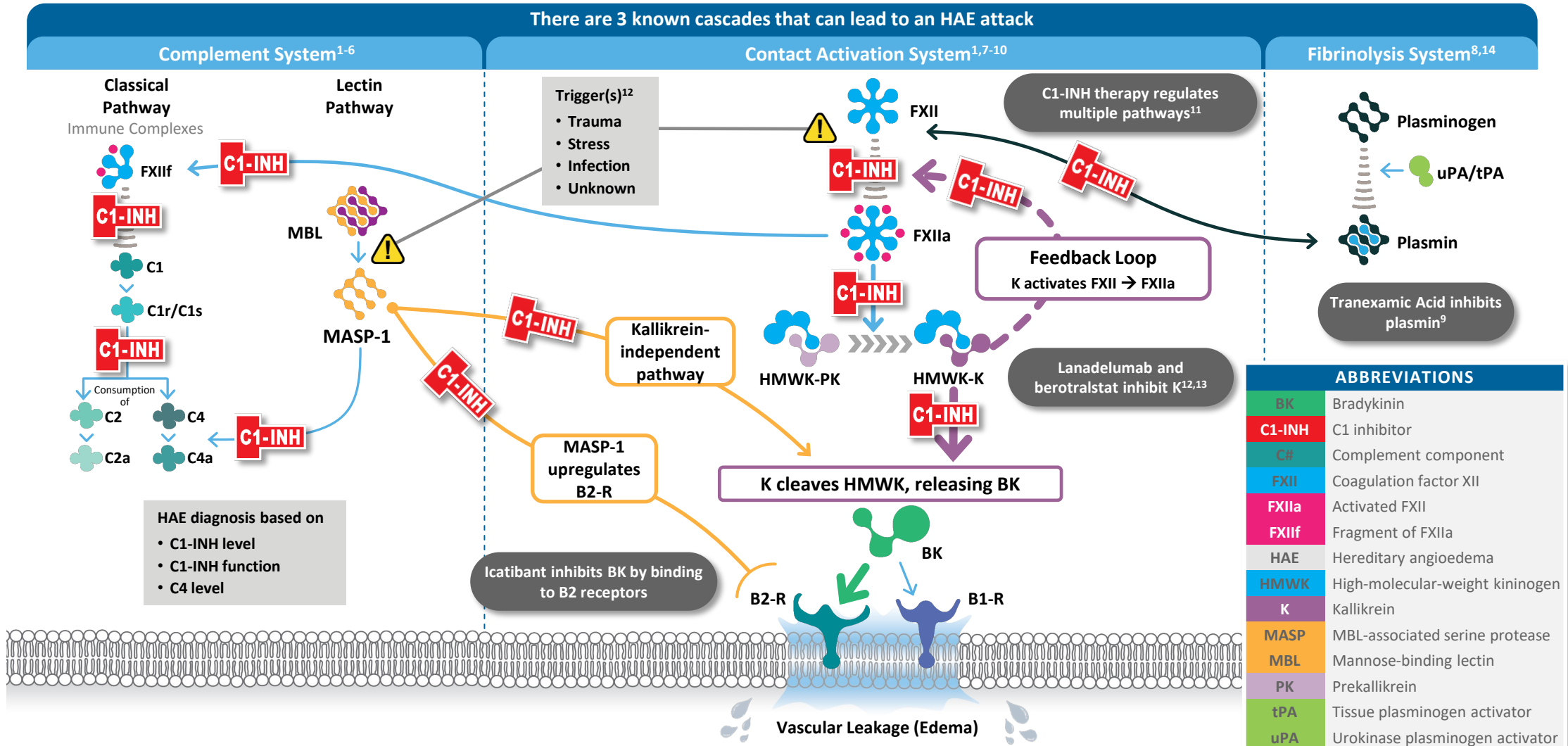
# Pipeline – multiple commercial stage rare disease products



 Pharming® | **35** years

**RUCONEST®**

# C1-INH targets the root cause of HAE



Adapted from a clinical cascade developed in partnership with Dr. Allen Kaplan. This is a current scientific understanding of the cascades. Clinical implications are unknown.



**Revenue US\$208m**  
(trailing 12 months)



**Strong 3Q23 performance**  
On track for low single digit  
2023 revenue growth



**The only recombinant treatment**  
that targets the root cause of HAE  
by replacing missing or  
dysfunctional C1-INH



**Well-tolerated and effective**  
treatment option for acute  
hereditary angioedema (HAE) -  
including breakthrough attacks



**Second most prescribed product**  
detailed for acute attacks



**97%: needed just 1 dose of**  
RUCONEST®<sup>1</sup>  
**93%: acute attacks stopped with**  
RUCONEST® for at least 3 days<sup>2</sup>



**Strong U.S. in-market demand –**  
over 70 new patient enrollments  
for 3 straight quarters



**Performing well in leading**  
revenue indicators in the U.S.:  
active patients, vials shipped, #  
physicians prescribing



Revenues increased 11% in 3Q23 (US\$60.2m) vs 3Q22  
Revenues increased 2% in 9M23 (US\$153.8m) vs 9M22



Performed well in leading revenue indicators in the U.S. including active patients, vials shipped, and number of physicians prescribing



Strong U.S. in-market demand – over 70 new patient enrollments for 3 straight quarters



On track for low single digit revenue growth for 2023



# Strong commitment to HAE community



Strong patient organization support since 2000

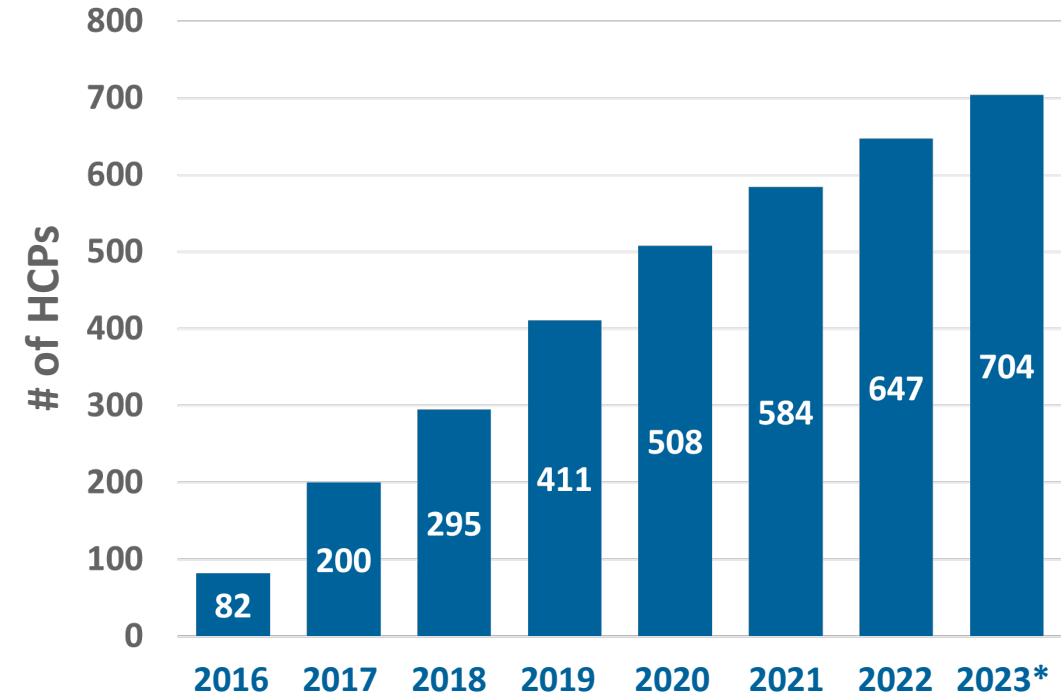


More than 700 U.S. physicians (and growing) prescribing RUCONEST®



>2,000 patients with HAE have been prescribed RUCONEST®

# of unique U.S. physicians prescribing



\*Data thru September 30, 2023





# APDS Overview

# APDS is a rare, primary immunodeficiency (PI) first characterized in 2013



Activated phosphoinositide 3-kinase delta (PI3K $\delta$ ) syndrome (APDS) affects >1500 patients\*

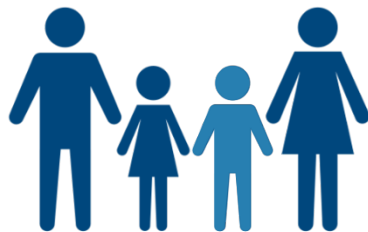
To date, Pharming has identified >640 of these patients in key global markets

(as of June 30, 2023, for U.S., Europe, U.K., Japan, Canada, Australia and Israel)



Until now, treatments for APDS have addressed the symptoms of the disease which manifest early in childhood, but not the root cause of APDS

Without an indicated treatment specifically for APDS, physicians could only manage symptoms



The signs and symptoms of APDS vary widely, even among family members with the same genetic variant, resulting in potential delays in diagnosis and care



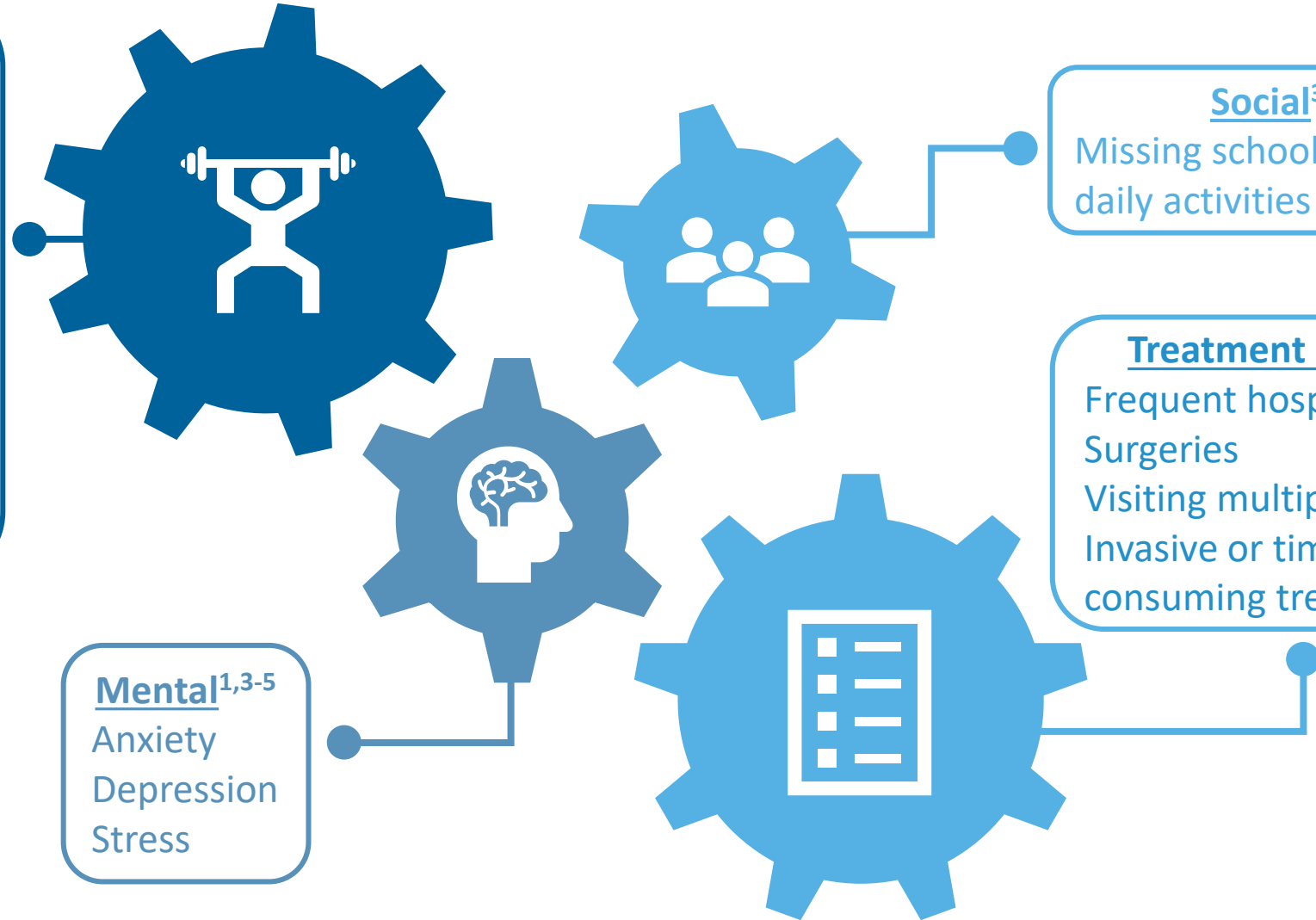
A genetic test can provide a definitive diagnosis of APDS

\*Size based on estimate of 1.5 APDS patients per million (based on available literature) for U.S., Europe, U.K., Japan, Canada, Australia and Israel

# APDS can impact many facets of life

## Physical<sup>1,2</sup>

Frequent infections  
Swollen glands  
Shortness of breath  
Coughing/wheezing  
Chest or joint pain  
Fatigue  
Inability to exercise  
Hearing loss  
Diarrhea  
Skin problems



## Social<sup>3,4</sup>

Missing school, work, or daily activities

## Treatment Burden<sup>1-4</sup>

Frequent hospitalizations  
Surgeries  
Visiting multiple doctors  
Invasive or time-consuming treatments

## Mental<sup>1,3-5</sup>

Anxiety  
Depression  
Stress

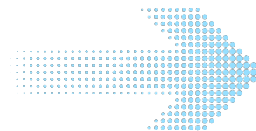
APDS, activated phosphoinositide 3-kinase  $\delta$  syndrome.

1. Coulter TI, et al. *J Allergy Clin Immunol.* 2017;139(2):597-606. 2. Elkaim E, et al. *J Allergy Clin Immunol.* 2016;138(1):210-218. 3. Rider NL, et al. *J Clin Immunol.* 2017;37(5):461-475.

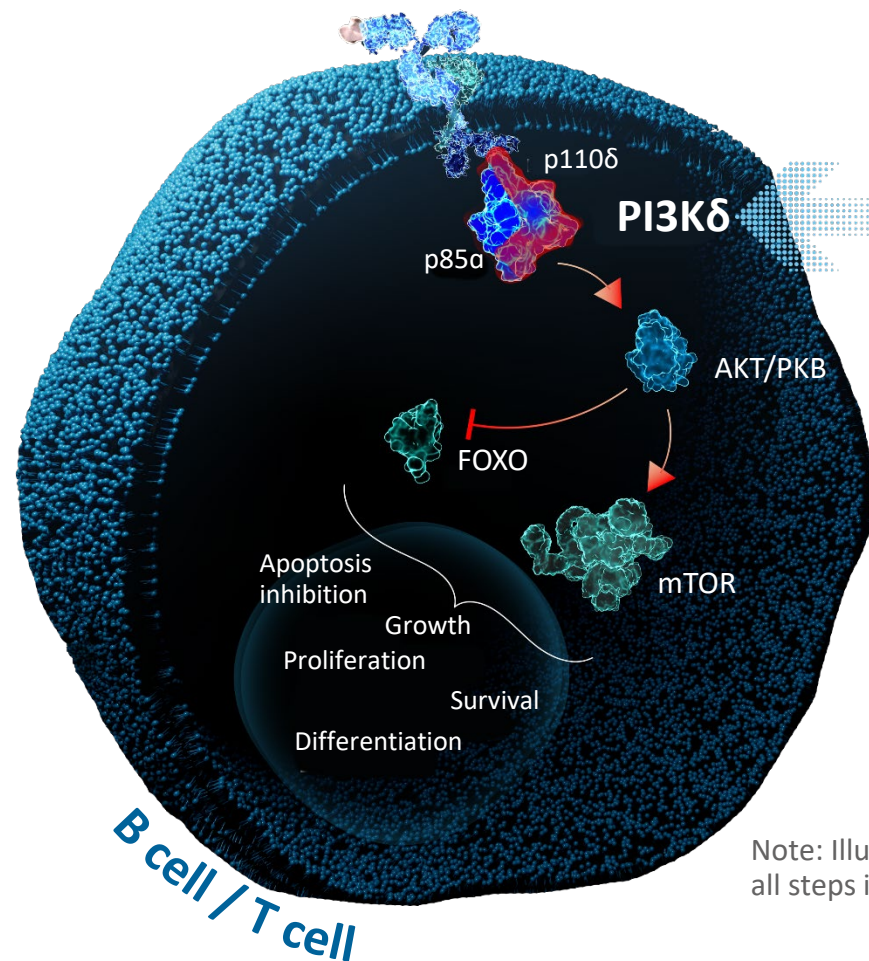
4. Jiang F, et al. *Allergy Asthma Clin Immunol.* 2015;11:27. 5. Kuburovic NB, et al. *Patient Prefer Adherence.* 2014;8:323-330.

# Genetic defect leads to PI3K $\delta$ hyperactivity, disrupting immune cell balance

Hyperactive PI3K $\delta$  results in dysregulated B and T cell development<sup>1-3</sup>

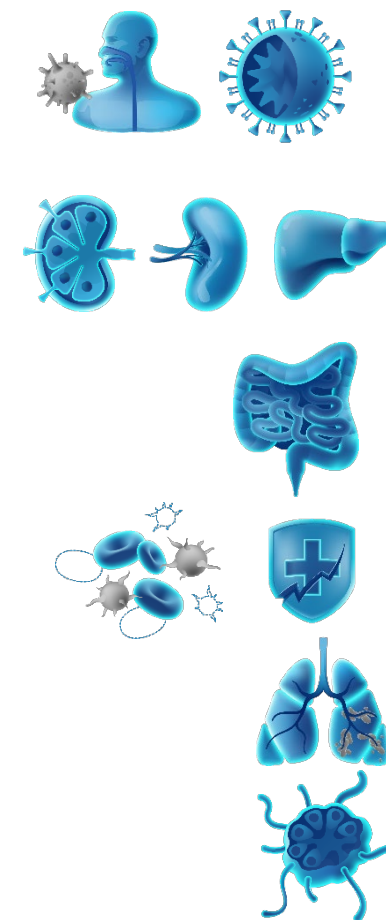


Immune imbalance leads to diverse signs and symptoms<sup>1,4-6</sup>



The PI3K $\delta$  enzyme is at the beginning of a complex signaling pathway

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



## Severe, recurrent, persistent infections

- Sinopulmonary
- Herpesvirus (especially EBV and CMV)

## Lymphoproliferation

- Lymphadenopathy
- Splenomegaly/hepatomegaly
- Nodular lymphoid hyperplasia

## Enteropathy

## Autoimmunity

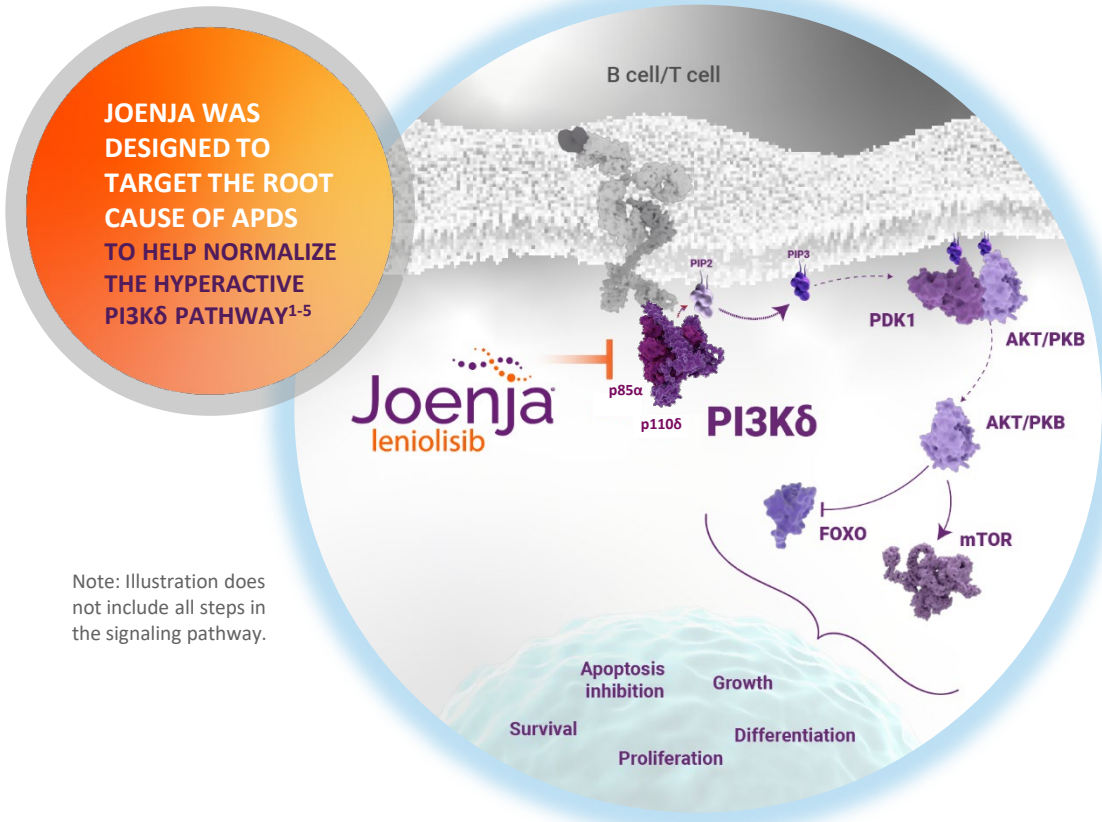
- Cytopenias
- Autoimmune disorders
- Autoinflammatory disorders

## Bronchiectasis

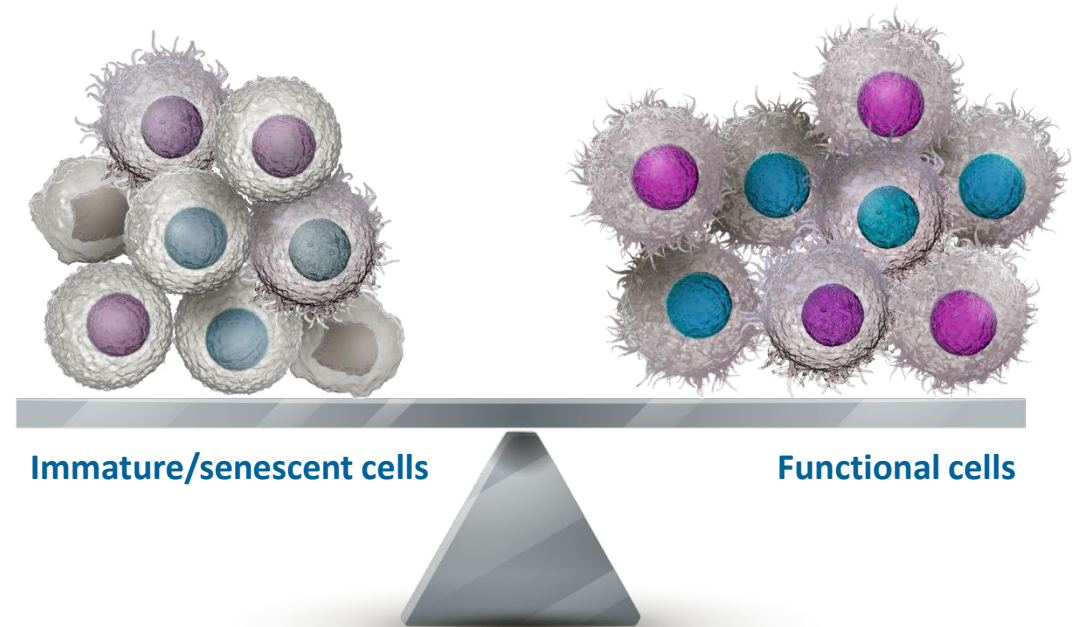
## Lymphoma

FOXO, forkhead box O; mTOR, mammalian target of rapamycin; PI3K $\delta$ , 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.



Joenja<sup>®</sup> facilitates a balanced PI3Kδ pathway to support proper immune function<sup>6</sup>



This is a graphical representation of a complex biological process.

AKT/PKB, protein kinase B; FOXO, forkhead box O; mTOR, mammalian target of rapamycin; p85α, the regulatory subunit of the PI3Kδ enzyme; p110δ, the catalytic subunit of the PI3Kδ enzyme.  
 1. Fruman DA, et al. *Cell*. 2017;170(4):605-635. 2. Okkenhaug K, Vanhaesebroeck B. *Nat Rev Immunol*. 2003;3(4):317-330. 3. Hoegenauer K, et al. *ACS Med Chem Lett*. 2017;8(9):975-980. 4. Rao VK, et al. *Blood*. 2017;130(21):2307-2316. 5. Rao VK, et al. *Blood*. 2023;141(9):971-983. 6. Nunes-Santos CJ, et al. *J Allergy Clin Immunol*. 2019;143(5):1676-1687.



**Joenja<sup>®</sup> (leniolisib)**

# U.S. launch of Joenja<sup>®</sup>: a much-needed treatment for patients with APDS and another win for Pharming

Joenja<sup>®</sup> (leniolisib) is a prescription medicine that is used to treat activated phosphoinositide 3-kinase delta (PI3K $\delta$ ) syndrome (APDS) in adults and pediatric patients 12 years of age and older

In a randomized placebo-controlled trial of patients with APDS

- Joenja<sup>®</sup> met both primary end points with significant efficacy results
- Demonstrated significant improvement in other secondary and exploratory parameters

There were no drug-related serious adverse events or study withdrawals in Joenja<sup>®</sup> trials

Joenja<sup>®</sup> reported additional findings from an ongoing long-term open-label extension study interim analysis: reductions/discontinuations in IRT and reduction in infection rates

Extension study interim analysis demonstrated safety consistent with the randomized, controlled trial. We continue to collect observational long-term data on lymphadenopathy, naive B cells and IgM

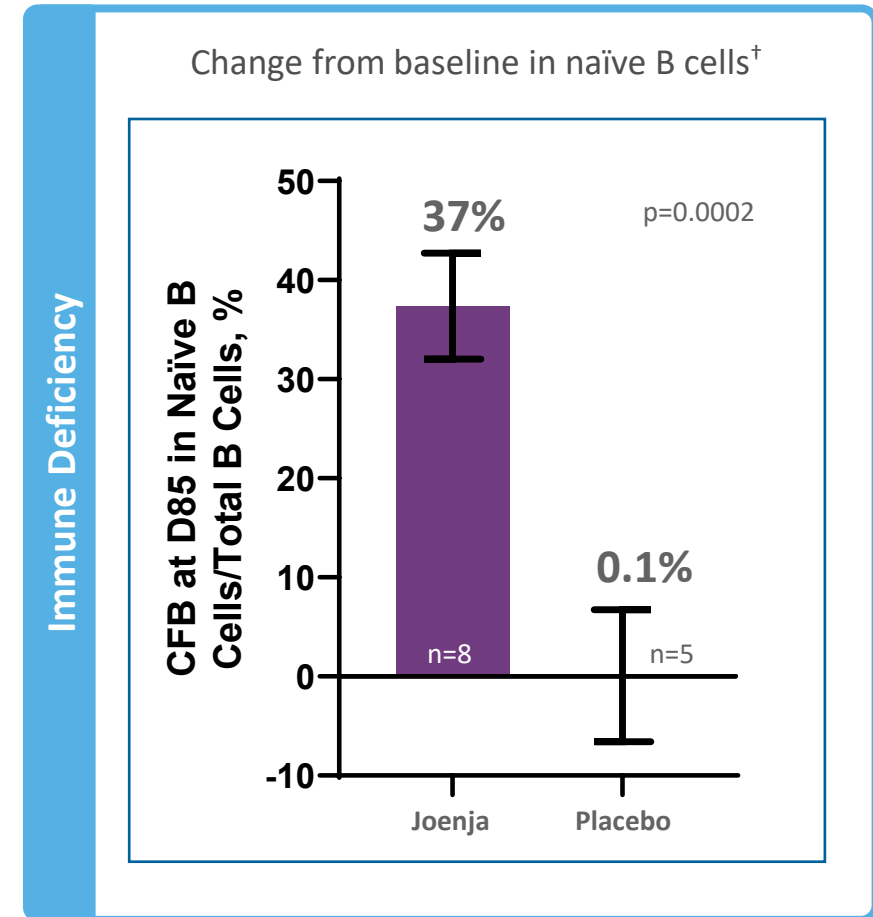
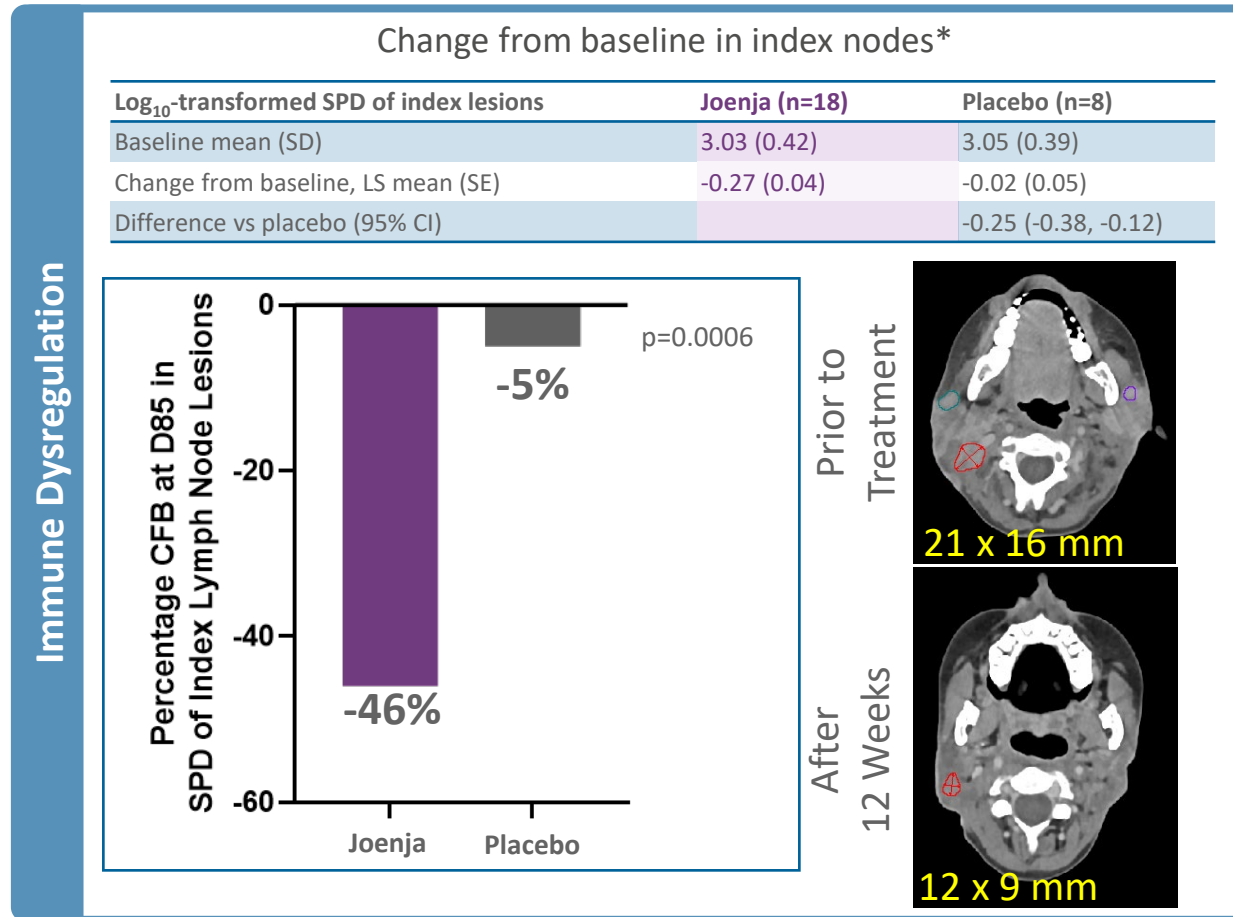
Strong start to Joenja<sup>®</sup> launch with 76 enrollments & 63 patients on paid therapy as of September 30, 2023





# 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



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.

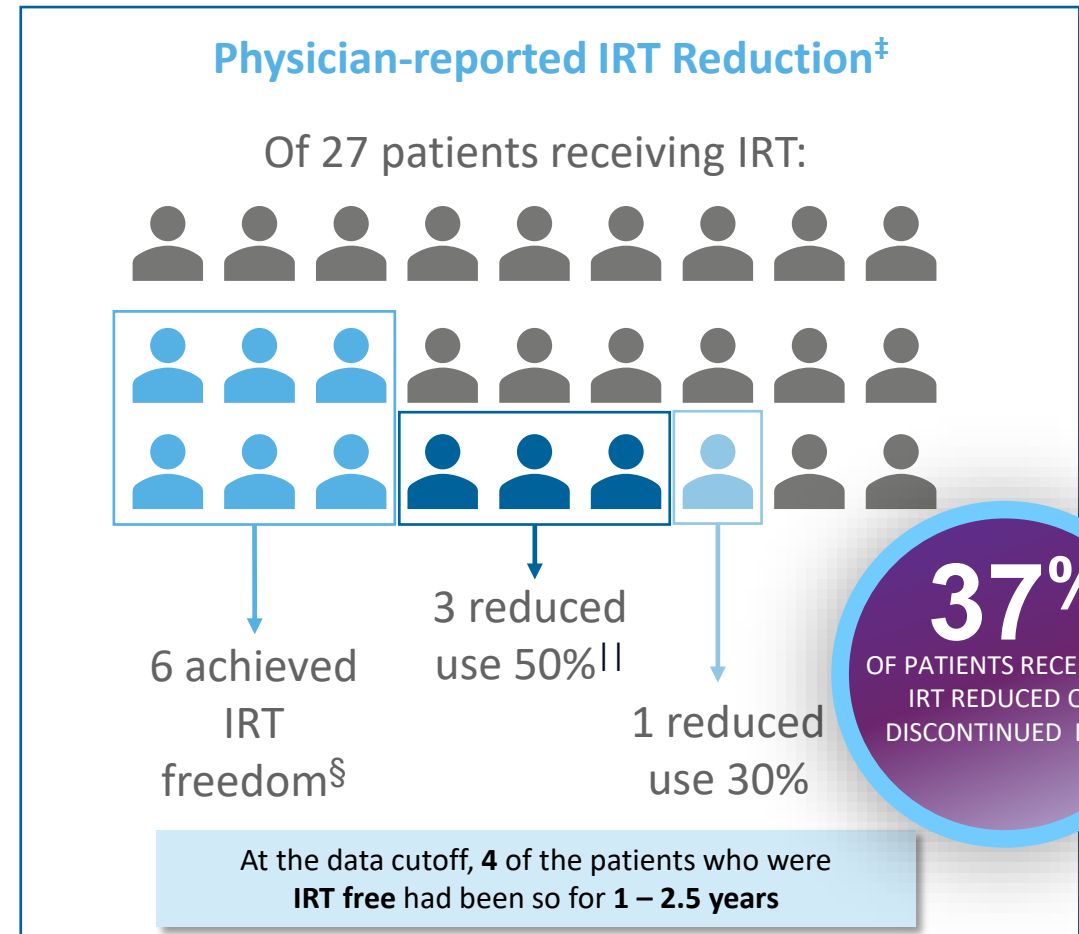
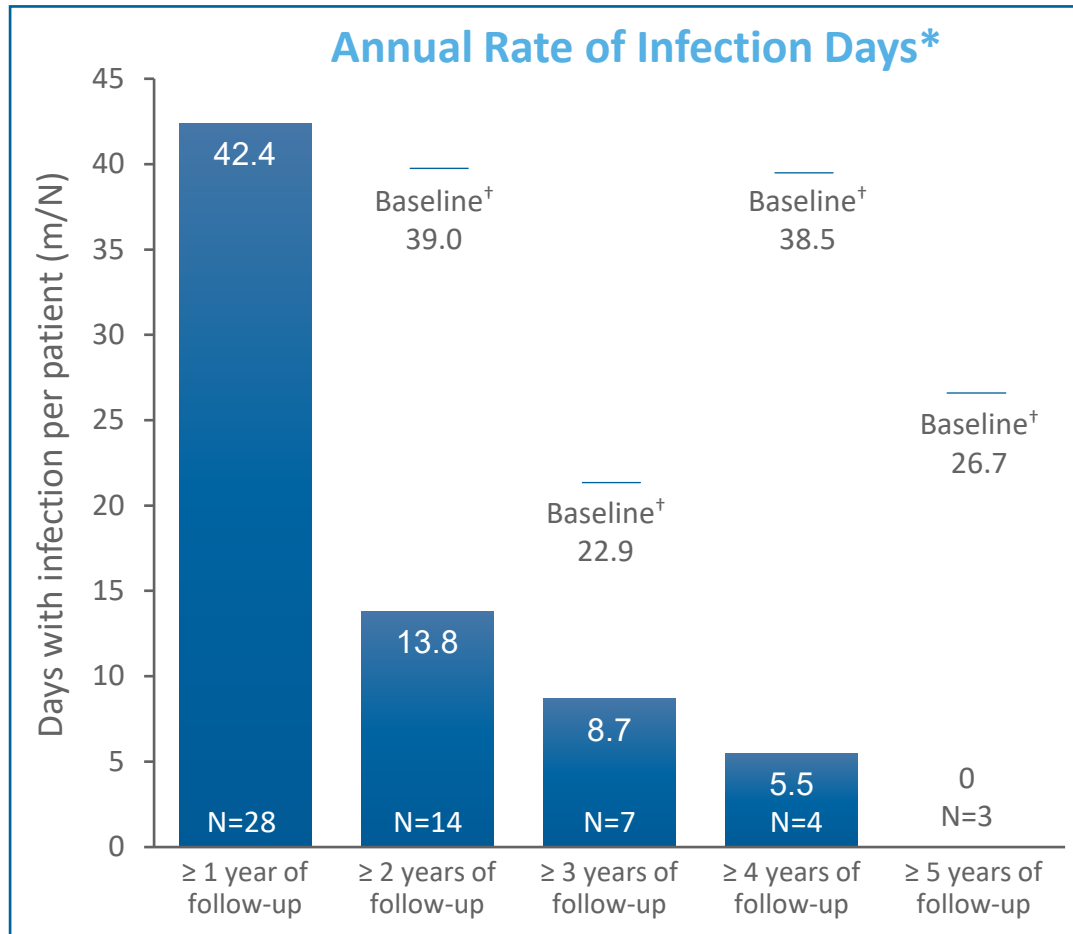
\*The analysis excluded 2 patients from each treatment group due to protocol deviations and 1 Joenja patient having complete resolution of the index lesion identified at baseline.

†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](http://joenja.com)

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



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.

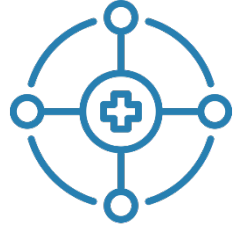
\*Infections that developed during the study were reported as adverse events. Investigators were requested to inquire about signs and symptoms of infections at each visit, with a particular focus on bacterial enterocolitis. Patients were not provided an infection diary to document infections occurring 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](http://joenja.com)



## Patient Identification

- Work with HCPs to further identify patients and get them tested
- APDS clinical educators assist with family mapping



All about **APDS**  
Activated PI3K Delta Syndrome



## Patient Access

- Dedicated support and education resources through the APDS Assist patient support program
- APDS Assist to help patients navigate coverage to ensure all eligible patients receive access to treatment
- Partnered exclusively with PANTHERx Specialty Pharmacy
- Starter and Bridge program enables rapid access while navigating coverage
- Copay Assistance and Patient Assistance Programs for eligible patients ensure affordability to care

- ◆ Strong commercial execution 6 months into U.S. launch
- ◆ Continue to add enrollments  
76 enrollments, of which 63 patients on paid therapy at end 3Q23
- ◆ All but one pre-existing OLE/EAP patients enrolled or are on paid therapy  
37 patients on paid therapy were previously untreated patients or naïve
- ◆ 3Q23 revenues: US\$6.5 million  
9M23 revenues: US\$10.3 million
- ◆ Significant focus on genetic family testing  
Ramp up in 4Q23 and 1Q24
- ◆ Productive ongoing engagement with both national and regional payers





Europe – CHMP opinion on MAA expected 1Q24 (approval ~ 2 months later)\*



UK – MHRA filing expected 1Q24\*\*



Japan clinical study – 1st patient enrolled Aug 2023



AUS, CAN, ISR submissions under regulatory review

CAN & AUS approval 2Q24\*\*\*  
ISR approval 1H24\*\*\*



Pediatric study for 4 to 11 years: enrollment majority (11/15) complete



Pediatric study for 1 to 6 years ongoing (first patient dosed)



Named patient program ongoing



Leniolisib development for PIDs with immune dysregulation (start 1<sup>st</sup> Phase 2 trial 2Q24)

\* Received CHMP Day 180 list of outstanding issues in July. CHMP will consult an Ad-hoc Expert Group (AEG) given the rarity of the disease and the unmet medical need for the treatment of APDS patients. Approval is subject to positive outcomes of the EMA CHMP review.

\*\* Pharming intends to file an MAA through the International Recognition Procedure (IRP), on the basis of the US FDA approval. MHRA would have 110 days from the date the IRP submission is validated to review and issue its decision.

\*\*\* Subject to positive AUS, CAN, ISR decisions



## Medical education to raise awareness of APDS and share leniolisib data

- ◆ Conferences and congresses
- ◆ Abstracts
- ◆ Publications



## Genetic testing

- ◆ Sponsored, no-cost testing program



- ◆ Genetic counselors to assist with testing and reviewing results
- ◆ Partnering with genetic testing companies to identify previously and newly diagnosed APDS patients



## Family testing

- ◆ Inherited disease\* but most APDS patients do not have diagnosed family members
- ◆ Patients may not be aware of genetics or have access to specialty physicians
- ◆ Cooperating with clinicians to encourage family testing
- ◆ Patients can request a genetic test through partner Genome Medical (if suspect APDS for themselves or family members)
- ◆ Reduces barrier for easier testing of those suspected with APDS

\*APDS genes are autosomal dominant meaning there is a 50% chance that a blood relative of an APDS patient may also carry that gene and in turn have APDS.

# Helping diagnose APDS patients: Variant of Uncertain Significance (VUS) resolution

## Genetic testing frequently leads to inconclusive results - previously unseen genetic variants:



Patients have clinical symptoms compatible with APDS, but genetic variant test is inconclusive



Frustrating for patients and clinicians

Need to determine if Variant of Uncertain Significance (VUS) causes APDS

## Pharming initiatives/partnerships to resolve VUSs



### Variant Curation

- ◆ ClinGen expert panels develop gene/disease specific thresholds and criteria for classifying variants
- ◆ Partnership with Genomenon to develop Genomic Landscape (comprehensive, systematic review of all published variant data)



### Functional testing

- ◆ Improve access to directly measure PI3K pathway activity in patient blood samples
- ◆ Sharing of results via public databases (ClinVar)



### Multiplexed assays of variant effect (MAVE)

- ◆ Test nearly all possible variants in a single experiment
- ◆ Generate variant effect map, including variants already found and those not yet found (proactive)



## ◆ AMCP Nexus (October 2023)

- *A Real-world Comparison of Health Care Resource Utilization and Health Care Costs Among Patients With Activated PI3K-Delta Syndrome Versus a Control Cohort of Patients Without Activated PI3K-Delta Syndrome in the United States*



## ◆ ACAAI (November 2023)

- *Mortality in Patients With Activated Phosphoinositide 3-Kinase Delta Syndrome, a Systematic Literature Review*



**IPIC2023**

INTERNATIONAL  
PRIMARY  
IMMUNODEFICIENCIES  
CONGRESS

## ◆ IPIC (November 2023)

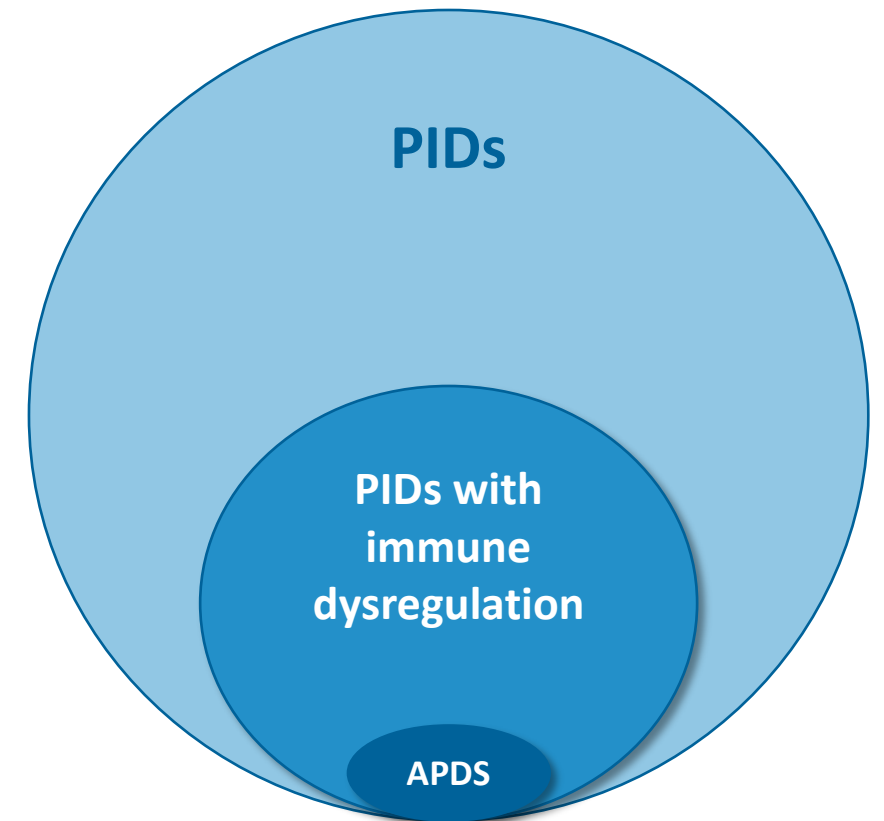
- *Results of a second interim analysis of an ongoing single-arm open-label extension study of leniolisib in activated PI3K delta syndrome: long-term efficacy and safety through to March 2023.*
- *Complicated course of activated PI3K delta syndrome-1 ameliorated by leniolisib: a case study.*
- *Gastrointestinal manifestations in patients with activated PI3K delta syndrome (APDS) treated with leniolisib.*
- *Assessing long-term treatment with leniolisib and its effects on bronchiectasis in patients with activated PI3K delta syndrome (APDS).*



## PIDs are a broad group of disorders<sup>1</sup> with key features:

- ❖ Genetic basis, i.e., not secondarily caused by another disease  
*'Inborn Errors of Immunity' (IEI) is used interchangeably with PID*
- ❖ An increased risk of infection may be the predominant manifestation, due to poor immune system function
- ❖ PID patients may have a predominance of immune dysregulation, for example: lymphoproliferation and autoimmunity<sup>2</sup>

**APDS is an example of a PID with immune dysregulation**

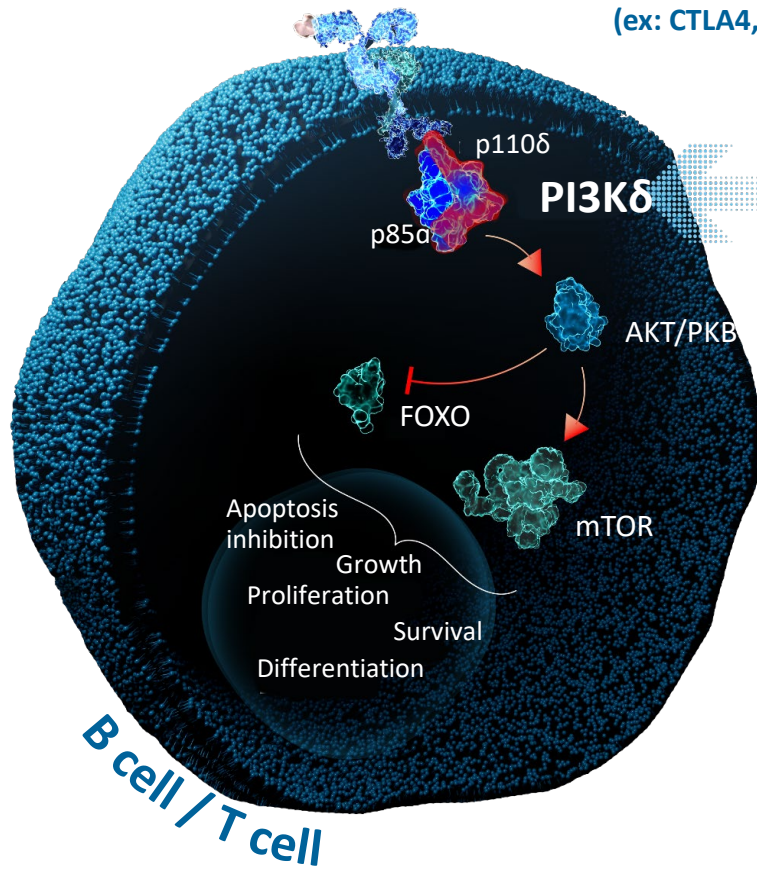


*Not to scale with population sizes*

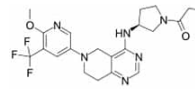
1. Bousfiha et al 2022 IUIS categorization  
2. Chan and Torgerson 2020 Curr Opin Allergy Clin Immunol 20(6): 582-590

# Given importance of PI3K $\delta$ in B & T cells, immune dysregulation in PIDs can occur via alterations in PI3K $\delta$ signaling

## Altered PI3K $\delta$ signaling can occur in multiple PID genetic disorders beyond APDS (ex: CTLA4, PTEN, FAS)



### leniolisib



**High unmet medical need**  
- no approved therapies other than Joenja® (leniolisib) for APDS: SOC immunosuppressives (e.g. rapamycin) have limited efficacy and significant tolerability concerns

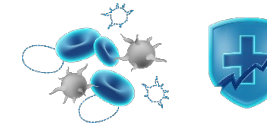
Note: Illustration does not include all steps in the signaling pathway.

## Clinical manifestations, disease onset and severity similar to APDS



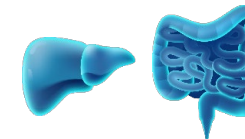
### Lymphoproliferation

- Lymphadenopathy
- Splenomegaly/hepatomegaly
- Nodular lymphoid hyperplasia



### Autoimmunity

- Cytopenias
- Autoimmune disorders
- Autoinflammation



### GI Disease

- Autoimmune enteropathy
- Nodular regenerative hyperplasia



### Pulmonary Disease

- GLILD
- Bronchiectasis



### Infections

- Sinopulmonary
- Herpesvirus



### Lymphoma

FOXO, forkhead box O; mTOR, mammalian target of rapamycin; PI3K $\delta$ , 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.

- ◆ Based on APDS experience, leniolisib has potential to be an effective & tolerable chronic treatment approach for PIDs with immune dysregulation
- ◆ Leniolisib, by reducing PI3K $\delta$  activity, should help rebalance immune dysregulation in PIDs, positively impacting clinical manifestations including lymphoproliferation and autoimmunity
- ◆ Initial development in PID genetic disorders with immune dysregulation linked to PI3K $\delta$  signaling in lymphocytes with similar clinical phenotypes to APDS, e.g. PTEN<sup>1</sup>, ALPS-FAS<sup>2</sup>, CTLA4<sup>3</sup>
  - Epidemiology suggests prevalence of ~5/million
  - FDA review / feedback received on clinical trial plans
- ◆ Phase 2 proof of concept clinical trial to commence 2Q 2024

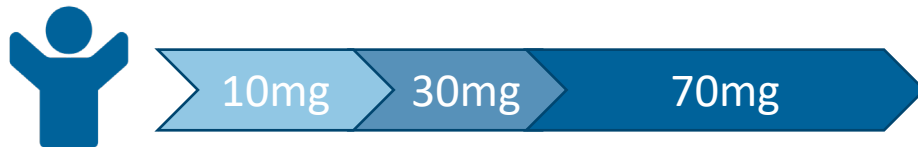
1. Eissing M, Ripken L, Schreibelt G, Westdorp H, Ligtenberg M, Netea-Maier R, Netea MG, de Vries IJM, Hoogerbrugge N. PTEN Hamartoma Tumor Syndrome and Immune Dysregulation. Transl Oncol. 2019;12(2):361-367

2. Rao and Oliveria Blood 2011

3. Westerman-Clark et al 2021; Schwab C, Gabrysch A, Olbrich P, Patiño V, Warnatz K, et al. Phenotype, penetrance, and treatment of 133 cytotoxic T-lymphocyte antigen 4-insufficient subjects. J Allergy Clin Immunol. 2018;142(6):1932-1946

## Phase 2 proof of concept clinical trial – single arm, open-label, dose range-finding study

Ph2 (N=12)



- Primary: Safety & Tolerability
- Secondary/Exploratory: PK/PD, efficacy measures
- 10/30/70 mg: 4/4/12 wks treatment, respectively
- Pick Best Dose regimen for Ph3



National Institute of Allergy and Infectious Diseases











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)



# Financials and Outlook

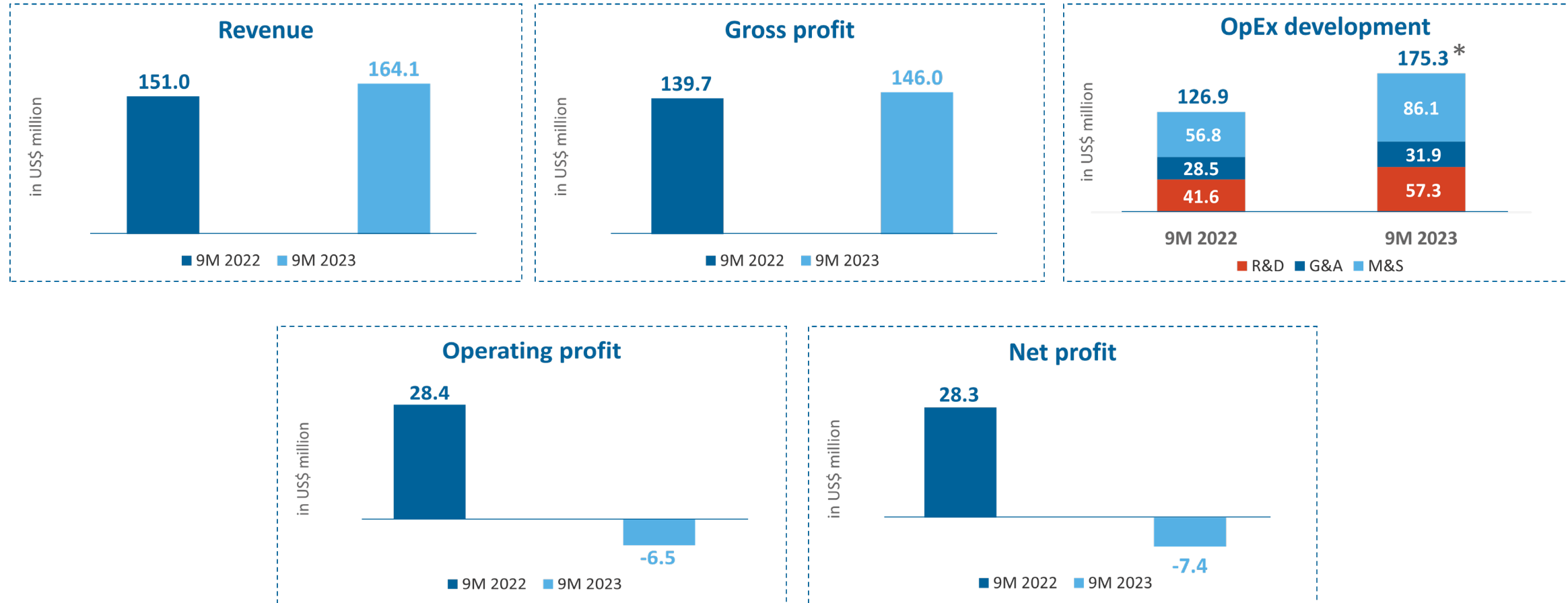
# Financial highlights: 3Q 2023 vs 3Q 2022

<b>TOTAL REVENUES</b> 3Q 2022	US\$54.2 million		<b>TOTAL REVENUES</b> 3Q 2023	US\$66.7 million	
<b>GROSS PROFIT</b> 3Q 2022	US\$51.9 million		<b>GROSS PROFIT</b> 3Q 2023	US\$58.4 million	
<b>OPERATING COSTS</b> 3Q 2022	US\$(44.7) million		<b>OPERATING COSTS</b> 3Q 2023	US\$(56.8) million	
<b>OPERATING PROFIT (LOSS)</b> 3Q 2022	US\$7.8 million		<b>OPERATING PROFIT (LOSS)</b> 3Q 2023	US\$1.9 million	
<b>NET PROFIT (LOSS)</b> 3Q 2022	US\$9.1 million		<b>NET PROFIT (LOSS)</b> 3Q 2023	US\$3.5 million	



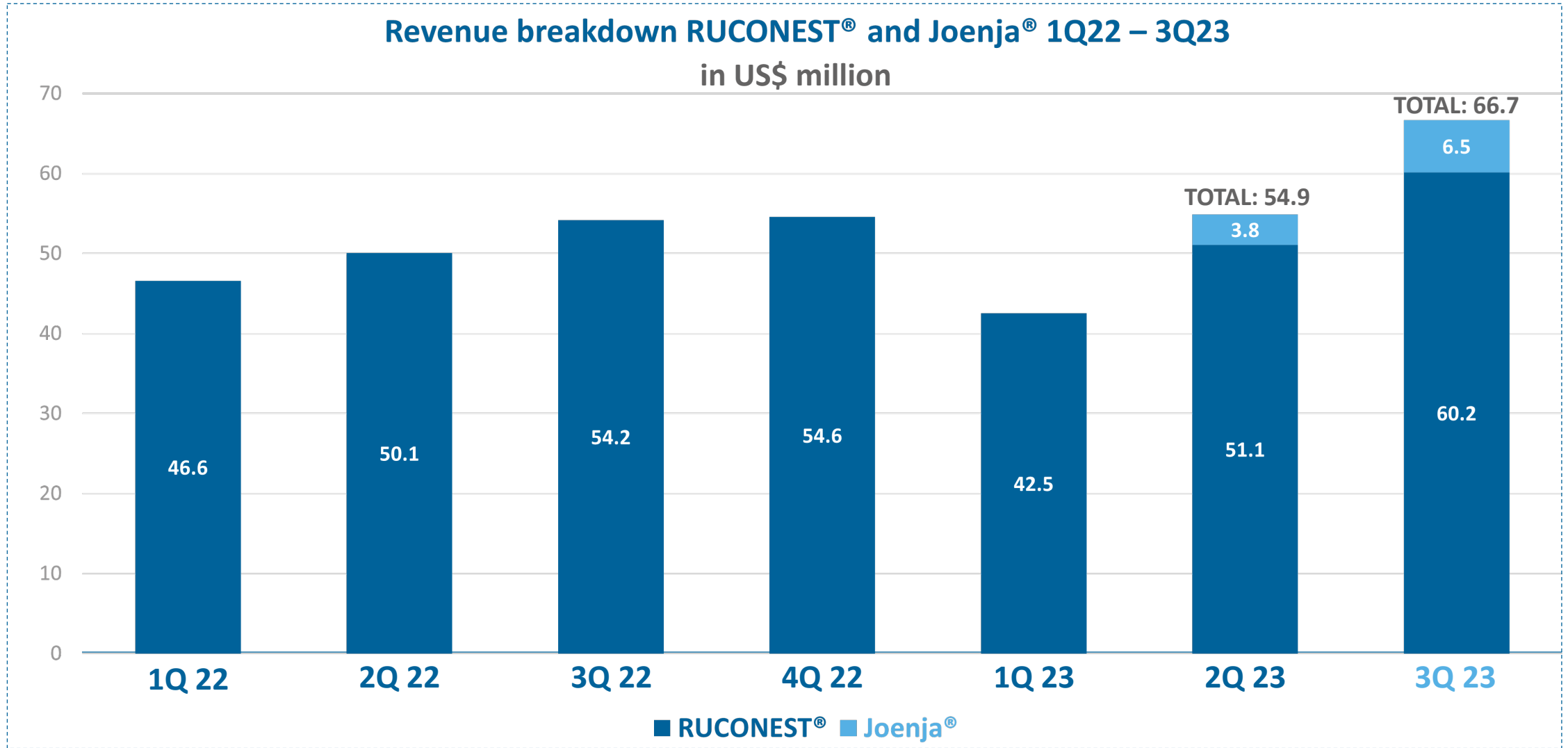
Cash and cash equivalents, together with restricted cash and marketable securities, increased from US\$194.1M at the end of 2Q23 to US\$199.2M at the end of 3Q23

# Financial highlights: 9M 2023 vs 9M 2022



\*2Q23 marketing and sales expenses includes US\$10M milestone payments paid

# RUCONEST® and Joenja® driving revenue growth







On track for low single digit growth in RUCONEST® revenues



Joenja® approved by FDA March 24, 2023, commercializing in U.S. since early April 2023



CHMP opinion in 1Q24, marketing authorization in Europe ~2 months later\*



File leniolisib with UK's MHRA in 1Q24 following IRP route\*



Continued operating cost investments to accelerate future growth



Announced plans to develop leniolisib for PIDs with immune dysregulation



Investment and continued focus on in-licensing or acquisitions of mid to late-stage opportunities in rare diseases

\* Pharming intends to file an MAA through the International Recognition Procedure (IRP) on the basis of the US FDA approval..



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