Pharming Group N.V.

Corporate Presentation

May 2024

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 2023 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2023, 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.

Building a leading global rare disease biopharma company

Pharming®

Market RUCONEST® for acute HAE attacks in key markets – U.S. focus

Positive cash flow from RUCONEST® revenue funds Joenja® (leniolisib) launches & pipeline development

- FY23 revenue US$227.1M
- 1Q24 revenue US$46.0M (+8%)
- Increase in patients and prescribers driving growth
- Patients reliant on RUCONEST® despite increased therapy options

Global approvals and commercialization of Joenja® (leniolisib) for APDS

Successful commercialization of Joenja® (leniolisib) – first and only FDA approved treatment for APDS – U.S. launch April 2023

- Revenue FY23 US$18.2M
  1Q24 US$9.6M (+21% vs. 4Q23)
- Strong focus on patient finding
- Israel approval (April 2024)
- Regulatory reviews ongoing in EUR, U.K., CAN, AUS
- Pediatric and Japan clinical trials

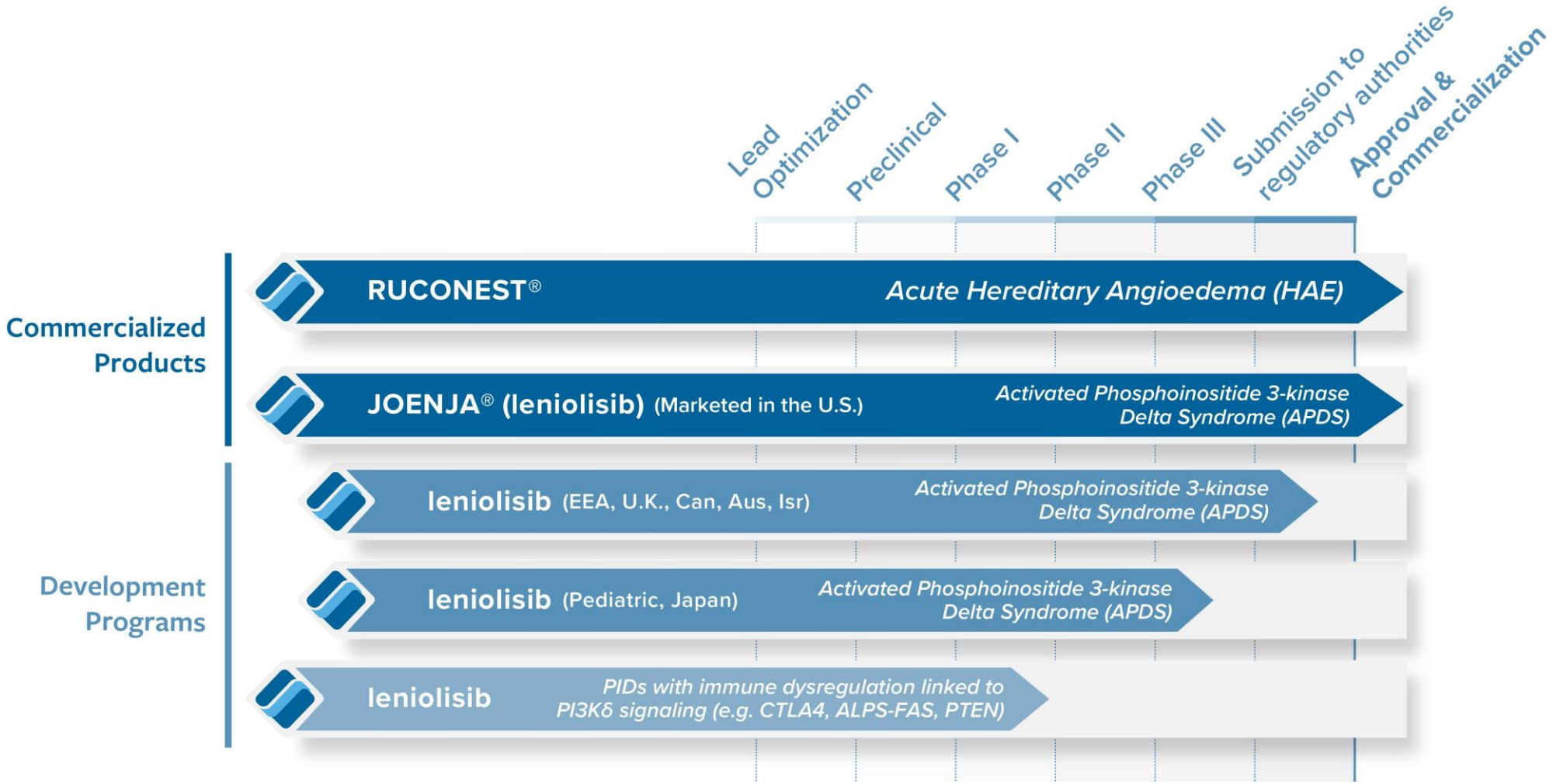
Ongoing pipeline development and management of rare disease assets

Advance internal projects and rare disease in-licensing and acquisition strategy

- Leniolisib development for PIDs with immune dysregulation beyond APDS – preparing Ph2
- BD focus on clinical programs in immunology, hematology, respiratory and gastroenterology
- OTL- 105 discontinued

2024 Total Revenue Guidance - $280 – $295M (14 – 20% growth)
Driven by Joenja®

Pipeline – multiple commercial stage rare disease products



Joenja® (leniolisib) franchise – multi-year growth potential

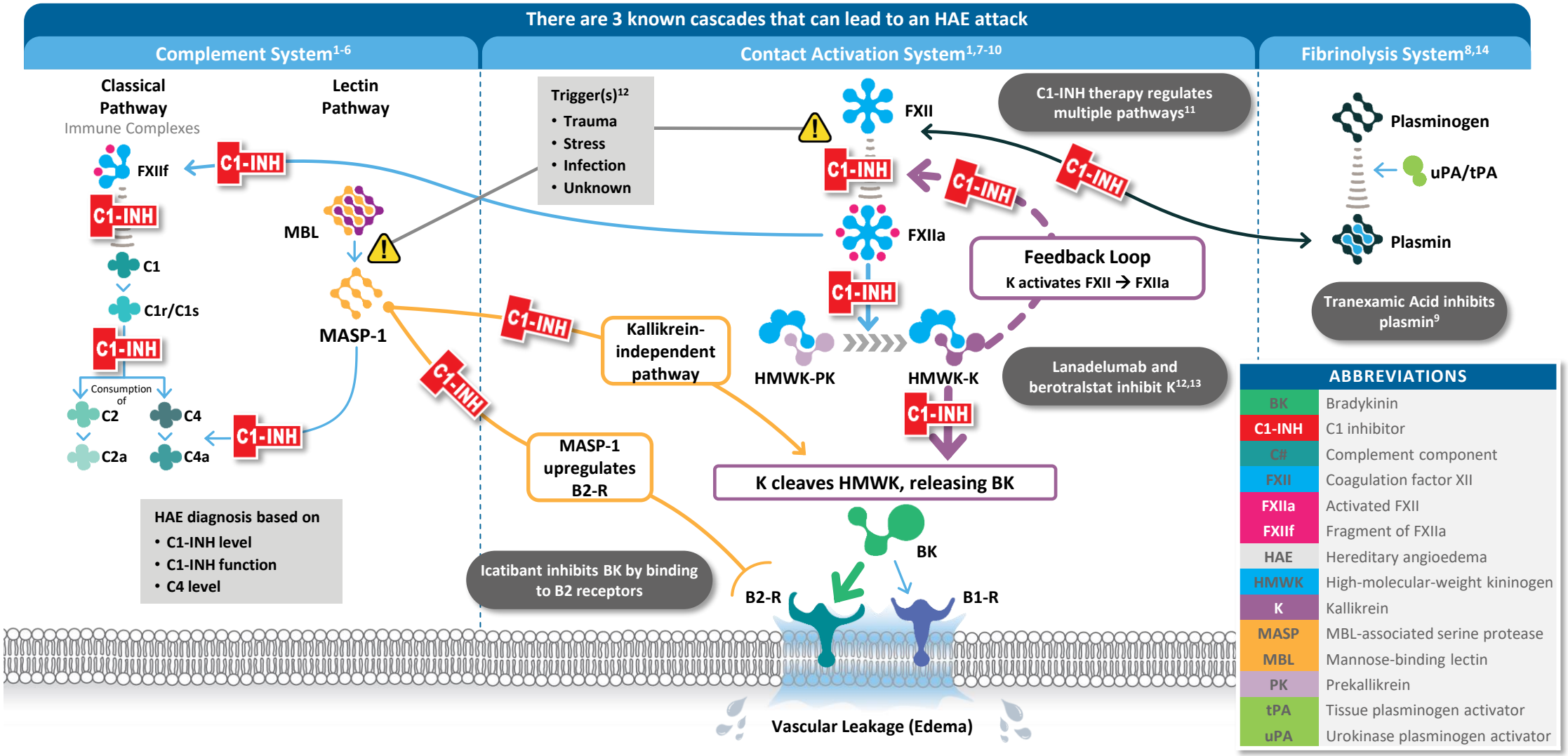
Joenja® U.S. (APDS)	Leniolisib (APDS)	Leniolisib for Primary Immunodeficiencies (PIDs)
• Marketed (12+) • Significant portion of identified patients on paid therapy • Ongoing patient finding and VUS resolution efforts	• Patients on early access/ named patient programs • Global expansion / regulatory reviews • Pediatric studies	• Phase II POC trial in PIDs with immune dysregulation linked to PI3Kδ signaling • Symptoms similar to APDS

Prevalence: **~1.5 / million ~2,000 patients** | **~5 / million**

Pharming®

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.

RUCONEST® (rhC1INH): trusted treatment cornerstone for HAE

Pharming®

- The only recombinant treatment that targets the root cause of HAE by replacing missing or dysfunctional C1-INH
- Second most prescribed product for acute attacks
- Well-tolerated and effective treatment option for acute hereditary angioedema (HAE) - including breakthrough attacks
- 97%: needed just 1 dose of RUCONEST®[1]
  93%: acute attacks stopped with RUCONEST® for at least 3 days[2]
- Strong U.S. in-market demand –
  New enrollments up 25% in FY23
  Almost 70 enrollments in 1Q24
- Performing well in leading U.S. revenue indicators: active patients, vials shipped, physicians prescribing (744, +15 vs. 2023)
- Revenue:
  FY23 US$227.1M (+10%)
  1Q24 US$46.0M (+8%)
- Continued growth in 2024, strong positioning vs. acute orals in late-stage development

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.

Pharming®

Joenja® (leniolisib)

U.S. launch of Joenja®: a much-needed treatment for APDS patients and another achievement for Pharming

Joenja® (leniolisib) is a prescription medicine that is used to treat activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older

In a randomized placebo-controlled trial of patients with APDS

- Joenja® 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® trials

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

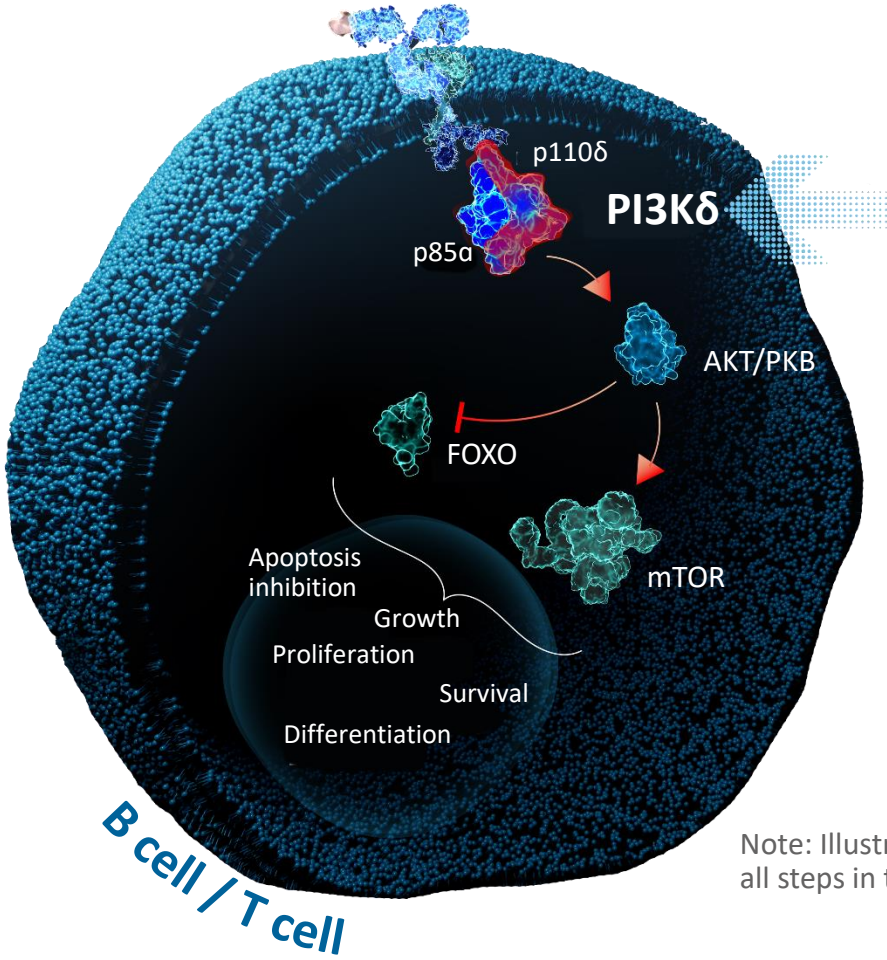
Extension study interim analysis demonstrated safety consistent with the randomized, controlled trial. We continue to collect observational long-term data on lymphadenopathy, naive B cells and IgM

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

Rao VK, et al. Blood. 2023;141(9):971-983
Rao VK, et al. Poster presented at: 64th Annual American Society of Hematology Annual Meeting; December 10-13, 2022; New Orleans, LA.

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

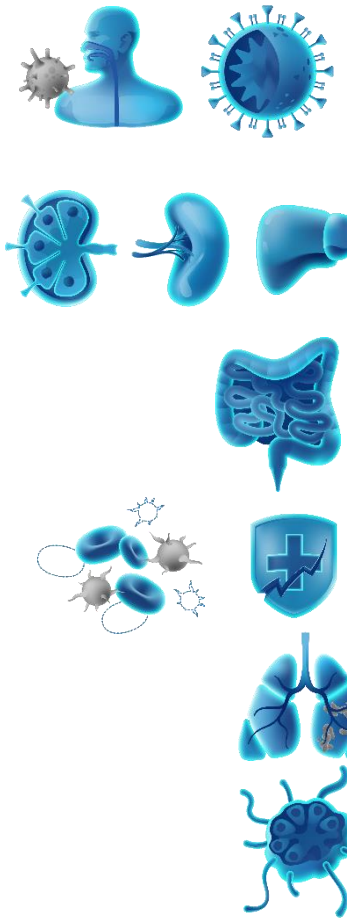
Hyperactive PI3Kδ results in dysregulated B and T cell development[1-3]



The PI3Kδ enzyme is at the beginning of a complex signaling pathway

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

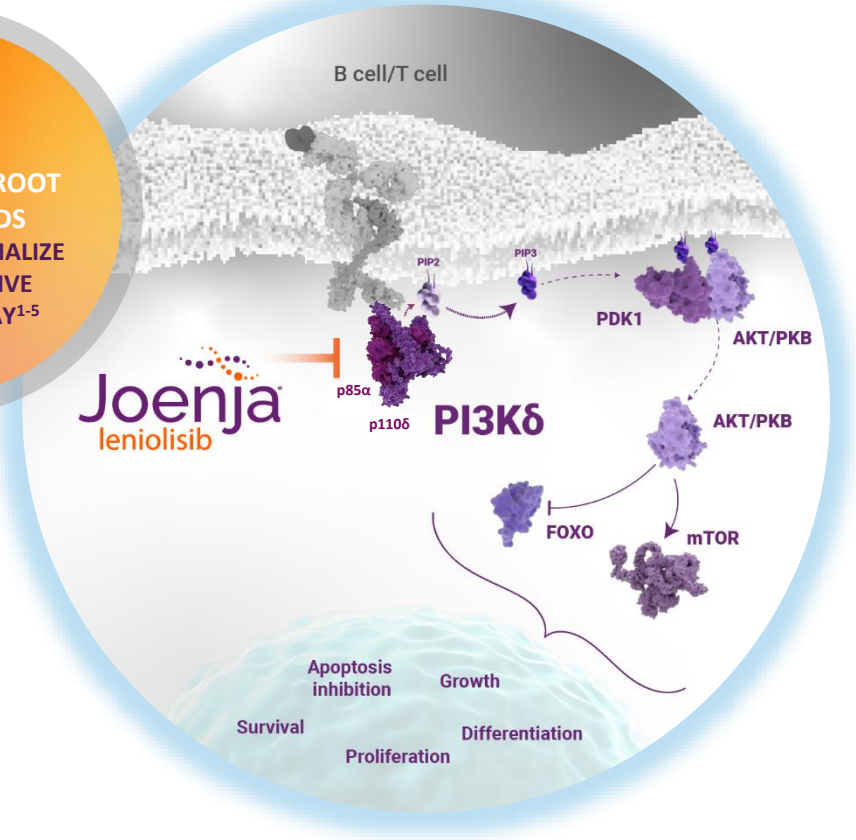
Lymphoma

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.

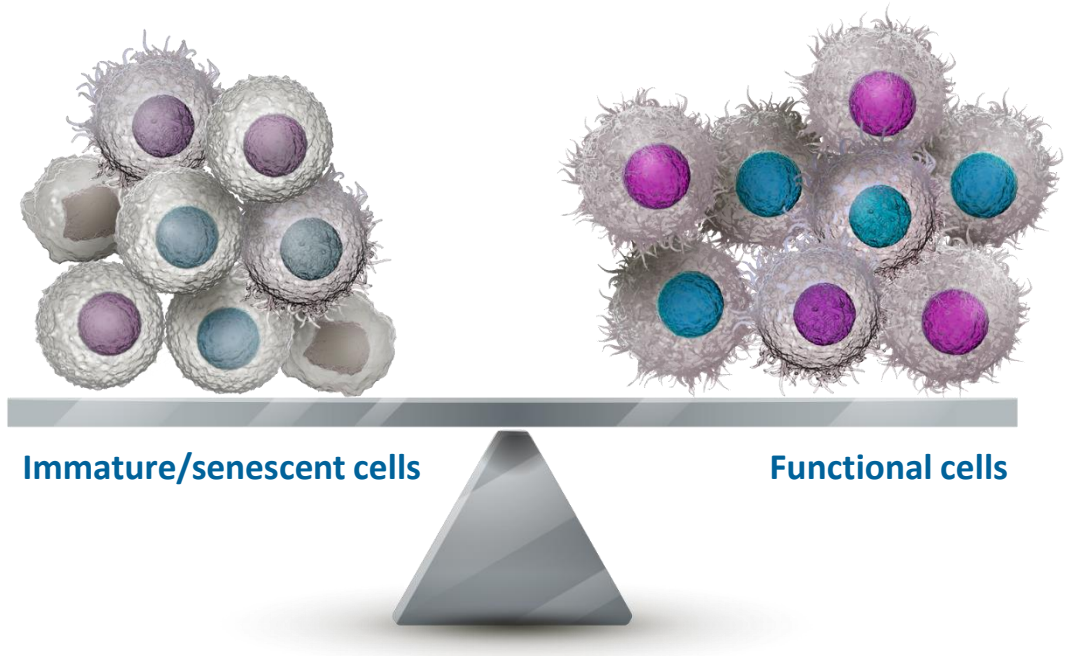
Joenja®: immune modulator that targets the root cause of APDS

JOENJA WAS DESIGNED TO TARGET THE ROOT CAUSE OF APDS TO HELP NORMALIZE THE HYPERACTIVE PI3Kδ PATHWAY[1-5]



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

Joenja® facilitates a balanced PI3Kδ pathway to support proper immune function[6]



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® (leniolisib) franchise – multi-year growth potential

Joenja® U.S. (APDS)	Leniolisib (APDS)	Leniolisib for Primary Immunodeficiencies (PIDs)
• Marketed (12+) • Found >220 of ~500 patients • 83 patients on paid therapy / 5 pending • >50 diagnosed patients (12+) not yet enrolled and >50 pediatric • Ongoing patient finding and VUS resolution efforts	• Global expansion / regulatory reviews • Pediatric studies • Found >840 patients globally • 138 patients on therapy (access programs and clinical studies)	• Phase II POC trial in PIDs with immune dysregulation linked to PI3Kδ signaling • Similar to APDS

Prevalence: **~1.5 / million ~2,000 patients** | **~5 / million**

- Joenja® U.S. and Europe / RoW access program revenues support 2024 guidance
- U.S. Pricing: 30-day supply $47,220, Annual cost (WAC) $566,640
- Global expansion focused on Europe, U.K., Japan, Asia Pacific, Middle East, and Canada

Joenja® U.S. launch: strong commercial execution

- Strong commercial execution 12 months into U.S. launch
- Continue to enroll and add patients
  83 patients on paid therapy at end 1Q24, with 5 additional enrollments pending authorization
  >50 diagnosed patients (12+) not yet enrolled and >50 pediatric
- FY23 revenue US$18.2M
  1Q24 revenue US$9.6M (+21% vs. 4Q23, includes US$1.1M Europe and RoW revenue)
- ~500 APDS patients in the U.S.*
  >220 diagnosed at end 1Q24 (+15 diagnosed, including via VUS resolution)
- Significant focus on genetic family testing
- Variant of uncertain significance (VUS) validation studies to complete in 4Q24
  focused on >1100 patients identified in the U.S. with VUSs

* Prevalence estimated at 1.5 patients per million population, based on available literature
As of December 31, 2023, Pharming has identified >840 diagnosed APDS patients in global markets
>730 of these patients are in key global launch markets in the U.S., Europe, the U.K., Japan, Asia Pacific, Middle East, and Canada with total prevalence of ~2000 APDS patients

Hiding in plain sight: Patient finding strategy

Medical education to raise awareness of APDS and share leniolisib data

- Conferences and congresses
- Abstracts
- Publications

AMCP NEXUS

American College of Allergy, Asthma & Immunology

IPIC2023 INTERNATIONAL PRIMARY IMMUNODEFICIENCIES CONGRESS

American Academy of Allergy Asthma & Immunology

Genetic testing

- Sponsored, no-cost testing program navigateAPDS by Pharming
- Assistance from Genetic counselors
- Partnering with genetic testing companies to identify APDS patients

Family testing

- Inherited disease* but most APDS patients do not have diagnosed family members
- Cooperating with clinicians to educate/encourage family testing
- Genetic testing offered through partner Genome Medical

VUS resolution

- Validation studies with various laboratories to confirm which Variants of Uncertain Significance (VUSs) should be classified as APDS
- Diagnose additional APDS patients amongst those who have clinical symptoms and a VUS test result (>1,100 patients in U.S.)**
- Variant curation (ClinGen, Genomenon)
- Functional testing (PI3K pathway activity)
- Multiplexed assays of variant effect (MAVE) studies
- Completion of studies during 4Q24

*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.
**To date Pharming has identified more than 1,100 patients in the U.S. with VUSs. As results become available, patients with validated variants could be diagnosed with APDS and be eligible for Joenja® treatment.

Joenja® – looking beyond FDA approval

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Europe – awaiting CHMP opinion on MAA

Israel marketing authorization received April 30, 2024

Japan clinical study: Patient enrollment is now complete

PMDA filing following completion of appropriate clinical trials

U.K., CAN, AUS submissions under regulatory review

Approvals in 2024-25* **

Pediatric study for 4 to 11 years

Enrollment completed

Pediatric study for 1 to 6 years ongoing

First patient dosed November 2023, enrollment continuing as planned

Expanded Access and Named Patient Programs

Initiate leniolisib development for PIDs with immune dysregulation (Phase II trial)

* In the U.K., Pharming filed an MAA on March 12, 2024 through the International Recognition Procedure (IRP) on the basis of FDA approval. The MAA was validated on April 17, 2024. The MHRA has 110 days from the date the IRP submission is validated, with an optional clock stop at Day 70, to review and issue its decision

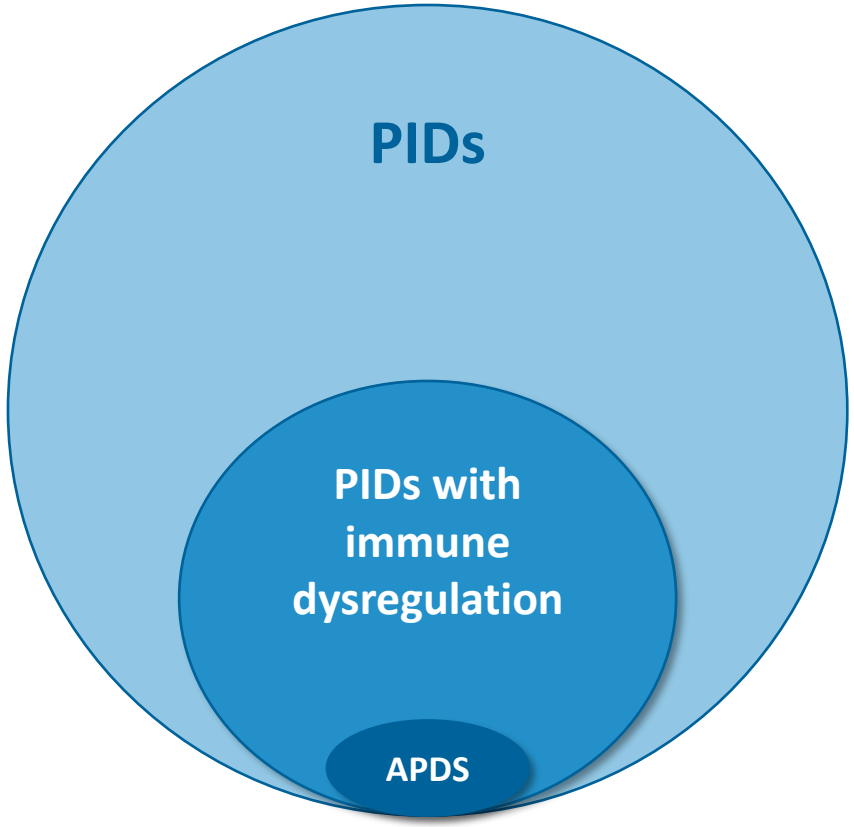
** Anticipate regulatory action in 2024 for Canada and in 2025 for Australia

Primary Immunodeficiencies (PIDs) with immune dysregulation

PIDs are a broad group of disorders[1] 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[2]

APDS is an example of a PID with immune dysregulation



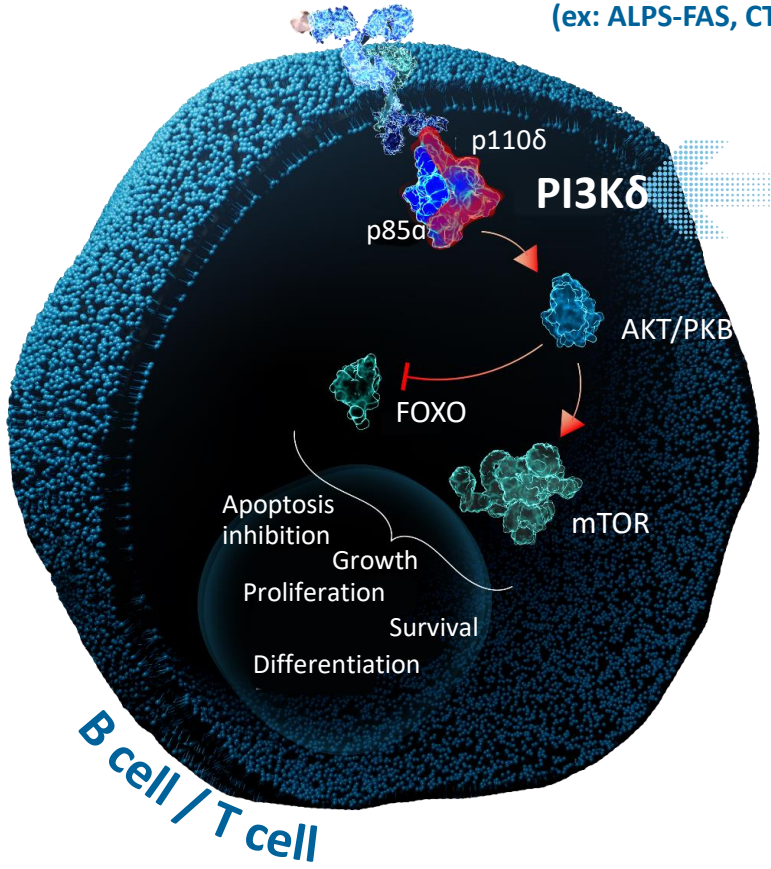
Not to scale with population sizes

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

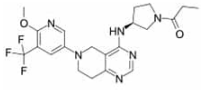
Given importance of PI3Kδ in B & T cells, immune dysregulation in PIDs can occur via alterations in PI3Kδ signaling

Altered PI3Kδ signaling can occur in multiple PID genetic disorders beyond APDS

(ex: ALPS-FAS, CTLA4, PTEN) [1-4]



leniolisib



High unmet medical need

- no approved therapies other than Joenja® (leniolisib) for APDS:

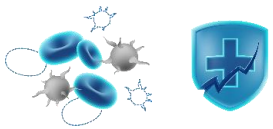
SOC immunosuppressives (e.g. rapamycin) have limited efficacy and significant tolerability concerns

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

Clinical manifestations, disease onset and severity similar to APDS [5-8]

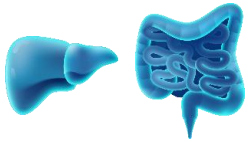
Lymphoproliferation

- 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

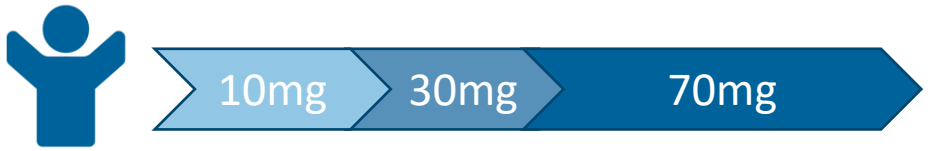
Lymphoma

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

1. Volkl et al. Blood 2016; 128(2):227-238. 2.Tsujita, et al. J Allergy Clin Immunol. 2016;138(6):1872-80. 3. Browning et al. J Med Genet. 2015;52(12):856-59. 4. Heindl et al. Gastroenterology 2012;142:1093-96. 5. Coulter TI, et al. *J Allergy Clin Immunol*. 2017;139(2):597-606. 6. Rao VK and Oliveria JB. Blood 2011; 118(22):5741-51. 7. Westerman-Clark et al 2021; Schwab C, Gabrysch A, Olbrich P, Patiño V, Warnatz K, et al. J Allergy Clin Immunol. 2018;142(6):1932-1946. 8. Eissing M, Ripken L, Schreibelt G, Westdorp H, Ligtenberg M, Netea-Maier R, Netea MG, de Vries IJM, Hoogerbrugge N. Transl Oncol. 2019;12(2):361-367

PIDs linked to PI3Kδ signaling – Phase II study design

Phase II proof of concept clinical trial – single arm, open-label, dose range-finding study (N=12)



- Patients with PIDs linked to PI3Kδ signaling, e.g. ALPS-FAS[1], CTLA4 haploinsufficiency[2], PTEN deficiency[3]
- 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

NIH 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)

1. Rao VK and Oliveria JB. How I treat autoimmune lymphoproliferative syndrome. Blood 2011; 118(22):5741-51
2. 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
3. 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

PIDs linked to PI3Kδ signaling – patient prevalence

Epidemiology of PIDs linked to PI3K signaling suggests treatable population of ~5/million[1]

Patients identified to date included in table below

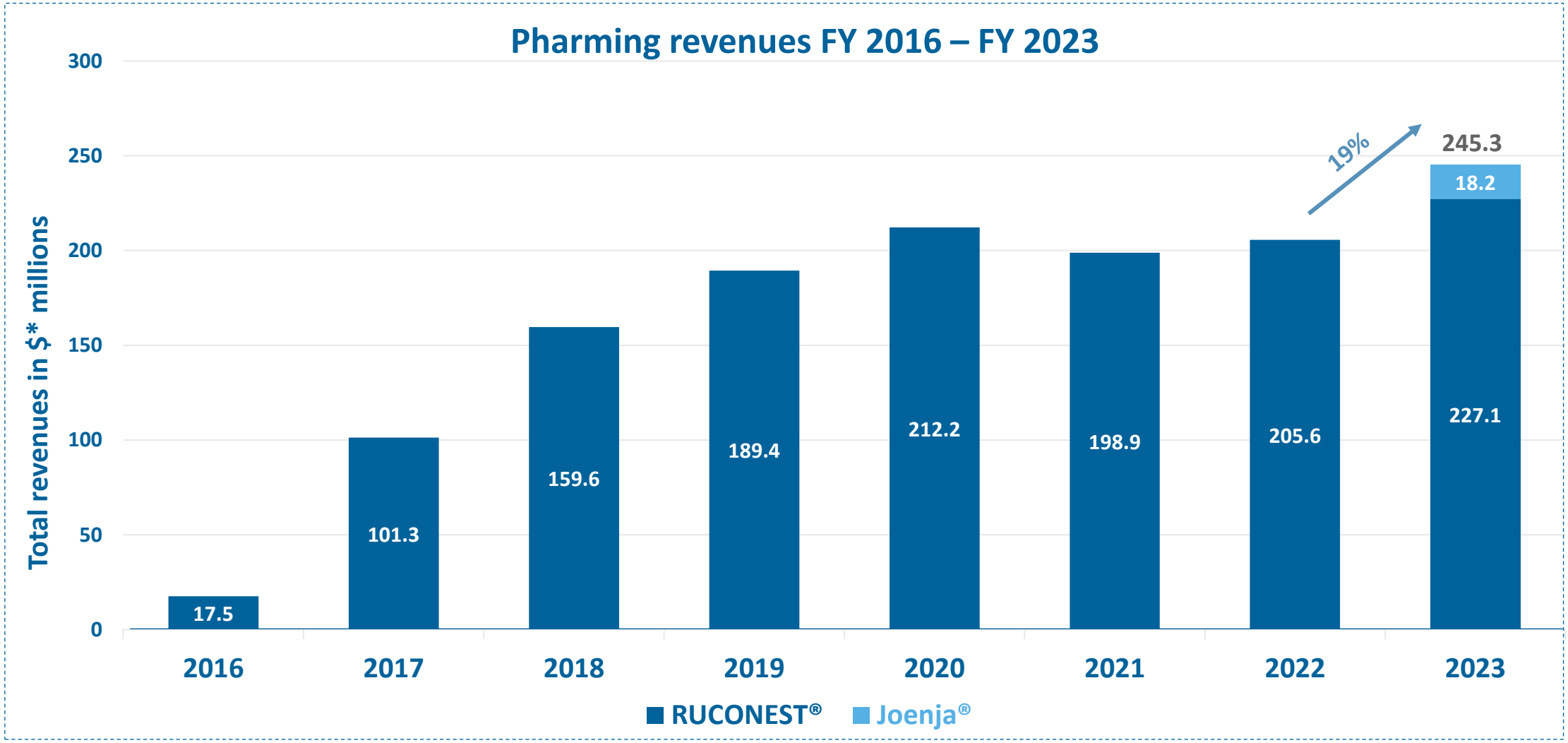
Genetic PID Type	Publication/cohort/registry	Cohort Size
ALPS-FAS	NIH protocol cohort ESID registry[2] Price et al 2014[3]	~500 236 150
CTLA4	Egg et al 2022[4] Schwab et al 2018[5] NIH protocol cohort ESID registry[2]	173 133 ~100 38
PTEN	All PTEN PID patients reported across publications	~88 [6]

1. Estimate of 5 patients per million is based on Pharming literature review, KOL feedback and review of patient registries. Estimate based on proportion of ALPS-FAS and CLTA4 haploinsufficiency patients deemed to be candidates for treatment.
2. Thalhammer et al J Allergy Clin Immunol 2021;148:1332-41
3. Price et al. Blood. 2014;123:1989-1999
4. Egg et al. J Allergy Clin Immunol 2022;149:736-746
5. Schwab et al. J Allergy Clin Immunol 2018;142:1932-1946
6. PTEN PID patient number tabulation from Pharming unpublished literature review completed Feb 2023. Patients may be double counted if reported in more than 1 publication.

Pharming®

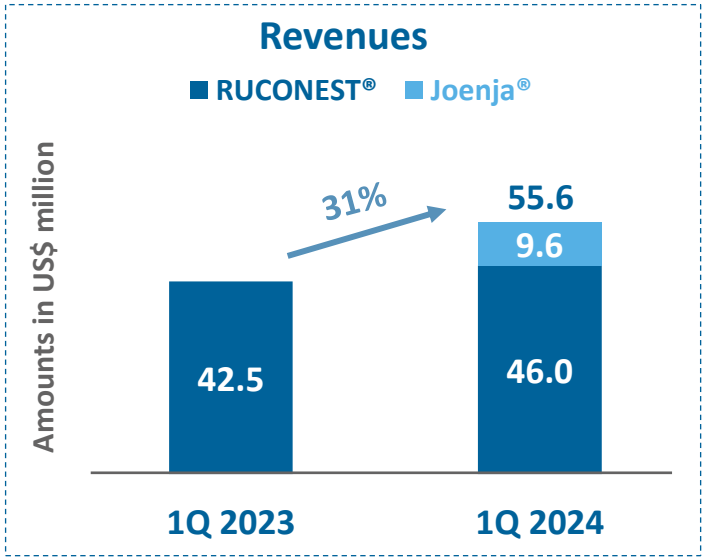
Financials and Outlook

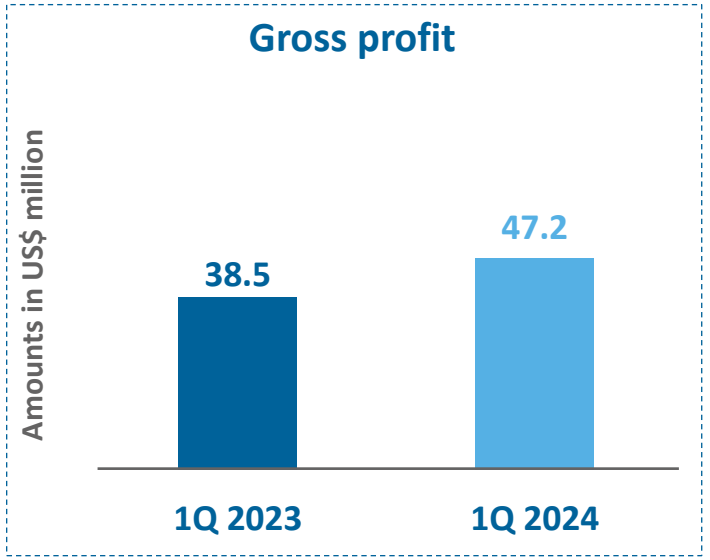
RUCONEST® and Joenja® driving revenue growth

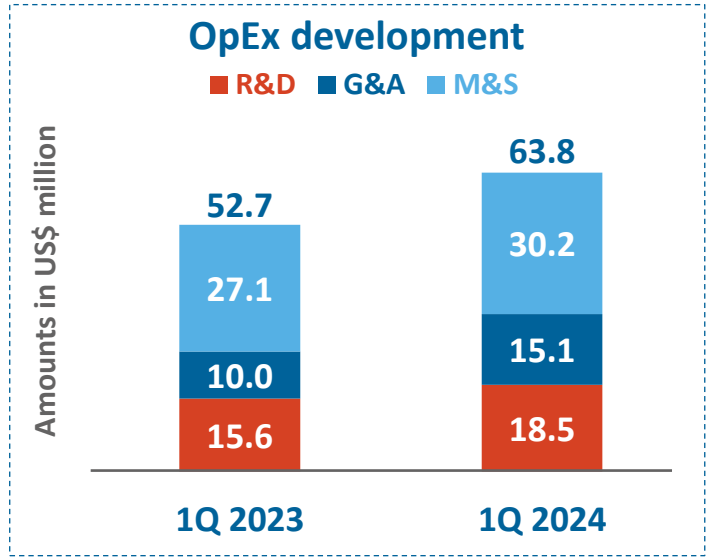


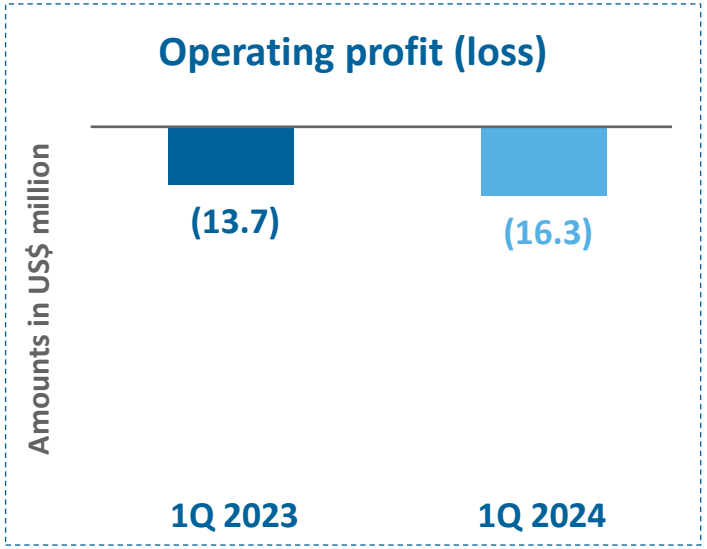
- From FY 2016 – FY 2020 Pharming Group reported earnings in EUR. Revenues during this time frame have been converted to USD. In 2021, Pharming Group began reporting earnings in USD.
- 4Q 2020 and 1Q 2021 quarterly fluctuations and volatility from COVID-19.

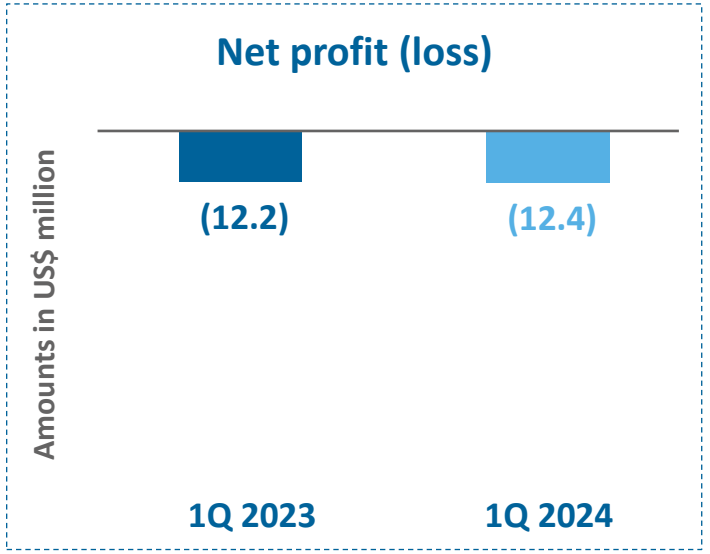
Financial highlights: 1Q 2024 vs 1Q 2023











Revenue breakdown by product and geographic segment

Amounts in US$ millions	1Q 2024			1Q 2023		
	RUCONEST®	Joenja®	Total	RUCONEST®	Joenja®	Total
Revenues						
US	44.8	8.5	**53.3**	40.9	-	**40.9**
Europe and RoW	1.2	1.1	**2.3**	1.6	-	**1.6**
Total Revenues	**46.0**	**9.6**	**55.6**	**42.5**	**-**	**42.5**

Pharming 2024 Outlook

- Total revenues between US$280 and US$295 million (14% to 20% growth), with quarterly fluctuations expected.
- Joenja® (leniolisib) U.S.: Continued progress finding additional APDS patients, supported by family testing and VUS validation efforts, and subsequently converting patients to paid therapy.
- Leniolisib ex-U.S.: Increasing revenues from commercial availability or through our Named Patient Program and other funded early access programs in key global markets.
- Completion of leniolisib clinical trials to support regulatory filings for approval in Japan and pediatric label expansion in key global markets.
- Progress towards regulatory approvals for leniolisib in the EEA, the U.K., Canada and Australia.
- Initiate and advance a Ph II clinical trial for leniolisib in PIDs with immune dysregulation linked to PI3Kδ signaling to significantly expand the long-term commercial potential of leniolisib
- Continued focus on potential acquisitions and in-licensing of clinical stage opportunities in rare diseases (e.g. immunology, hematology, respiratory and gastroenterology)

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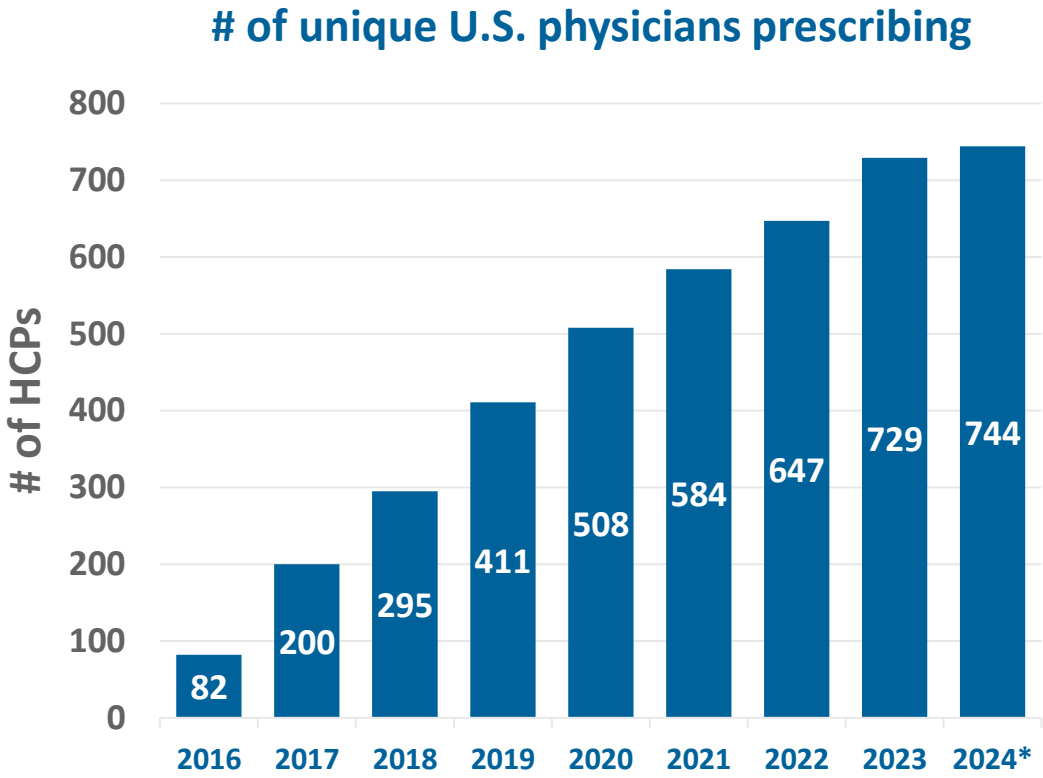
Appendix

RUCONEST® - Strong commitment to HAE community

Pharming®

- Strong patient organization support since 2000
- More than 740 U.S. physicians (and growing) prescribing RUCONEST®
- >2,000 patients with HAE have been prescribed RUCONEST®



*Data thru March 31, 2024

US HEREDITARY ANGIOEDEMA ASSOCIATION

HAEi HAE International

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

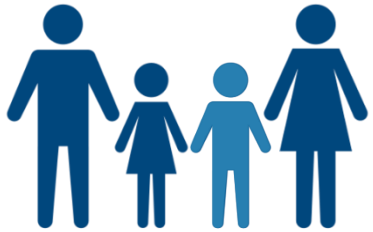
Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS)

Global prevalence estimated at 1.5 patients per million population*

To date, Pharming has identified >840 diagnosed APDS patients in select global markets**

(as of December 31, 2023)

A genetic test can provide a definitive diagnosis of APDS



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

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

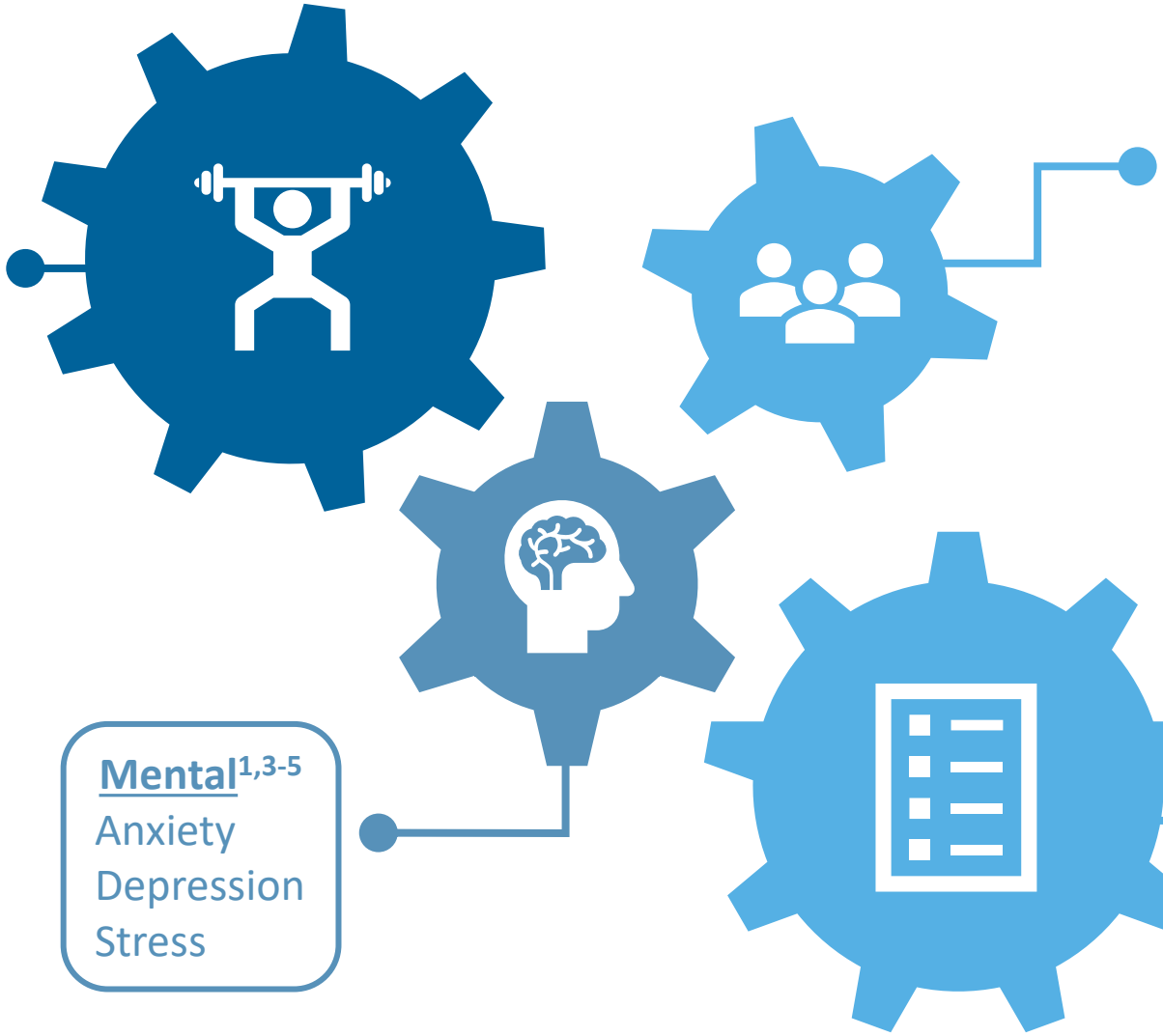
Without an indicated treatment specifically for APDS, physicians could only manage symptoms

*Size based on available literature

**>730 of these patients are in key global launch markets in the U.S., Europe, the U.K., Japan, Asia Pacific, Middle East, and Canada with total prevalence of ~2000 APDS patients

APDS can impact many facets of life

Physical[1,2]
Frequent infections
Swollen glands
Shortness of breath
Coughing/wheezing
Chest or joint pain
Fatigue
Inability to exercise
Hearing loss
Diarrhea
Skin problems



Social[3,4]
Missing school, work, or daily activities

Treatment Burden[1-4]
Frequent hospitalizations
Surgeries
Visiting multiple doctors
Invasive or time-consuming treatments

Mental[1,3-5]
Anxiety
Depression
Stress

APDS, activated phosphoinositide 3-kinase δ 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.

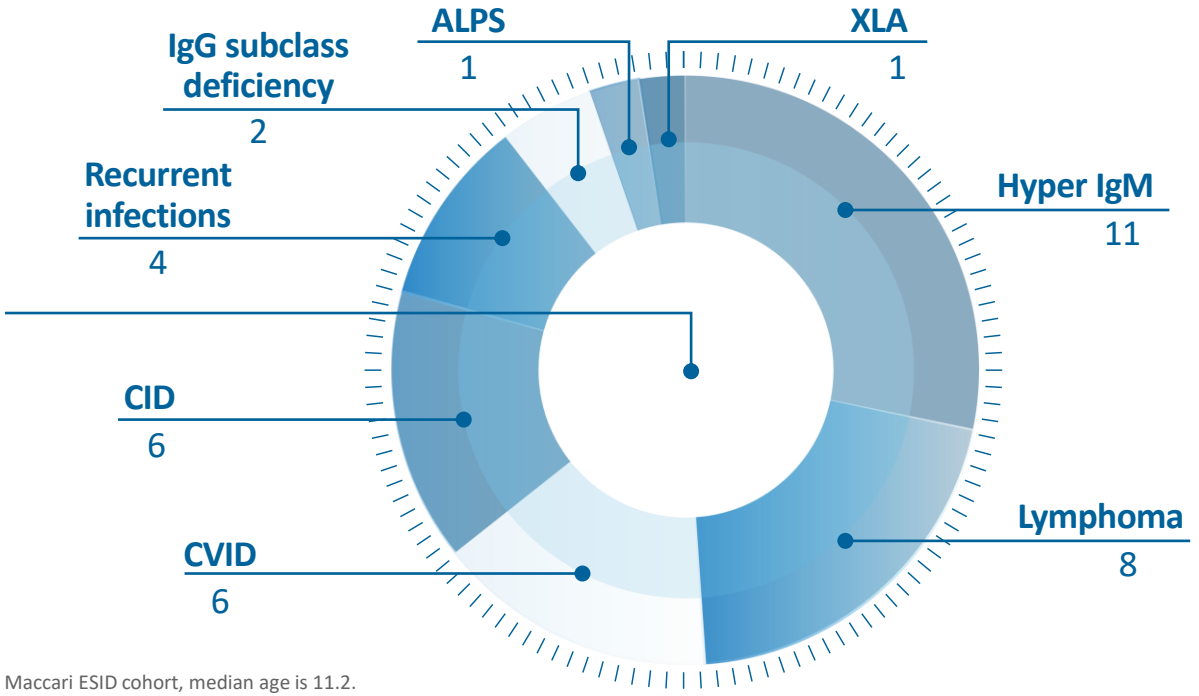
Heterogeneous, evolving symptomology can often lead to missed diagnoses

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]



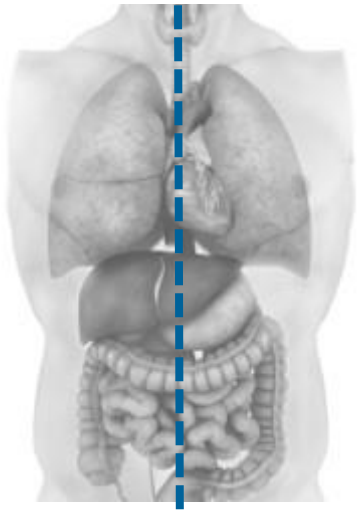
Improved identification of symptoms, increased genetic testing, and earlier diagnosis are needed

*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.

Management for APDS[1,2] prior to Joenja®

Immune Deficiency

- Antimicrobial prophylaxis
- Immunoglobulin replacement therapy



Immune Dysregulation

- Corticosteroids
- Other immunosuppressants
- mTOR inhibitors

None of these therapies are FDA-approved for APDS treatment

Hematopoietic stem cell transplant

APDS, activated phosphatidylinositol 3-kinase δ syndrome; IRT, immunoglobulin replacement therapy; mTOR, mammalian target of rapamycin; PI, primary immunodeficiency; PIRD, primary immune regulatory disorder.

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. Chan AY, et al. *Front Immunol*. 2020;11:239.
4. Chinn IK, et al. *J Allergy Clin Immunol*. 2020;145(1):46-69.

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.

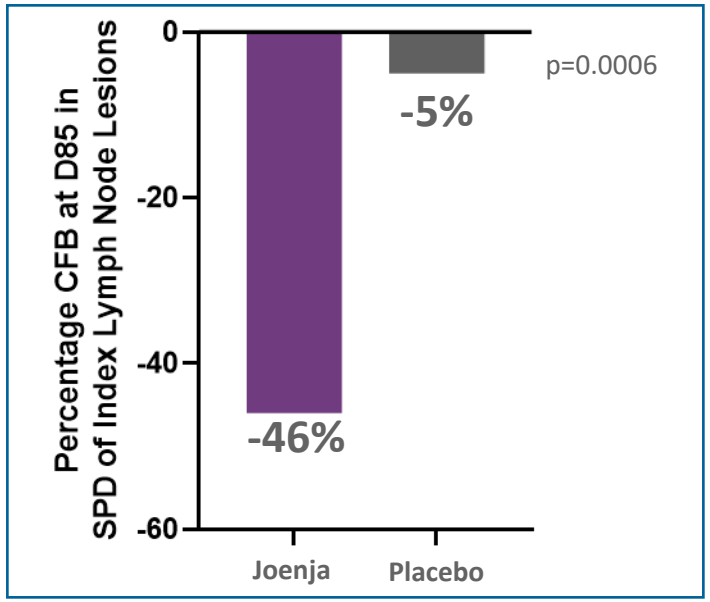
Joenja® addresses the underlying cause of APDS to help restore immune balance – Phase 3 co-primary endpoints

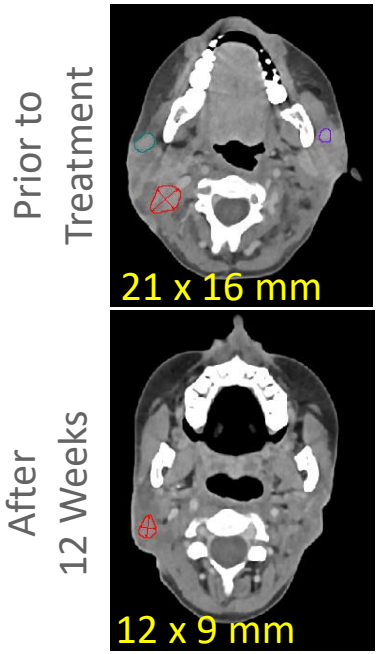
At 12 weeks Joenja® decreased lymphadenopathy and increased naïve B cells

Immune Dysregulation

Change from baseline in index nodes*

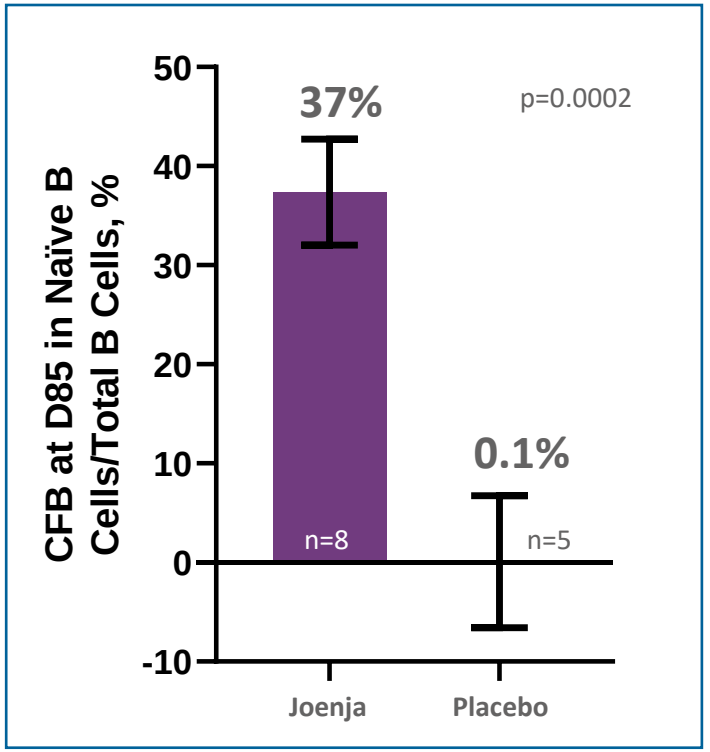
Log_{10}-transformed SPD of index lesions	Joenja (n=18)	Placebo (n=8)
Baseline mean (SD)	3.03 (0.42)	3.05 (0.39)
Change from baseline, LS mean (SE)	-0.27 (0.04)	-0.02 (0.05)
Difference vs placebo (95% CI)		-0.25 (-0.38, -0.12)





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

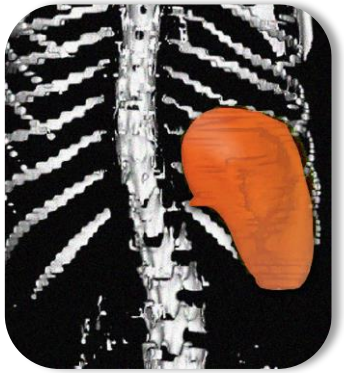
at week 12

27%

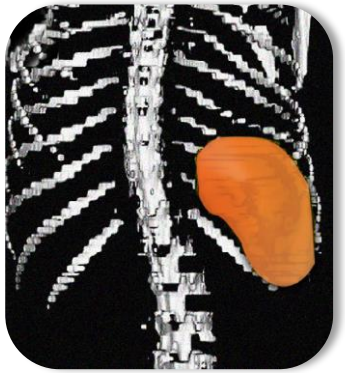
reduction in 3D spleen volume*

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



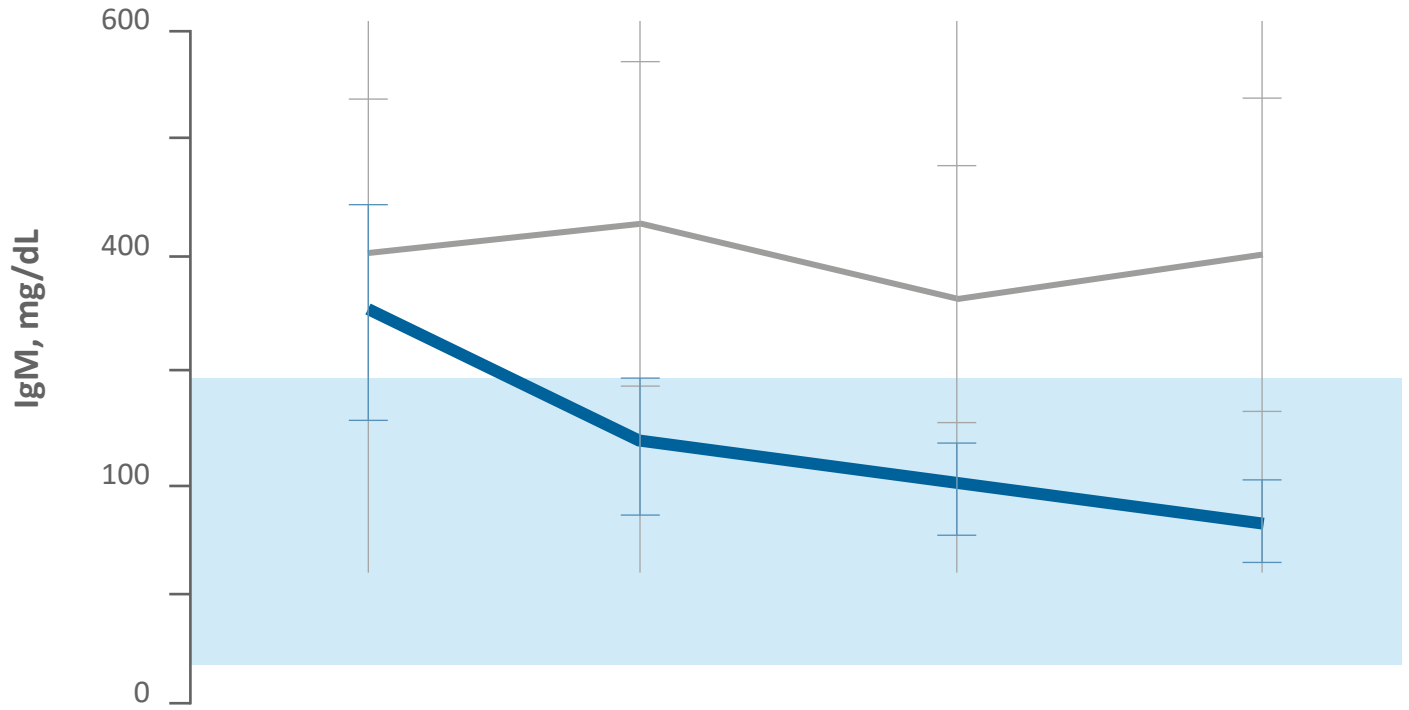
Actual patient images of a 17-year-old male. As individual results vary, images may not be representative of all patients.

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.

An exploratory end point showed Joenja® reduced IgM levels

Mean serum IgM rapidly reduced to within normal limits



		Baseline	Week 4	Week 8	Week 12
Joenja®	n	21	20	21	21
Placebo	n	10	10	10	10

- In the Joenja® arm, IgM was elevated above normal limits in 6 patients at baseline, and by week 12 was reduced in all, with 50% returning to within normal limits
- In contrast, IgM was elevated above normal limits at baseline in 4 patients in the placebo arm, and by week 12 levels remained stable or elevated, with 0% returning to within normal limits

Error bars are standard error of the mean. Safety analysis set (N=31) shown. Blue box indicates IgM normal range.
Soluble biomarkers, including IgM, were prespecified exploratory endpoints in the protocol. Although an observational decrease in IgM was noted in some patients, no statistical significance can be made from this analysis, and no conclusions should be drawn.
Rao VK, et al. Blood. 2023;141(9):971-983

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

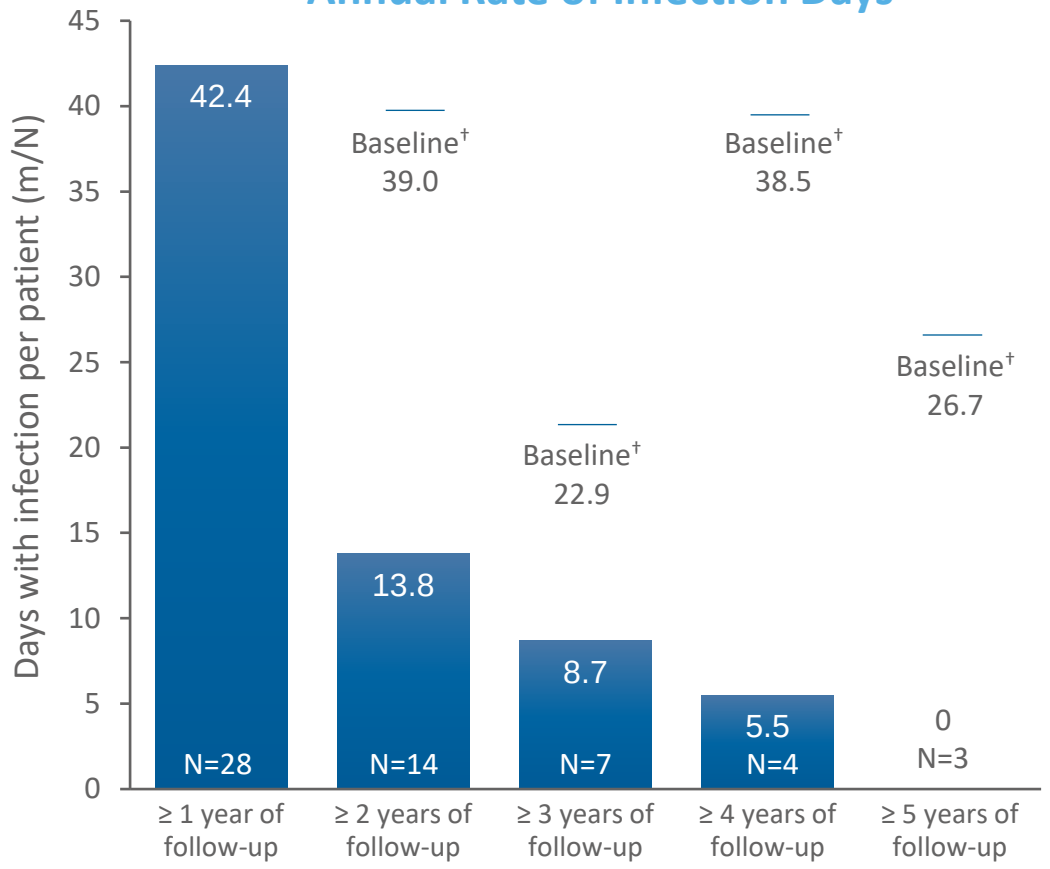
Across all trials[2]

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

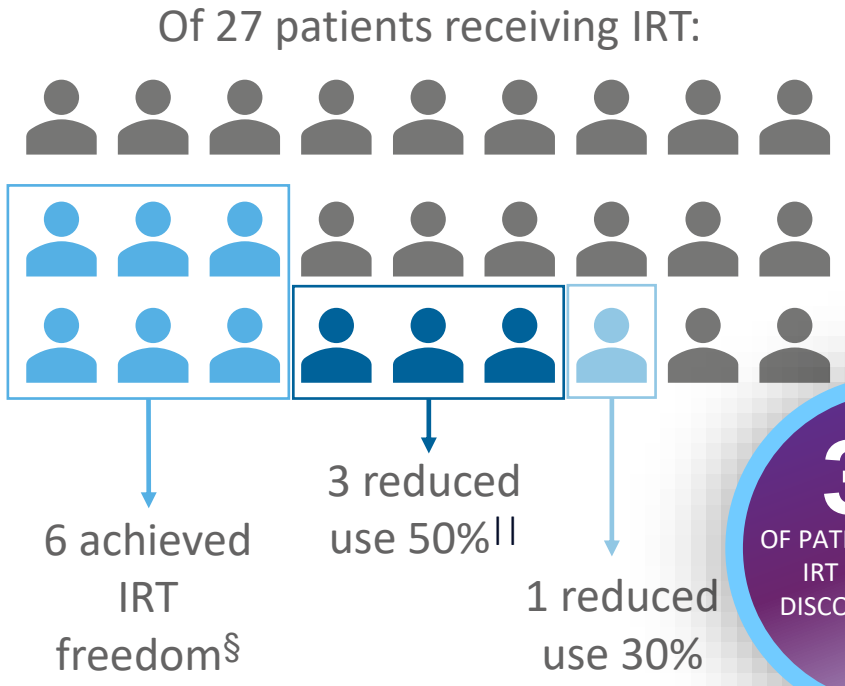
A patient with multiple occurrences of an AE is counted only once in the AE category. Only AEs occurring at or after first drug intake are included.
*Includes dermatitis atopic and eczema. †Includes tachycardia and sinus tachycardia.
AEs, adverse events; **ALT**, alanine aminotransferase; **AST**, aspartate 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.

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

Annual Rate of Infection Days*



Physician-reported IRT Reduction‡



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

Recent medical conference presentations (selected)

AMCP Nexus - Academy of Managed Care Pharmacy (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 - American College of Allergy, Asthma & Immunology (November 2023)

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

IPIC - International Primary Immunodeficiencies Congress (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).*

AAAAI - American Academy of Allergy, Asthma & Immunology (February 2024)

- *Clinical and Genetic Findings of Individuals Tested via the navigateAPDS Sponsored Genetic Testing Program*