



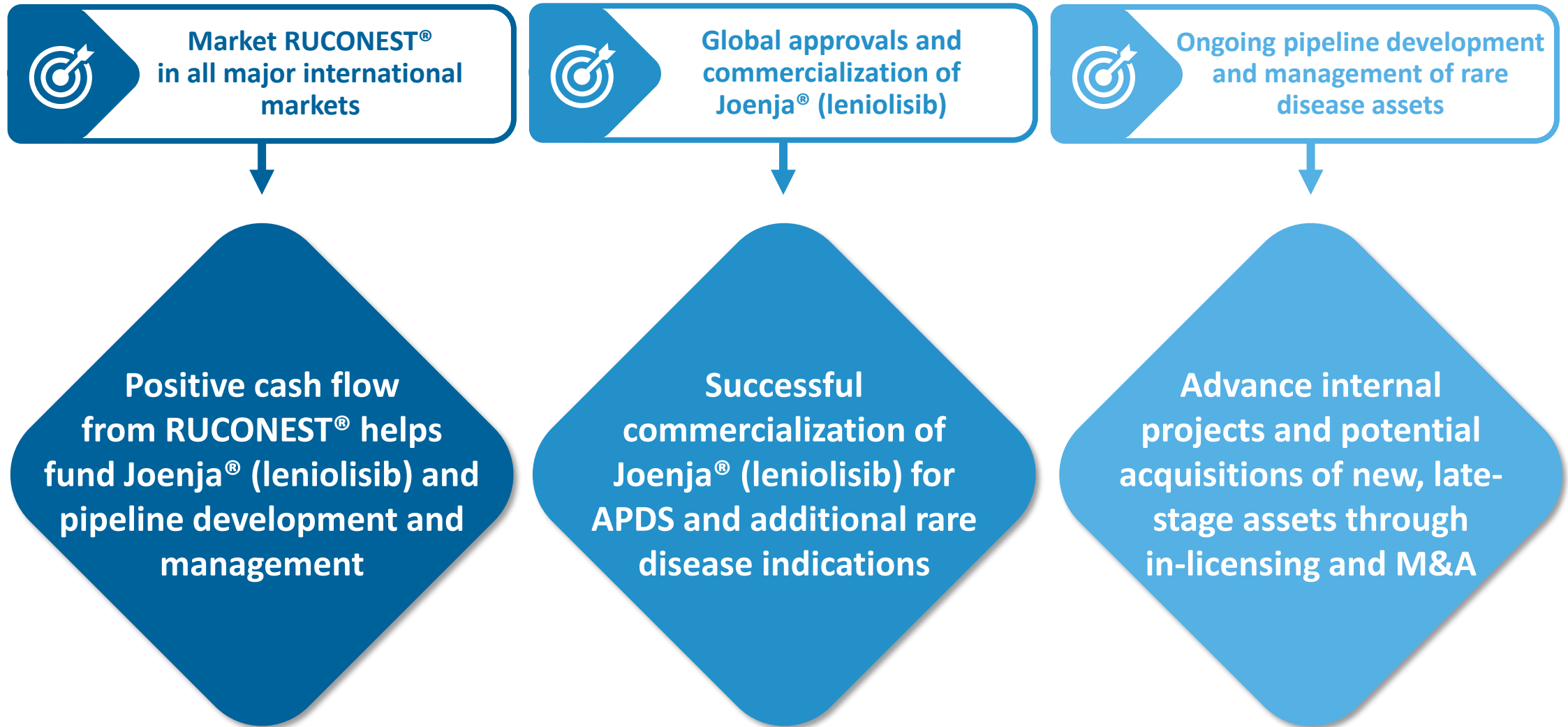
Pharming Group N.V.

Stifel European Healthcare
Summit

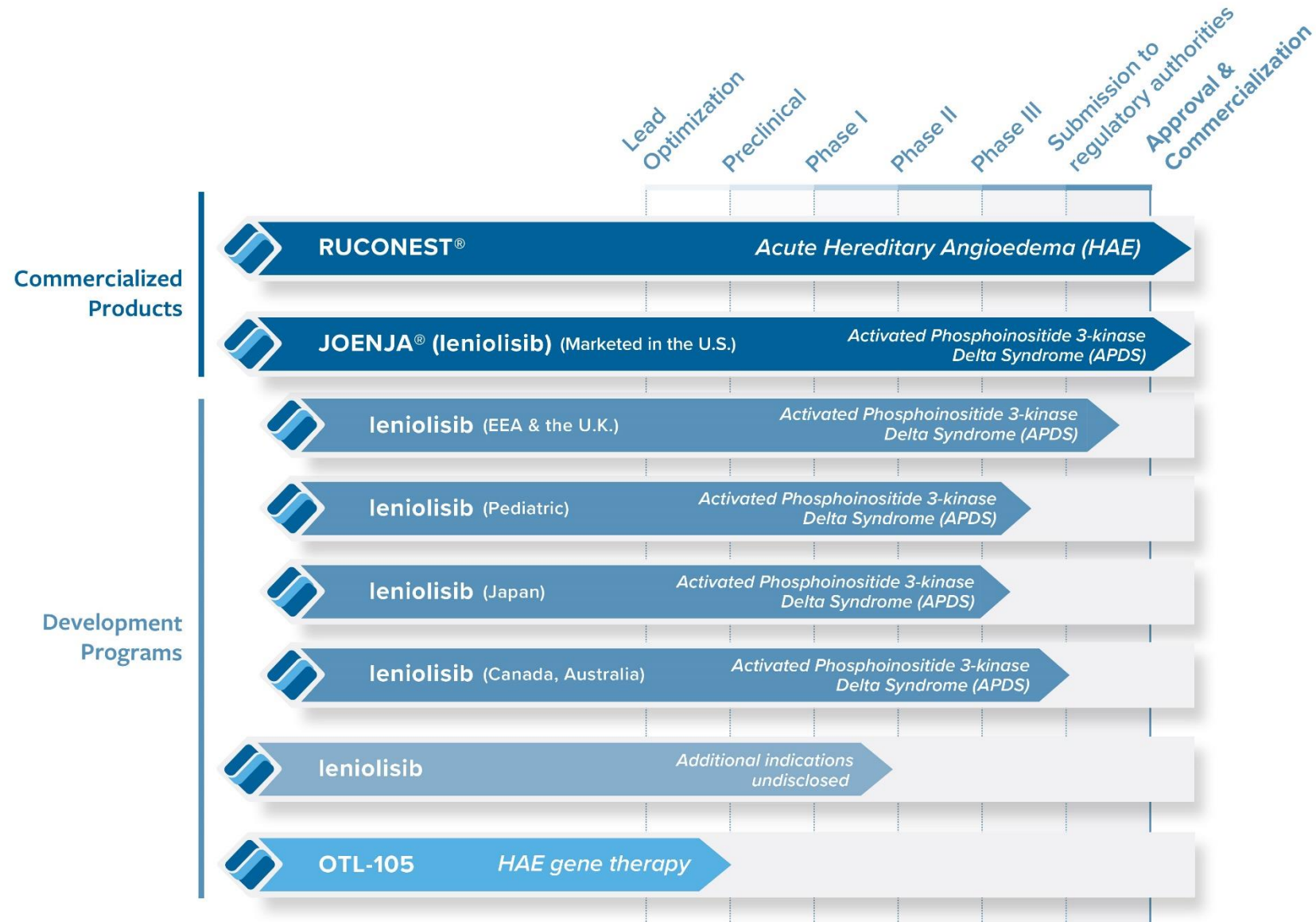
June 2023

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

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Pipeline – multiple commercial stage rare disease products





Dedicated sales force and marketing in US, EU, and MENA



Market access teams



Patient support and reimbursement teams



Disease educators and specialists for APDS and HAE



Medical Affairs teams

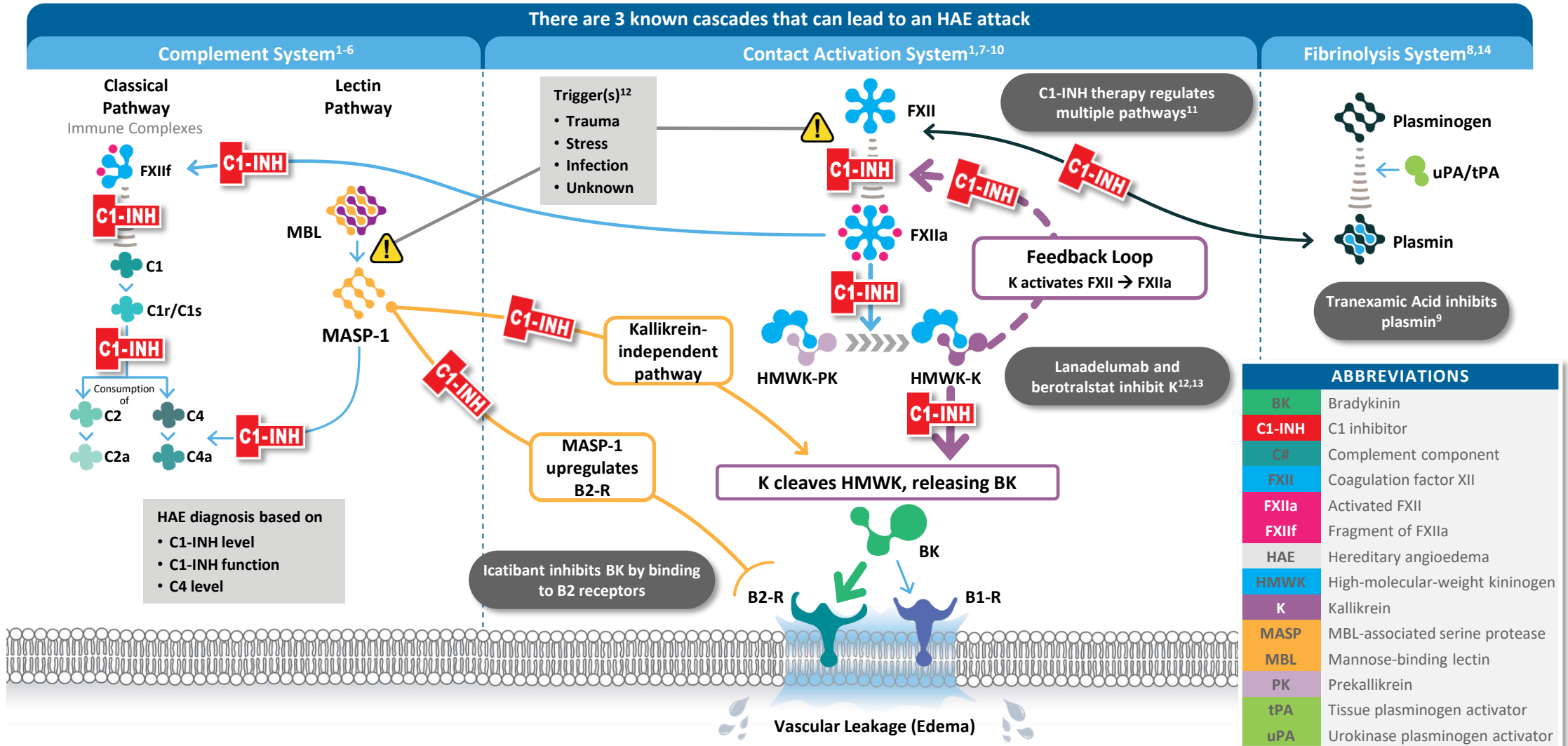


High conference penetration & Support for educational KOL speaker programs

 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.



RUCONEST® sales >US\$200m
(trailing 12 months)



Outlook of single digit revenue
growth for 2023



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% of acute attacks needed just
one dose of RUCONEST®¹



93% of attacks were stopped with
RUCONEST® for at least three days²



Patients are well managed and feel
confident to administer treatment
themselves³



Strong patient organization support since 2000



Over 700 physicians have prescribed RUCONEST® since 2014



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





APDS Overview

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



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

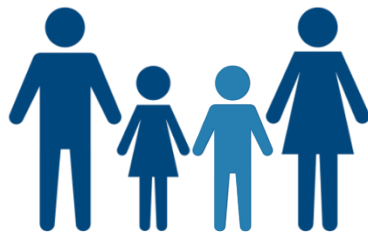
To date, Pharming has identified >500 of these patients

(as of December 2022 for US, Europe, UK, Japan, Canada, Australia)



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



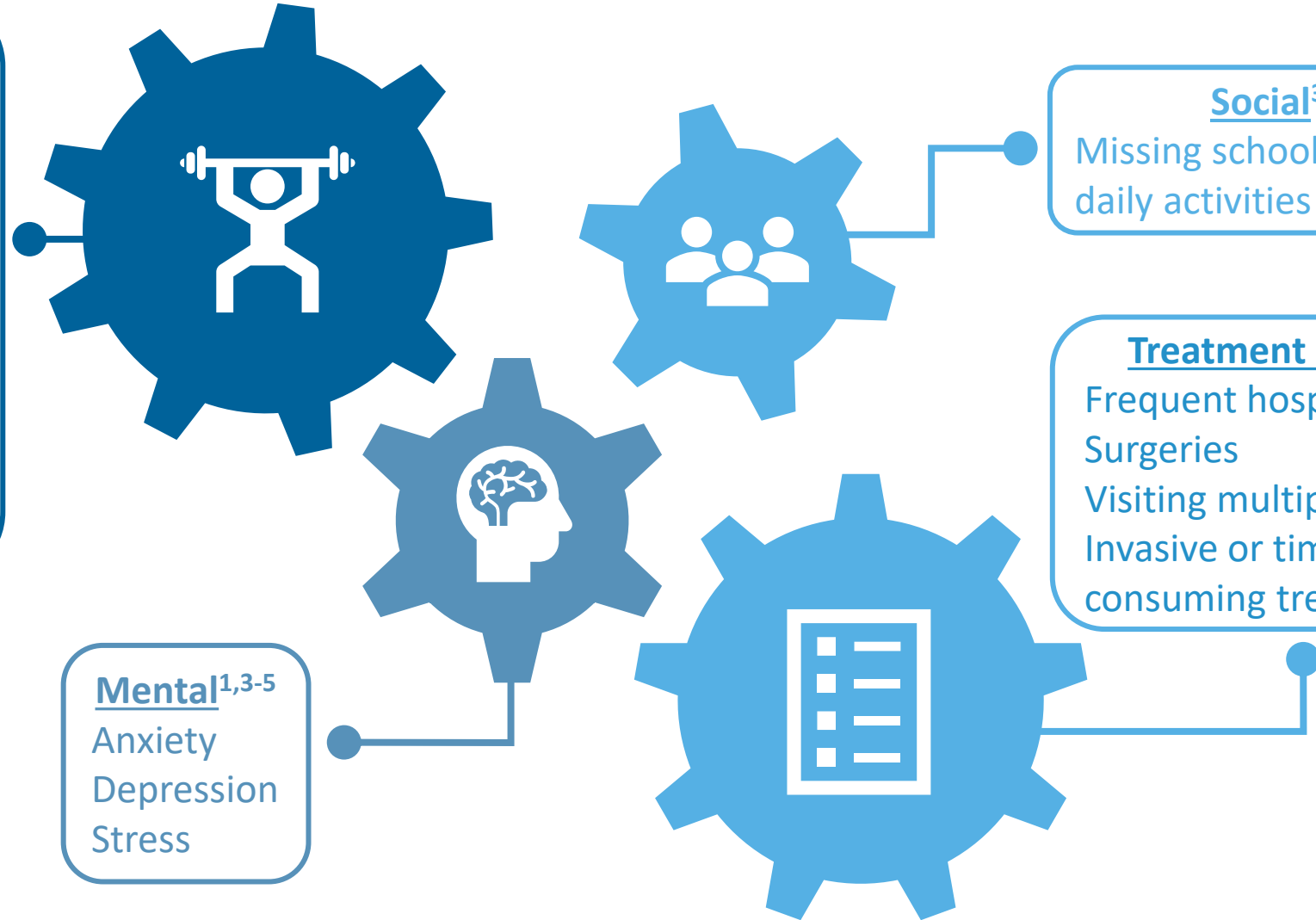
A genetic test can provide a definitive diagnosis of APDS

*Size based on estimate of 1.5 APDS patients per million (based on available literature) for US, Europe, UK, Japan, Canada and Australia

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 Burden¹⁻⁴

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.

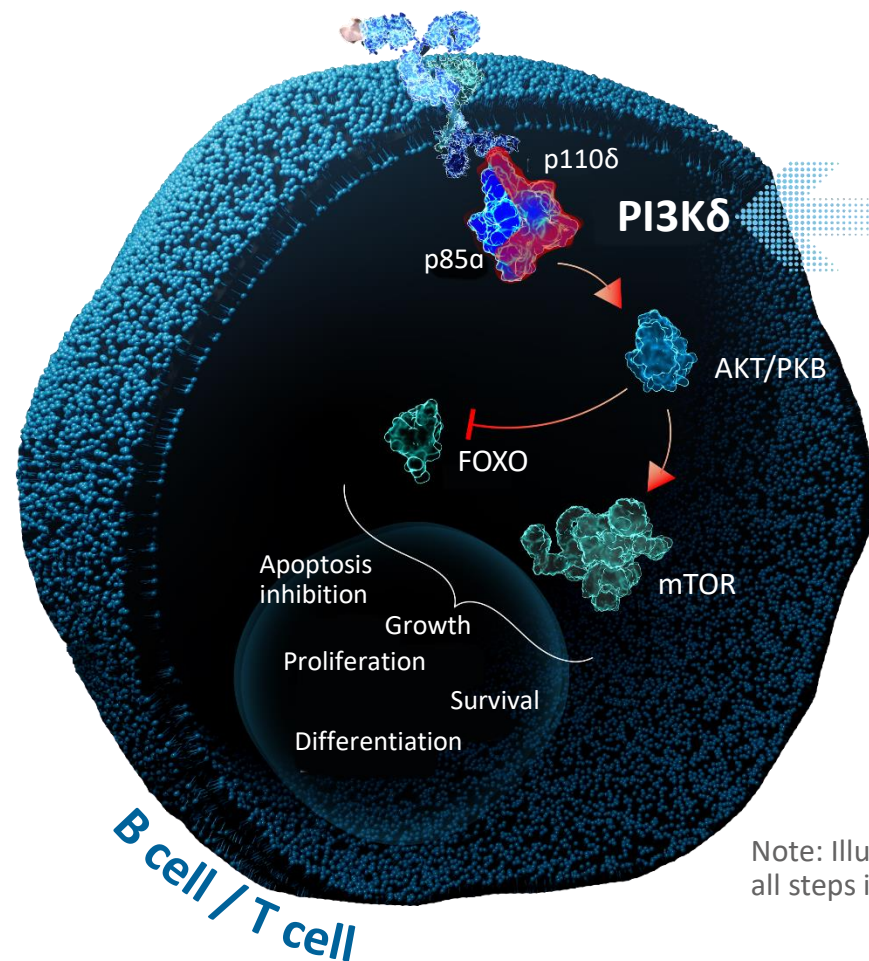
4. Jiang F, et al. *Allergy Asthma Clin Immunol.* 2015;11:27. 5. Kuburovic NB, et al. *Patient Prefer Adherence.* 2014;8:323-330.

Genetic defect leads to PI3K δ hyperactivity, disrupting immune cell balance

Hyperactive PI3K δ results in dysregulated B and T cell development¹⁻³

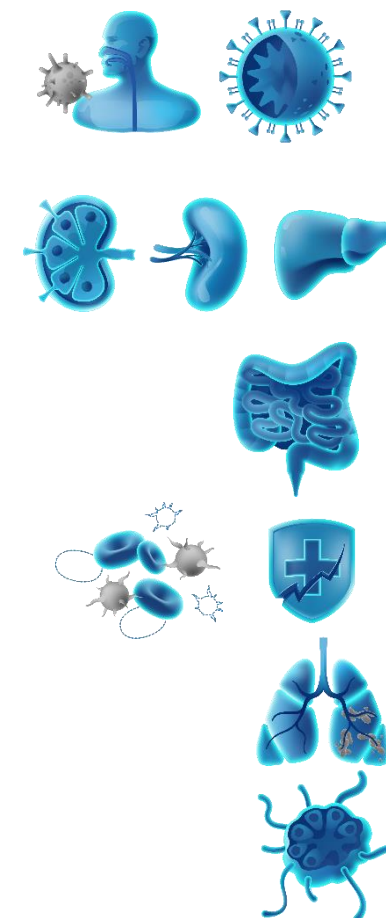


Immune imbalance leads to diverse signs and symptoms^{1,4-6}



The PI3K δ 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

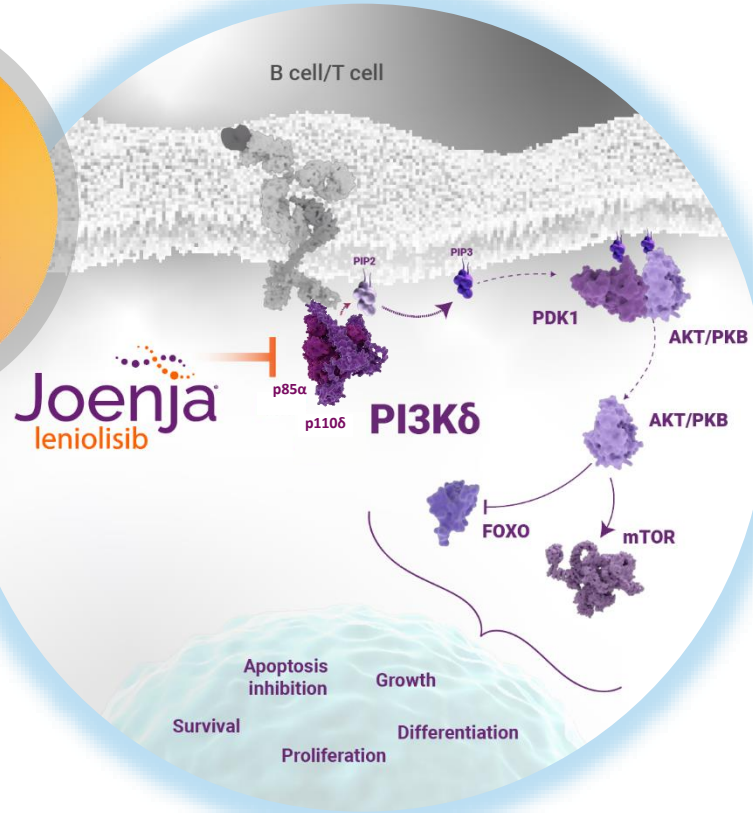
Lymphoma

FOXO, forkhead box O; mTOR, mammalian target of rapamycin; PI3K δ , 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.

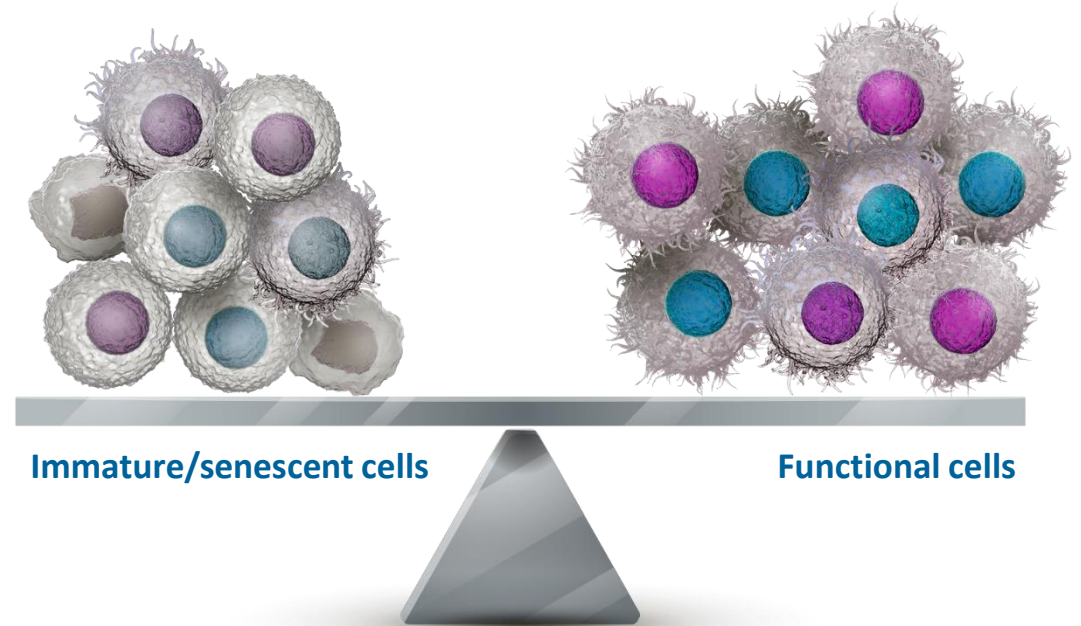
Joenja[®]: immune modulator that targets the root cause of APDS

JOENJA WAS DESIGNED TO TARGET THE ROOT CAUSE OF APDS TO HELP NORMALIZE THE HYPERACTIVE PI3Kδ PATHWAY¹⁻⁵



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

Joenja[®] facilitates a balanced PI3Kδ pathway to support proper immune function⁶



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)

FDA approval of Joenja®: a much-needed treatment for patients with APDS and another win for Pharming

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

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

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

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

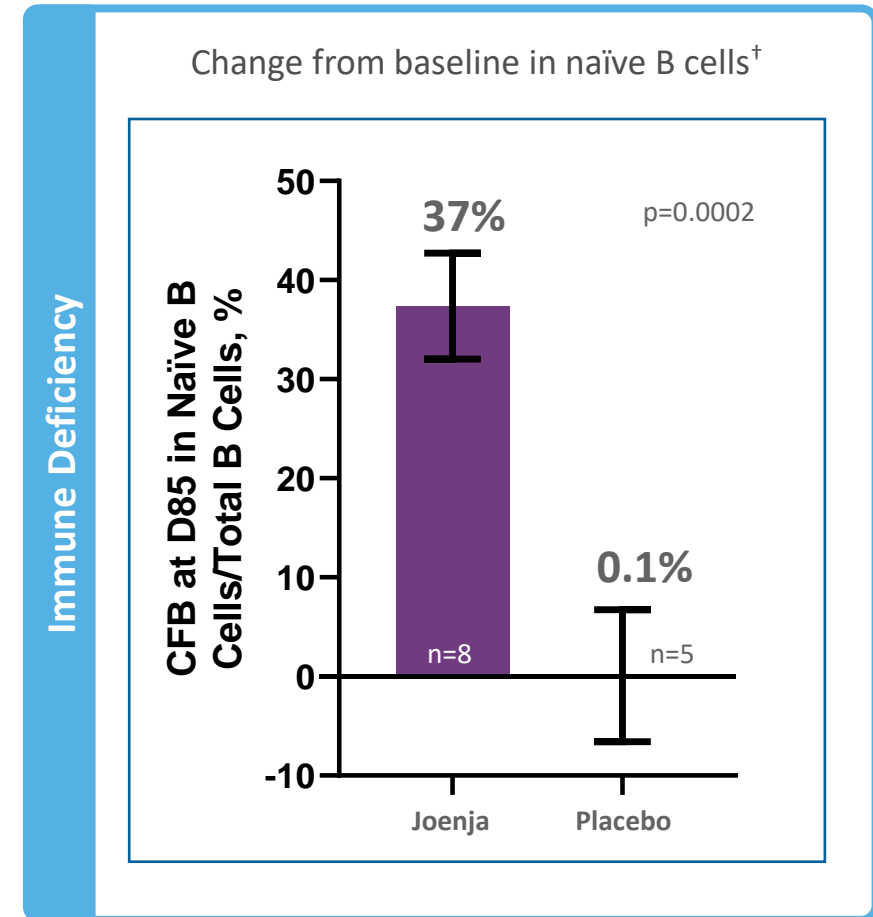
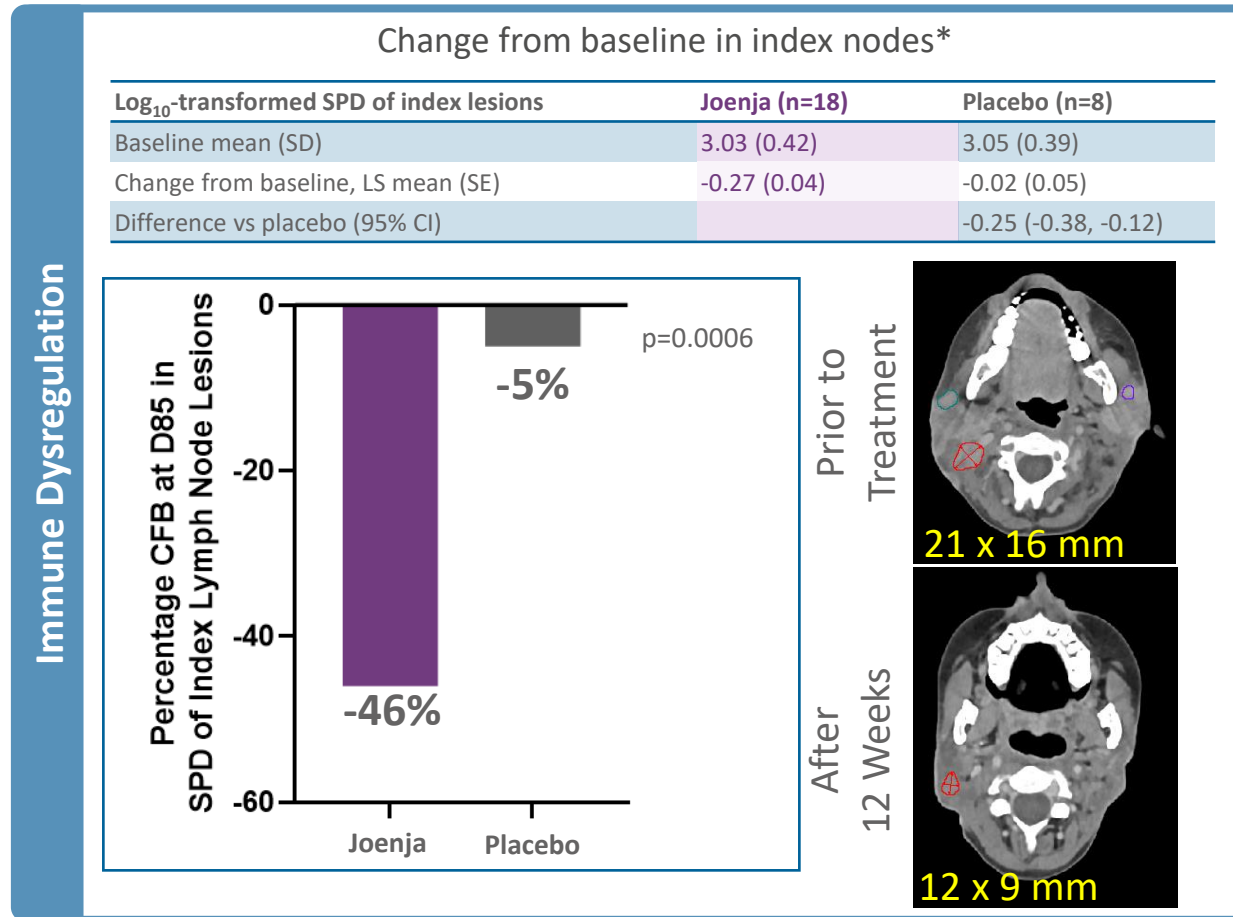
There were no drug-related serious adverse events or study withdrawals in Joenja® trials

Pharming is well-positioned to hit the ground running with Joenja®



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.

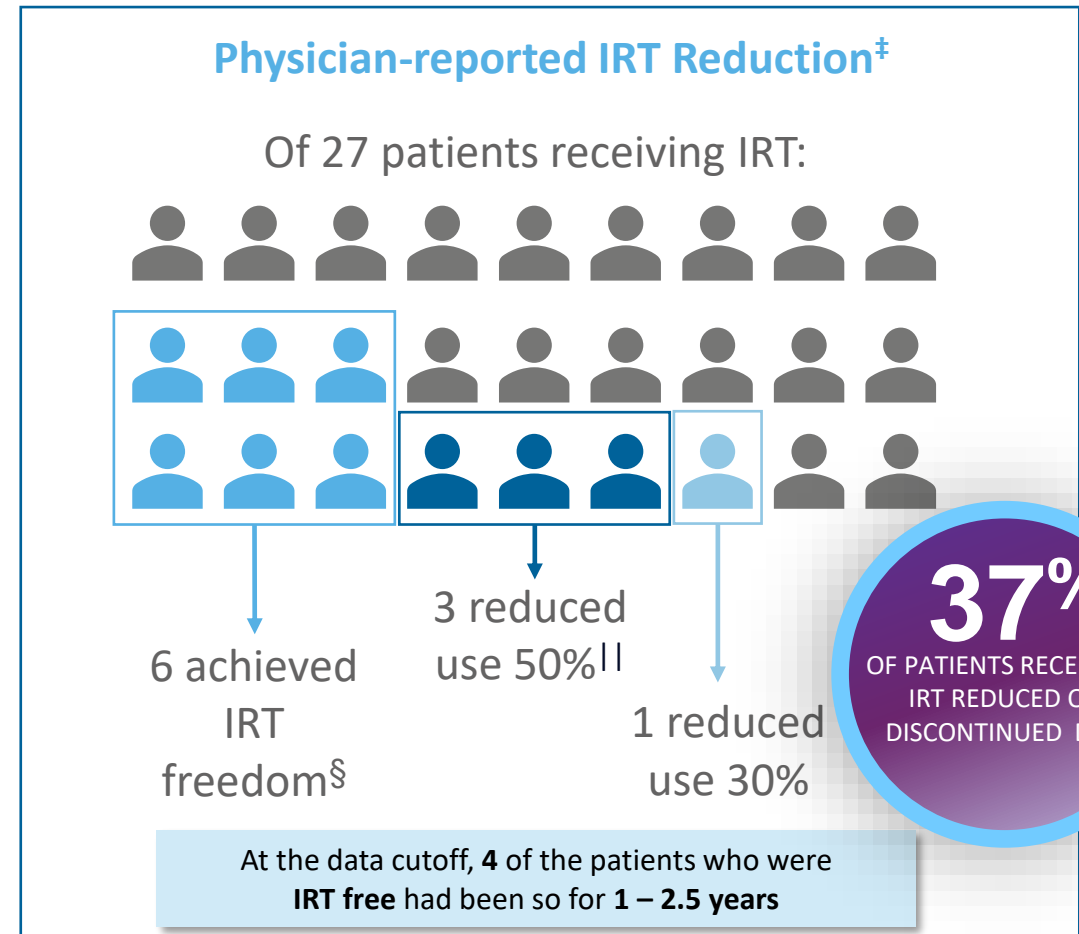
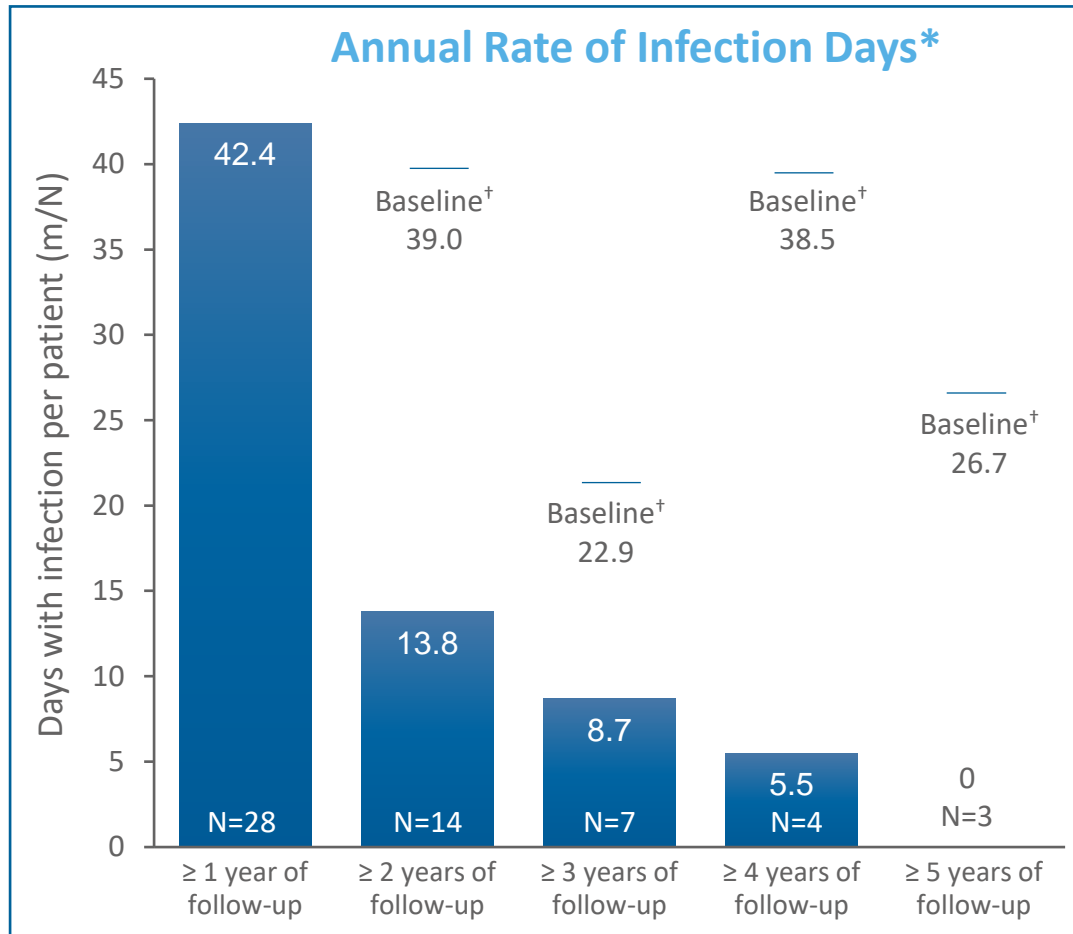
*The analysis excluded 2 patients from each treatment group due to protocol deviations and 1 Joenja patient having complete resolution of the index lesion identified at baseline.

†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

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. 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



Joenja[®] launched & reimbursed commercial shipments to patients commenced early April



Europe – CHMP opinion on MAA expected 2H23 (approval ~ 2 months later)



UK – MHRA filing expected 2H23 (approval ~2 months later)



Initiation of Japan clinical study in 1H23 (Orphan Drug Designation ODD granted May 2023)



Development ongoing for pediatric patients 4 to 11 years old



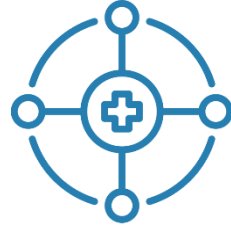
Initiation of second pediatric study in children 1 to 6 years in 3Q23



Commercial Field Team

Rare Disease Team of 27
focused on
Allergy/Immunology

Institutional Team of 27
focused on multiple
specialties



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



Support Services

- Dedicated support, education and resources for patients and caregivers through the APDS Assist patient support program
- APDS Care Coordinators provide support for onboarding, coverage assistance and financial support resources



Patient Access

- 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



Precision medicine targeting rare and genetically-defined patient population



First and only treatment indicated for APDS addressing high unmet need



Demonstrated efficacy and safety profile



Significant burden of disease

◆ Innovation:

- Pharming is committed to providing patients with rare disease the solutions they need

◆ Value:

- APDS is a progressive disease
- Joenja[®] designed to treat the root cause of APDS treating both immune deficiency and dysregulation

◆ 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

◆ Support:

- Pharming is committed to the APDS community through active grassroots engagement with advocacy groups such as the IDF and Jeffrey Modell Foundation

Annual Cost (WAC) – US \$547,500



Financials and Outlook



Strong underlying in-market demand for RUCONEST® including high, double digit, new patient enrollments in 1Q23



Disruptions have since resolved, but impacted February sales



Disruptions in reimbursement for some patients on U.S. government insurance programs impacted the entire HAE market in 1Q23



Pharming has since seen a recovery in sales



These market-wide factors caused a delay in shipments to patients



We are maintaining our outlook for low single digit RUCONEST® revenue growth in 2023



Strong start to our early April product launch



Pharming continues to engage with both national and regional payers



First commercial shipment of Joenja[®], with full reimbursement, ~two weeks after FDA approval



23 U.S. patients on paid therapy with Joenja[®] (through May 11, 2023)



The sales team continue to drive new patient enrollments



Good progress moving EAP and OLE patients to commercial drug



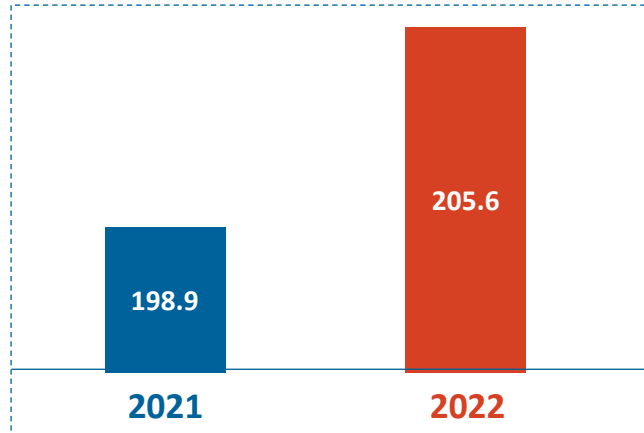
First revenues will be seen in the second quarter



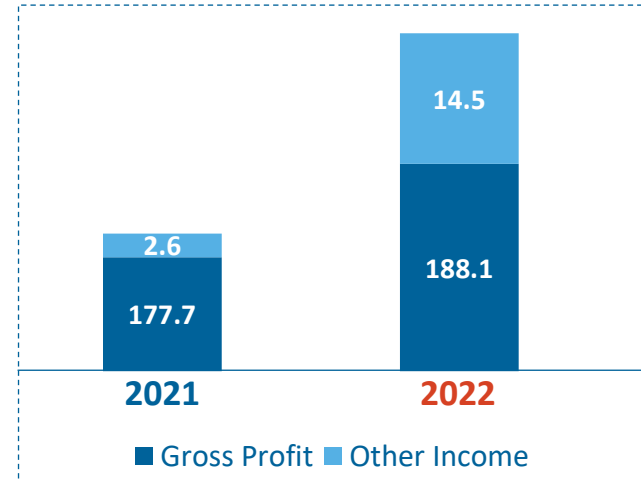
2Q 2023: \$10M commercial milestone payment and ~\$21.1M sale of PRV to Novartis

Pharming grew sales & investments in leniolisib

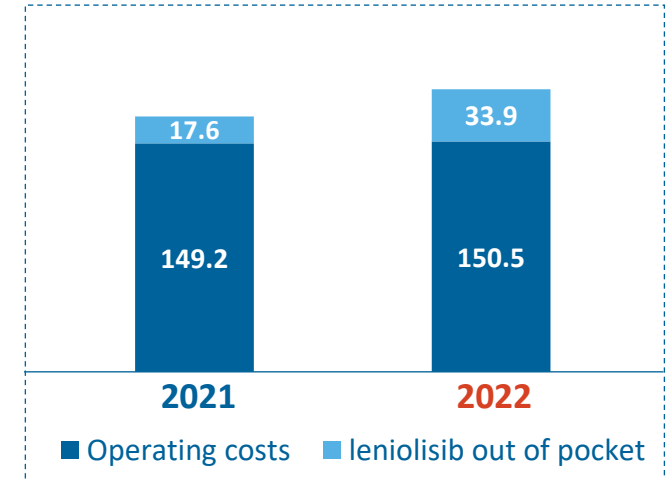
Revenue in US\$ million



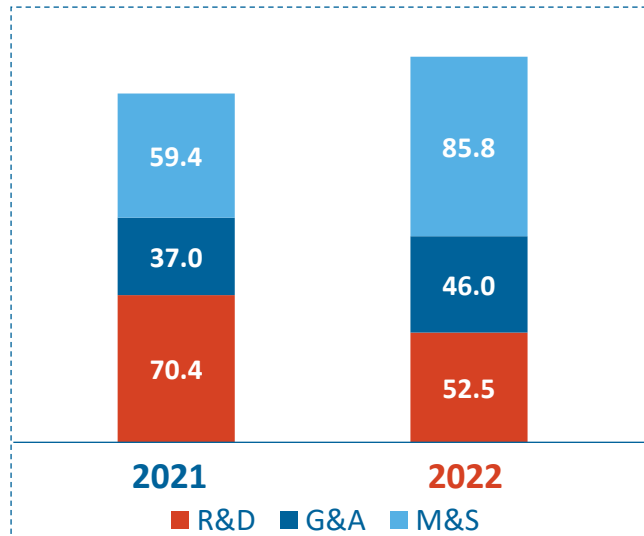
Gross Profit and Other Income in US\$ million



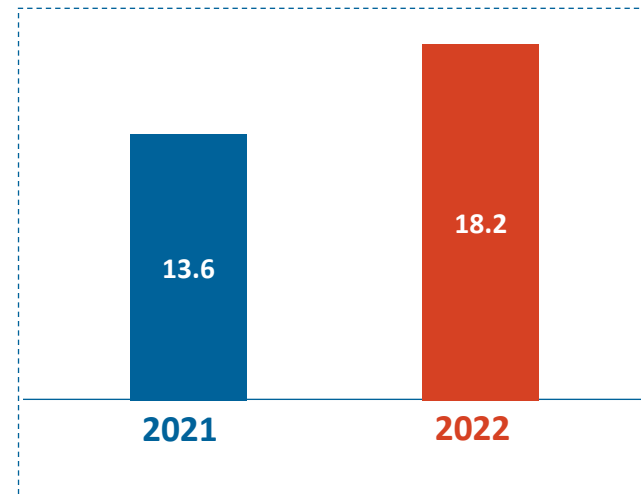
Operating costs in US\$ million



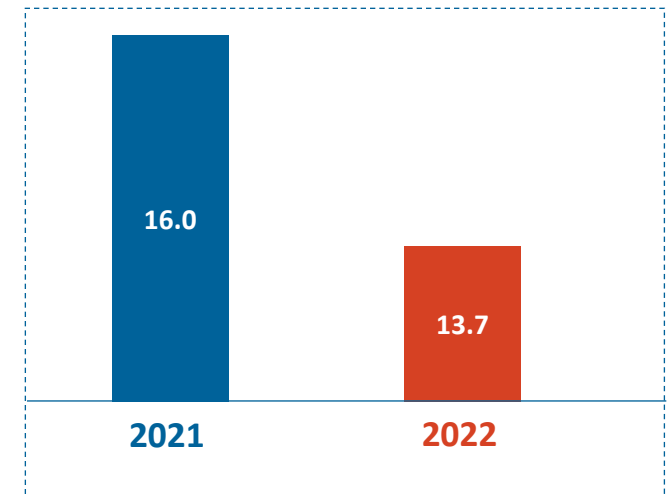
Cost category development in US\$ million



Operating Profit in US\$ million



Net Profit in US\$ million

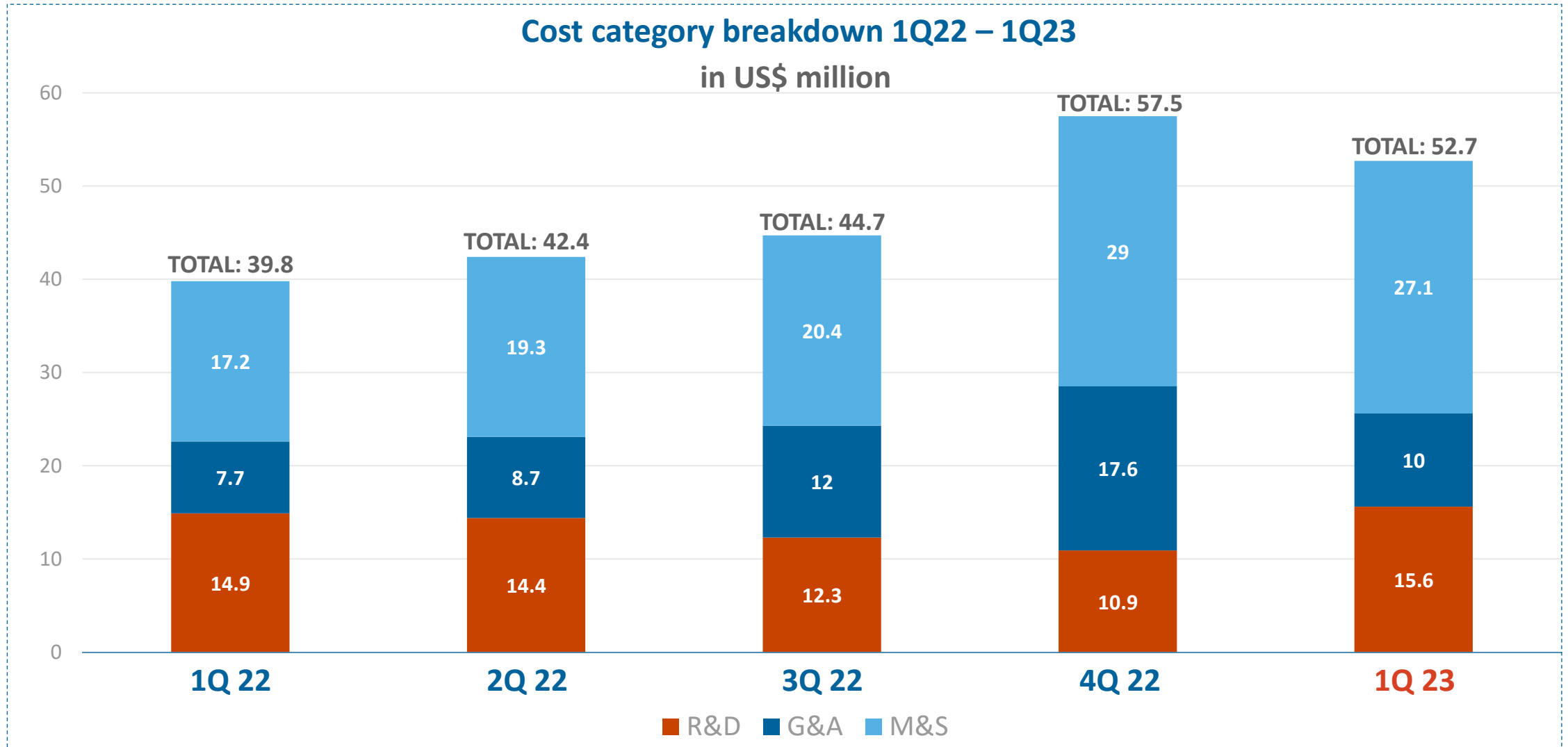


Financial highlights: 1Q 2023 vs 1Q 2022



Cash & Cash Equivalents (March 31, 2023): US\$184.8 million

Continued investment in the launch of Joenja





Continued low single-digit growth in RUCONEST® revenues



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



Positive CHMP opinion in 2H 2023, marketing authorization in Europe ~2 months later*



File leniolisib with UK's MHRA following ECDRP route*



Continued operating cost investments to accelerate future growth



Further details on our plans to develop leniolisib in additional indications to be provided in 2H 2023



Investment and continued focus on potential acquisitions and in-licensing of late-stage opportunities in rare diseases



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Pharming Group N.V.

Appendix

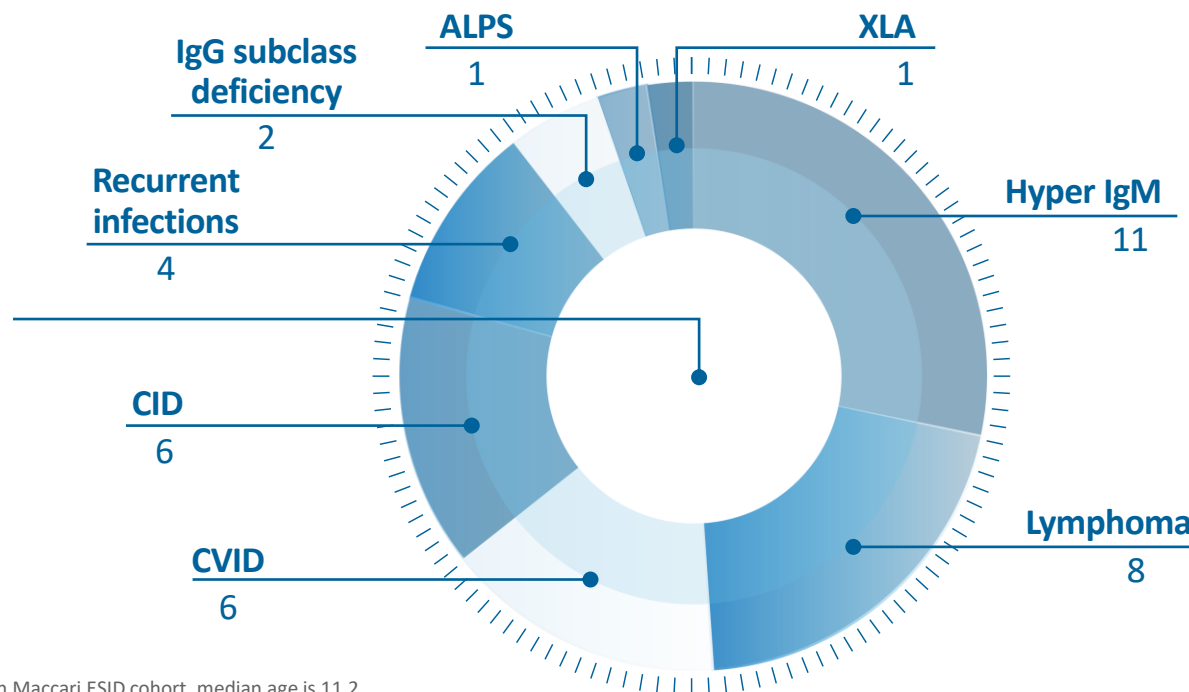
Heterogeneous, evolving symptomology can often lead to missed diagnoses

Timeline of the most common pathologies* seen in APDS¹⁻⁴

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



APDS has often been diagnosed as another PI or condition, causing delays in diagnosis¹



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.

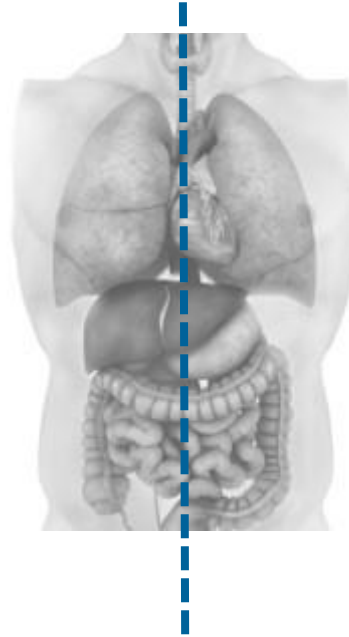
[‡]No median ages are available for these manifestations.

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.

Immune Deficiency

- Antimicrobial prophylaxis
- Immunoglobulin replacement therapy



Immune Dysregulation

- Corticosteroids
- Other immunosuppressants
- mTOR inhibitors

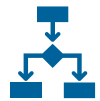
None of these therapies are FDA-approved for APDS treatment

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.

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 Evaluation³



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 log¹⁰-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.

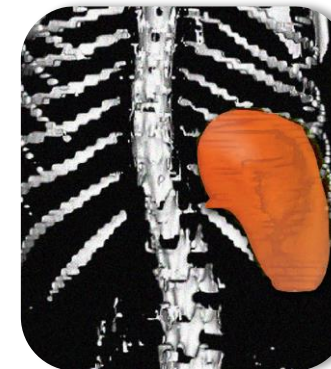
Secondary endpoint: Significant reductions in spleen size by 2D and 3D analysis compared to placebo

- 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: $-297, -76.2$), $P=0.0020$

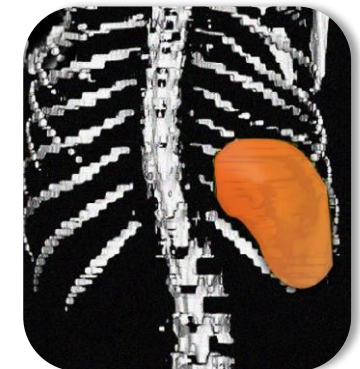
at week 12
27%
reduction in 3D spleen volume*

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.

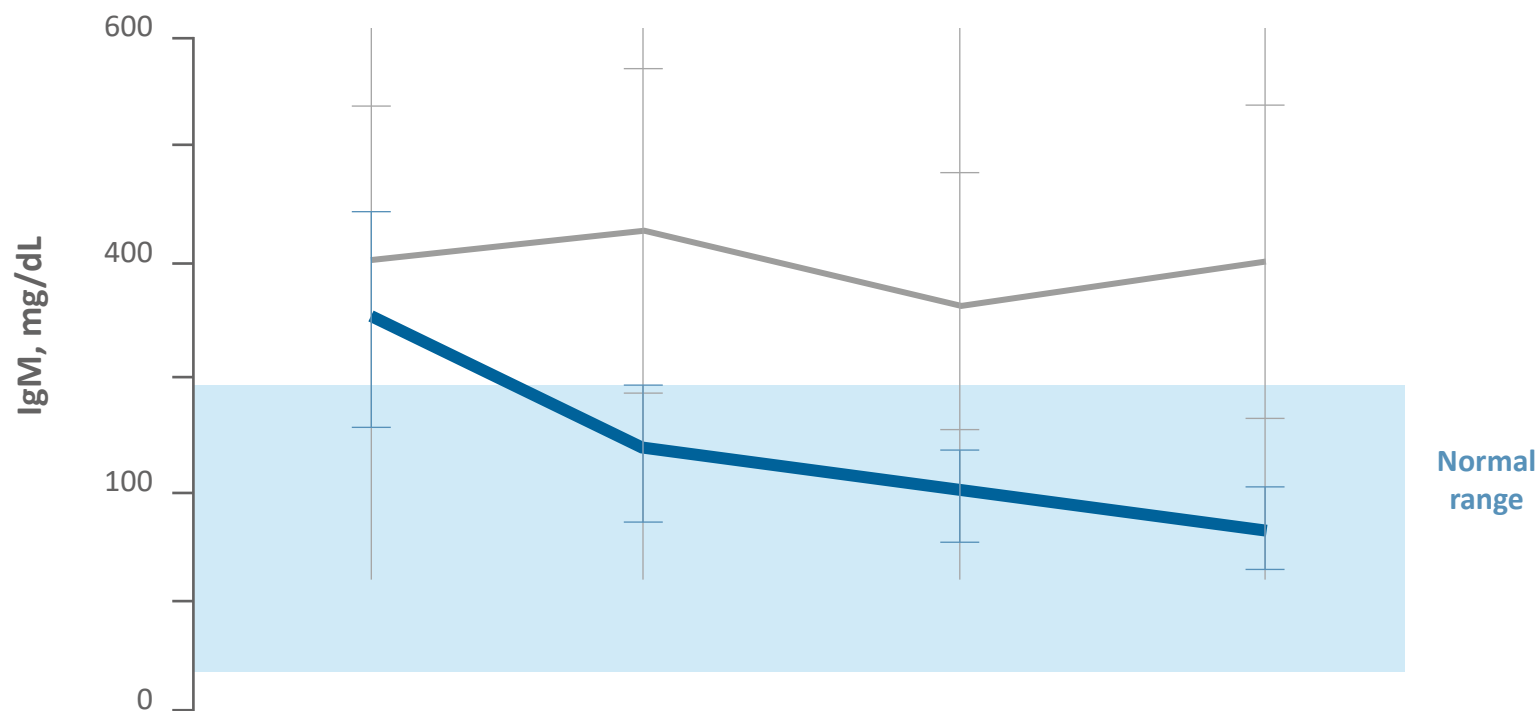
Rao VK, et al. Blood. 2023;141(9):971-983.

*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



- 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

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

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

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

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 Study³

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 trials²**
- 38 patients had a **median exposure of ~2 years**
 - 4 patients had **>5 years of exposure**



SI 1: Identify

Continue to identify HCPs and patients to expand networks with the support of patient advocacy partners



SI 2: Educate

Build knowledge of APDS and belief in PI3K δ inhibitor benefits by defining the disease, journey, and unmet needs



SI 3: Differentiate Joenja[®]

Differentiate Joenja[®] as a well-tolerated and efficacious treatment for APDS that targets the root cause of the disease



SI 4: Establish Access

Establish access that enables genetic testing and optimizes the Joenja[®] benefits and value proposition



>1500 APDS patients*

(as of December 2022 for US, Europe, UK, Japan, Canada, Australia)

>500 patients identified by Pharming to date

All about APDS
Activated PI3K Delta Syndrome



*Size based on estimate of 1.5 APDS patients per million population (based on available literature) for US, Europe, UK, Japan, Canada and Australia

Program Offerings



Cost & insurance

Providing insurance coverage assistance and financial support resources



Filling prescriptions

Coordinates prescription details with patient families/caregivers and HCP through single point of contact to assist in getting Joenja[®] dispensed on time



Support & education

Regularly touches base to help patient families/caregivers with their insurance, provides appropriate financial assistance options for eligible patients, and assists with prescription delivery

Dedicated, Experienced Support Team



APDS Assist Care Coordinators

Welcomes patient families/caregivers to APDS Assist and helps navigate coverage, access, and support options



APDS Clinical Educators (ACE)

Provides one-on-one education, support and resources for patients, caregivers and family members

Exclusive Specialty Pharmacy Model



Partnered exclusively with PANTHERx, specializing in rare and ultra-rare therapeutic areas

Process and fill Joenja[®] prescriptions with clinical pharmacists, available 24/7, to:

- Answer questions and offer treatment support for Joenja[®]
- Provide information about potential side effects and offer information support when appropriate

APDS Assist offers personalized coverage assistance, financial resources and prescription support to patients and caregivers starting and continuing Joenja[®] therapy



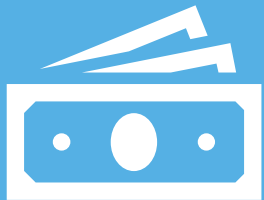
Starter Program

- Available to all newly enrolled patients
- Up to 30-day supply within one week of enrollment for most patients



Bridge Program

- Available for patients in which insurance has been verified
- Provides continuation of therapy when there is a gap in coverage while seeking payer approval



Copay Assistance

- Eligible patients with commercial insurance may pay as little as \$0 per month
- Assists with deductible, copay/co-insurance and out of pockets costs for Joenja®



Patient Assistance Program

- Continuation of coverage may be provided for uninsured patients or situations in which Joenja® is not covered by their insurance plan



Commercial Product Available mid-April 2023

APDS Assist patient support services now active



www.joenja-hcp.com/APDSAssist

1-877-796-2737 (APDS)

Joenja® NDC	71274-170-60
Supplied as	60-count bottle (30-day supply)

Wholesale acquisition cost (WAC)

Per tablet	\$750.00
Per mg	\$10.71
Per bottle	\$45,000.00