Pharming Group N.V.

H.C. Wainwright – Global Investment Conference

September 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

- Revenue FY23 US$227.1M
  2Q24 US$63.0M (+23% vs. 2Q23)
  1H24 US$109.0M (+16% vs. 1H23)
- 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
  2Q24 US$11.1M (+16% vs. 1Q24)
  1H24 US$20.7M (+44% vs. 2H23)
- Strong focus on patient finding
- Israel approval
- 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

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

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 • Growth potential from patient finding and VUS efforts	• Patients on early access/ named patient programs • Global expansion / regulatory reviews • Pediatric studies / label expansion	• Phase II POC trial in PIDs with immune dysregulation linked to PI3Kδ signaling • Symptoms similar to APDS • Seeking regulatory feedback on third PID indication

- APDS global prevalence:
  ~1.5 patients / million
  ~2,400 patients
- PIDs with immune dysregulation (PI3Kδ) global prevalence:
  ~5 patients / million

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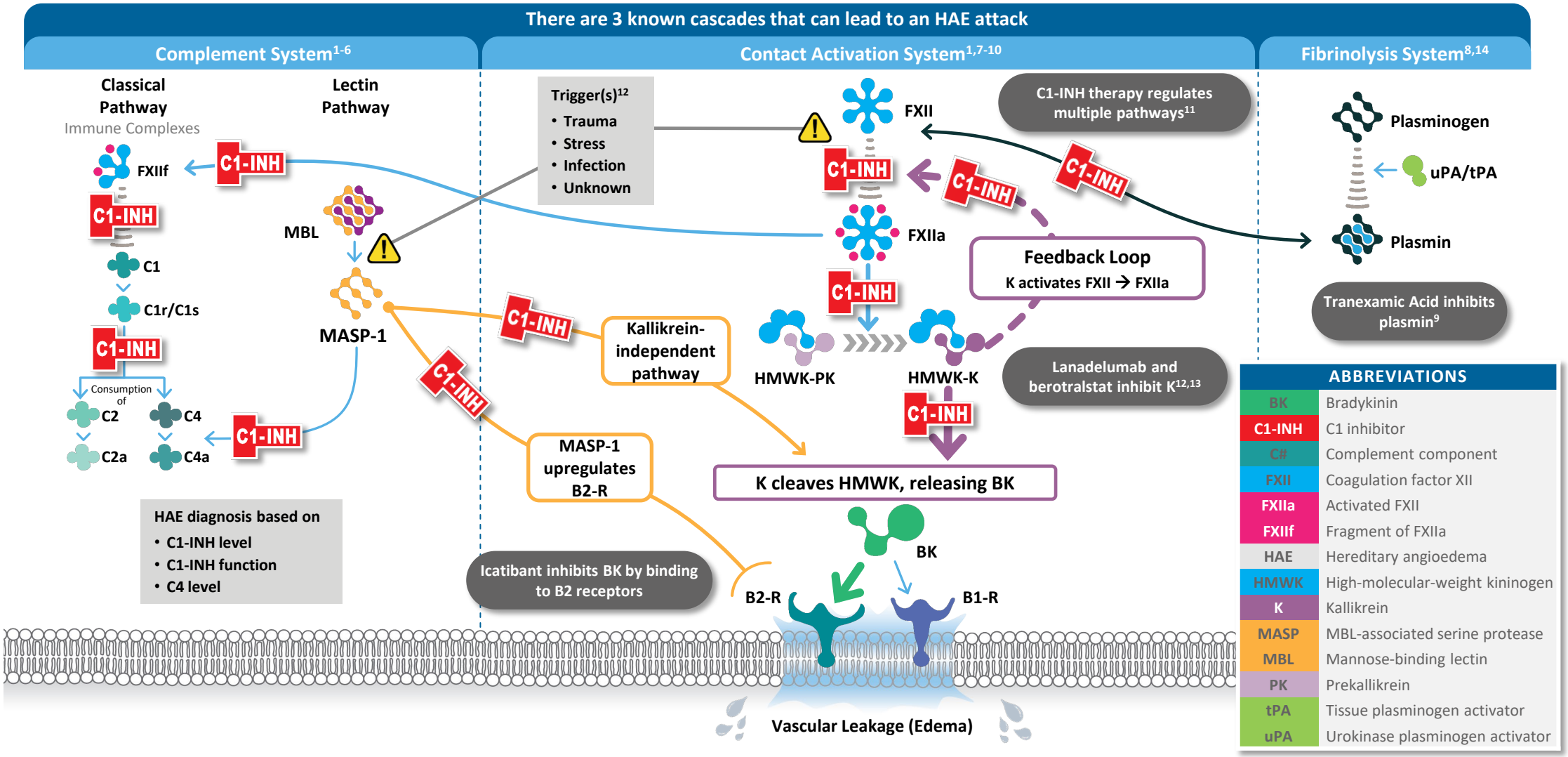
RUCONEST®

C1-INH targets the root cause of HAE

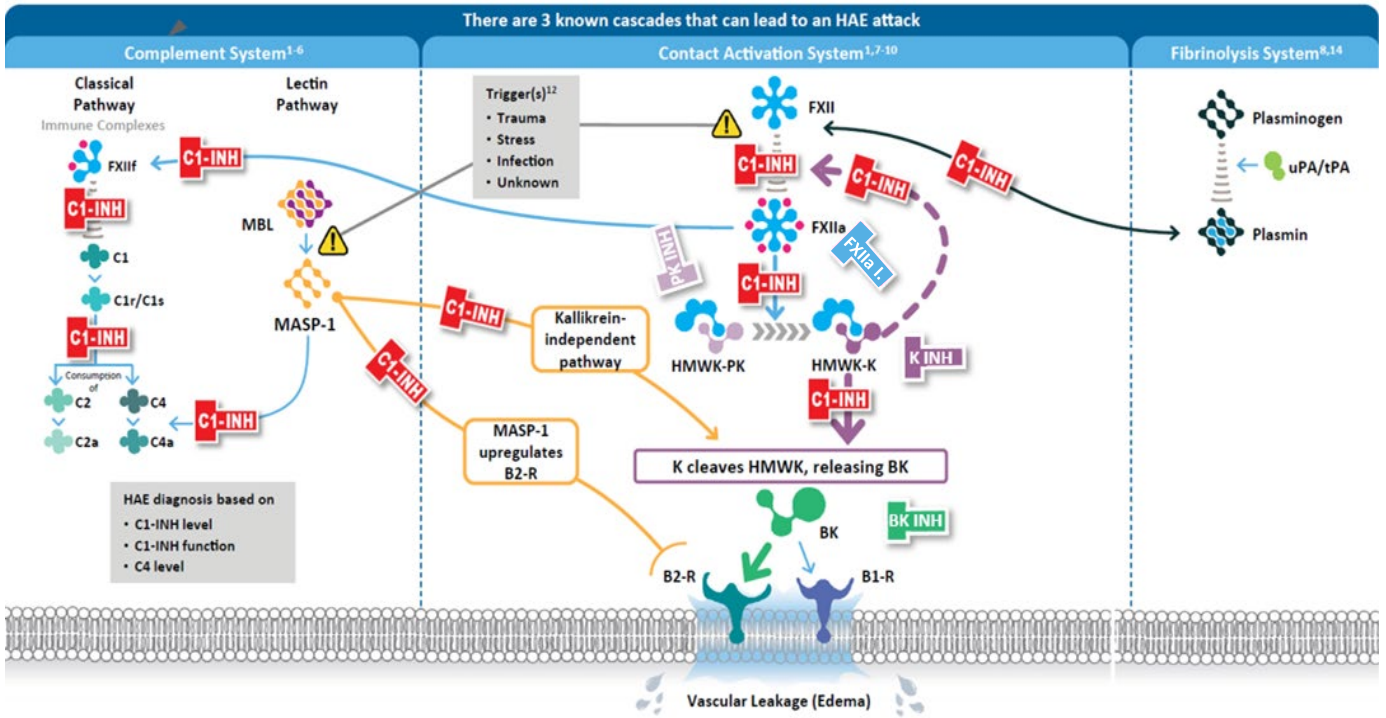


Adapted from a clinical cascade developed in partnership with Dr. Allen Kaplan. This is a current scientific understanding of the cascades. Clinical implications are unknown.

C1-INH targets the root cause of HAE

TARGET	BRAND NAME	GENERIC NAME	STATUS	TYPE
C1 Inhibitor	Ruconest	C1 esterase inhibitor (recombinant)	Marketed	OD
	Berinert	C1 esterase inhibitor (human)	Marketed	OD
	Haegarda	C1 esterase inhibitor (human)	Marketed	Prophy
	Cinryze	C1 esterase inhibitor (human)	Marketed	Prophy
Pre-Kallikrein	n/a	donidalorsen	Phase 3	Prophy
	n/a	NTLA-2002	Phase 1/2	Prophy
Plasma Kallikrein	Kalbitor	ecallantide	Marketed	OD
	Orladeyo	berotralstat	Marketed	Prophy
	Takhzyro	lanadelumab	Marketed	Prophy
	n/a	sebetralstat	NDA	OD
	n/a	STAR-0215	Phase 2	Prophy
FXIIa	n/a	garadacimab	BLA	Prophy
Bradykinin B2	Firazyr	icatibant	Marketed	OD
	n/a	deucrictibant (PHVS416)	Phase 3	OD
	n/a	deucrictibant (PHVS719)	Phase 2	Prophy

Overview of Marketed and In-Development Therapies and Their Targets Within the Three Known Cascades Leading to HAE Attacks



Source: Cascade 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

2nd most prescribed product for acute attacks
Typical patient: failed icatibant (BK inh) and on prophy Tx (K inh)

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
Over 100 enrollments in 2Q24 (vs. almost 70 in 1Q24)

Performing well in leading U.S. revenue indicators: active patients, vials shipped, physicians prescribing (765, +36 vs. 2023)

Revenue:
FY23 US$227.1M (+10%)
2Q24 US$63.0M (+23%)
1H24 US$109.0M (+16%)

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.

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Joenja® (leniolisib)

U.S. launch of Joenja®: first and only approved therapy for APDS, corrects the underlying immune defect

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

APDS is a complex syndrome caused by pathogenic variants of the PI3Kδ enzyme, with significant mortality

Joenja® is an oral, selective PI3Kδ inhibitor designed to help regulate the hyperactive signaling pathway

FDA approval (March 2023) based on randomized pivotal study and OLE study
U.S. launch (April 2023)

Joenja® is an oral immune modulator targeting the root cause of APDS

- Normalizes the hyperactive PI3Kδ pathway to correct the underlying immune defect in APDS patients
- Helps address both immune deficiency and immune dysregulation

No drug-related serious adverse events or study withdrawals in Joenja® trials
Clinical data and tolerability for long term treatment

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.

Joenja® U.S. launch: strong commercial execution

- Strong commercial execution 15 months into U.S. launch
- Continue to enroll and add patients on paid therapy in 2Q24
  91 patients on paid therapy at end 2Q24, with 2 additional enrollments pending authorization
- 2Q24 revenue US$11.1M (+16% vs. 1Q24)
  Includes US$0.9 M Europe and RoW
- 1H24 revenue US$20.7M (+44% vs. 2H23)
  Includes US$2.0M Europe and RoW
- ~500 APDS patients in the U.S.* with >230 diagnosed as of June 30, 2024
  +10 diagnosed patients in 2Q24, including patients diagnosed via VUS resolution
- Significant focus on genetic family testing
- Variant of uncertain significance (VUS) validation studies to complete in 4Q24
  focused on >1200 patients identified in the U.S. with VUSs

* Prevalence estimated at 1.5 patients per million population, based on available literature
As of June 30, 2024, Pharming has identified >870 diagnosed APDS patients in global markets
>780 of these patients are in key global launch markets in the U.S., Europe, the U.K., Japan, Asia Pacific, Middle East, Latin America and Canada with total prevalence of ~2,400 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 (>1,200 patients in U.S.)**
- Variant curation (ClinGen, Genomenon)
- Functional testing (PI3K pathway activity)
- Multiplexed assays of variant effect (MAVE) studies (complete 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 1,200 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.

VUS by the numbers

VUSs frustrate patients and doctors, limiting diagnosis of genetic diseases such as APDS

Pharming is aware of **~1,200 US patients** harboring *PIK3CD/R1* VUSs

- This figure will continue to grow over time
- VUS are identified at ~4x the rate of likely pathogenic/pathogenic (LP/P) variants
- Similar VUS frequencies expected worldwide
- Published literature, which includes more than 1.5 million patients, showed that 20% of reclassified VUSs are upgraded to LP/P
- Pilot study in 25 VUS patient samples - findings consistent with APDS identified in 5 patients (20%) including patient preparing for enrollment

No systemic initiatives exist to resolve *PIK3CD/R1* VUSs, yet these patients remain a significant opportunity to identify incremental patients with APDS

Joenja® – looking beyond FDA approval

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

Israel marketing authorization received April 30, 2024

U.K MHRA decision expected in the fourth quarter 2024*

CAN, AUS submissions under regulatory review
Australia approval in 2025**

Japan clinical study: Patient enrollment is now complete
PMDA filing following completion of appropriate clinical trials

Pediatric studies
4 to 11 years - Enrollment completed
1 to 6 years - 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. Pharming received MHRA Day 70 Request for Further Information on July 3, 2024. There were no major objections. Upon Pharming's satisfactory response to MHRA requests, it is expected that the MHRA will issue its decision in the fourth quarter of 2024.
** Anticipate regulatory action in 2025 for Australia

Joenja® (leniolisib) franchise – strong 3-5 year growth potential

Joenja® U.S. (APDS)	Leniolisib (APDS)	Leniolisib for Primary Immunodeficiencies (PIDs)
• Marketed (12+) • Found >230 of ~500 patients • 91 patients on paid therapy • >50 diagnosed patients (12+) not yet enrolled and >50 pediatric • Growth potential from patient finding and VUS efforts	• Found >870 patients globally • Global expansion / regulatory reviews • Pediatric studies / label expansion (>25% patients) • 150 patients in EAP, clinical studies, and NPP	• Phase II POC trial in PIDs with immune dysregulation linked to PI3Kδ signaling • Similar to APDS • Seeking regulatory feedback on third PID indication

Prevalence: **~1.5 / million ~2,400 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, Latin America and Canada

Leniolisib for PIDs with immune dysregulation

- **Primary Immunodeficiencies (PIDs) are a broad group of disorders with key potential features:**
  - Genetic basis
  - immune dysfunction → increased risk of infection
  - Immune dysregulation → lymphoproliferation and autoimmunity
  - High morbidity and mortality

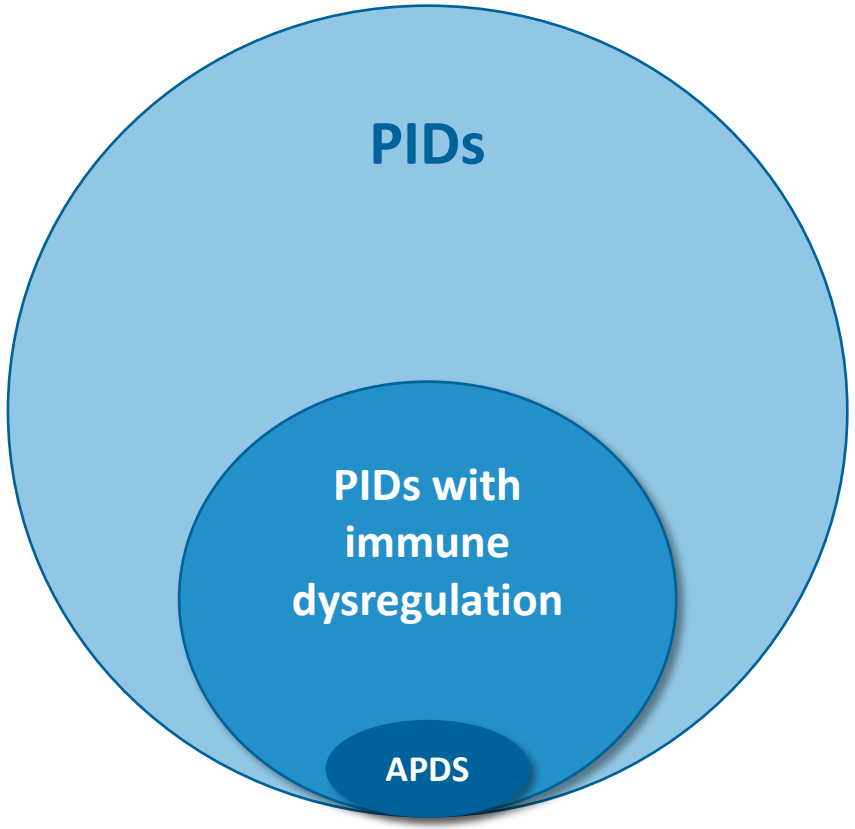
- **Pharming developing leniolisib for PIDs with immune dysregulation beyond APDS**

PIDs with immune dysregulation linked to PI3Kδ signaling

- Multiple PIDs with alterations in PI3Kδ signaling
- Clinical manifestations, disease onset and severity similar to APDS
- No approved therapies
- Phase II proof of concept clinical trial starting shortly

Next indication

- Obtaining regulatory feedback on proposed clinical development plan

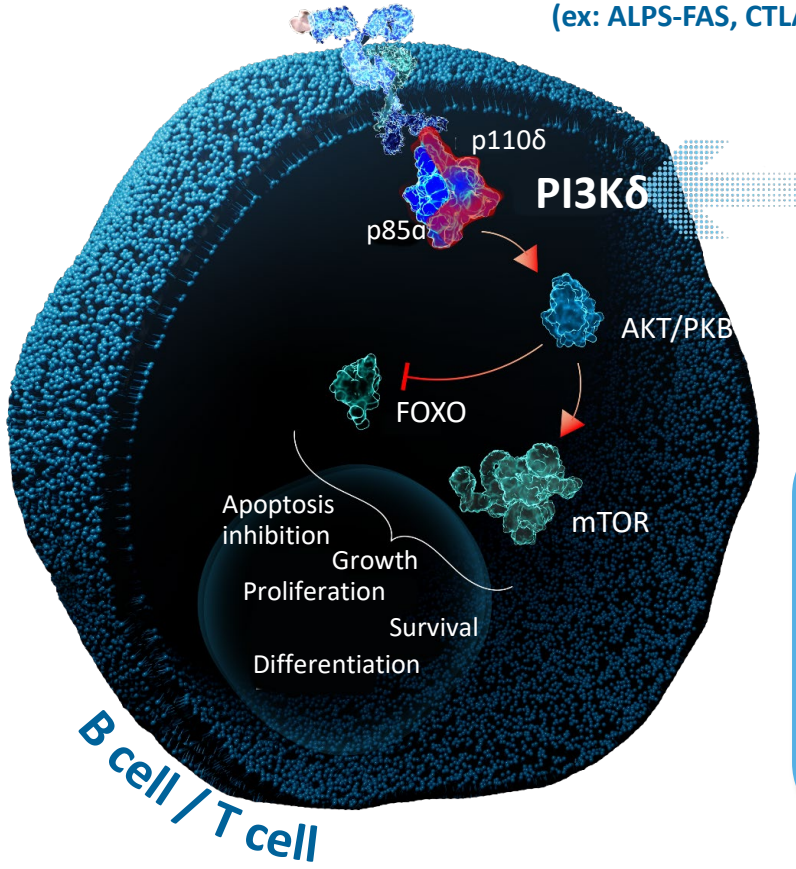


Not to scale with population sizes

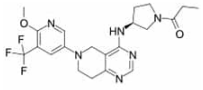
Given importance of PI3Kδ in B & T cells, immune dysregulation in PIDs can occur via alterations in PI3Kδ signaling

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

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



leniolisib



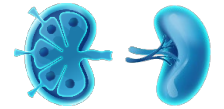
High unmet medical need

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

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

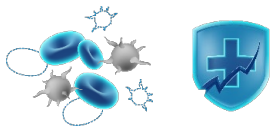
Note: Illustration does not include all steps in the signaling pathway.

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



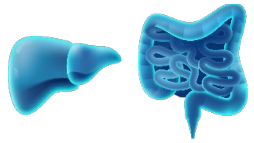
Lymphoproliferation

- 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

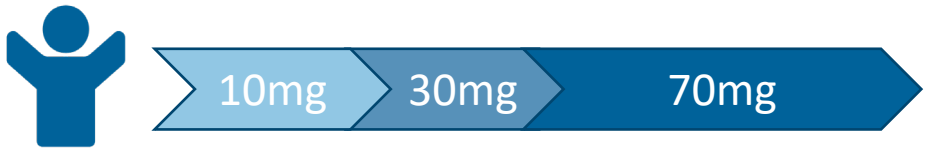
Lymphoma

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] (treatable population ~5/million)
- Primary: Safety & Tolerability
- Secondary/Exploratory: PK/PD, efficacy measures
- 10/30/70 mg: 4/4/12 wks treatment, respectively
- Pick Best Dose regimen for Phase III

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

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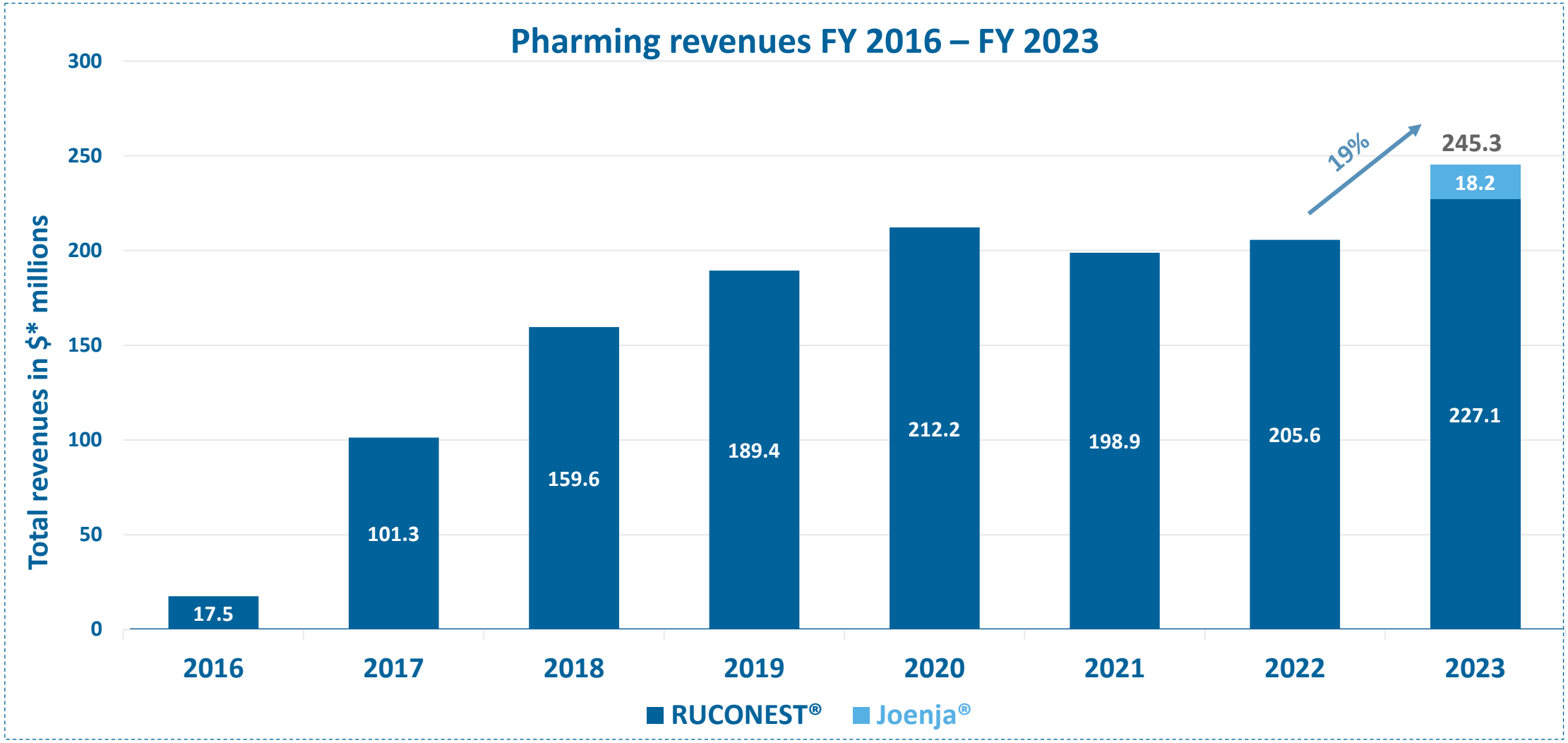
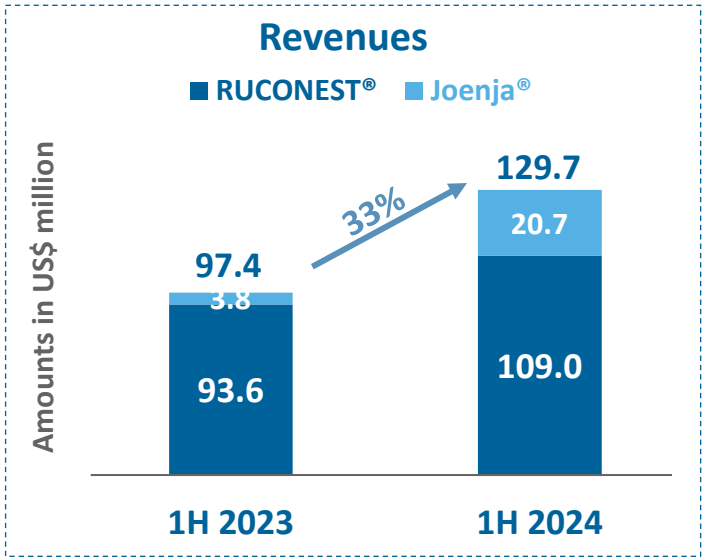
Financials and Outlook

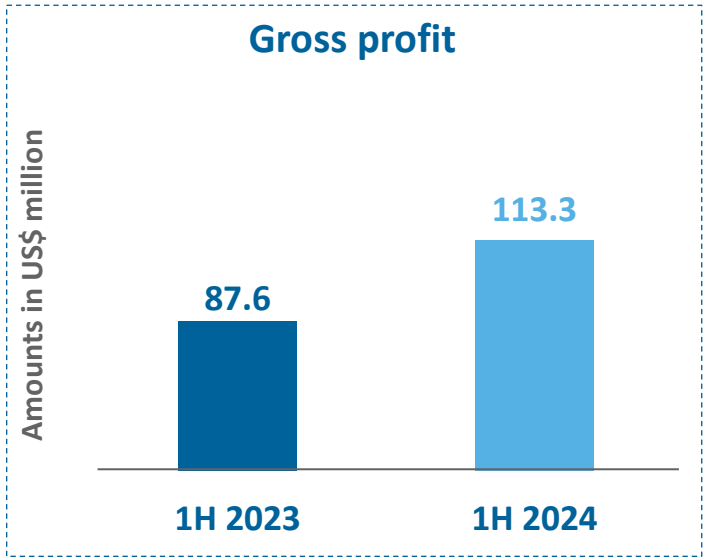
RUCONEST® and Joenja® driving revenue growth

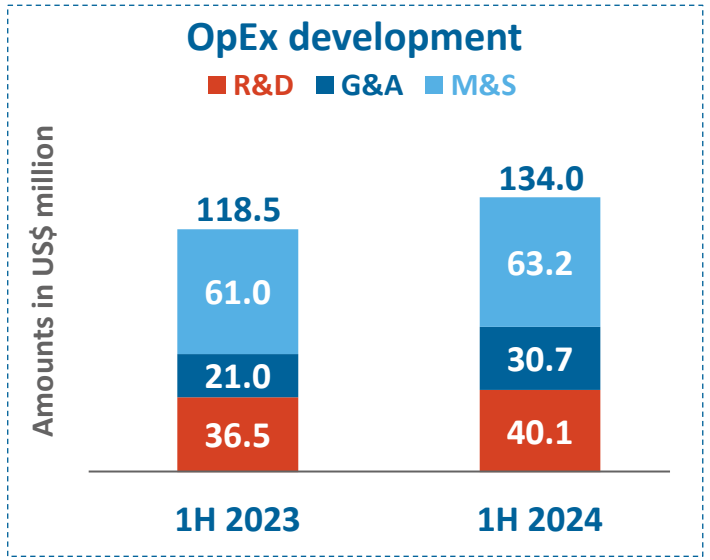


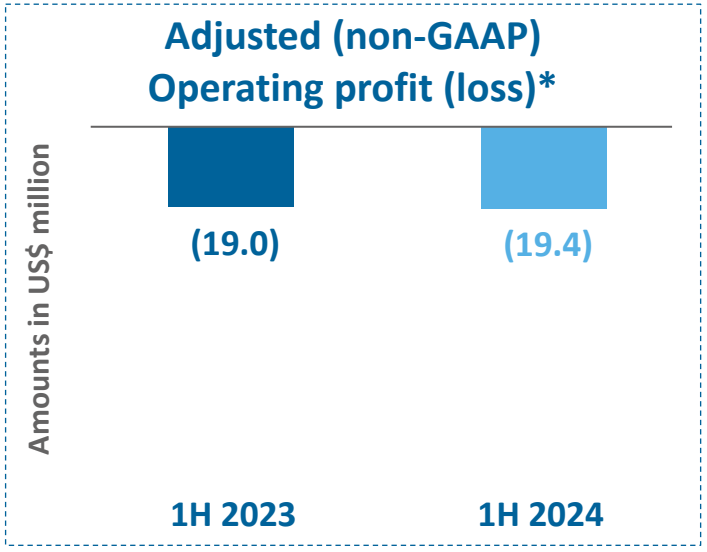
- From FY 2016 – FY 2020 Pharming Group reported earnings in EUR. Revenues during this time frame have been converted to USD. In 2021, Pharming Group began reporting earnings in USD.
- 4Q 2020 and 1Q 2021 quarterly fluctuations and volatility from COVID-19.

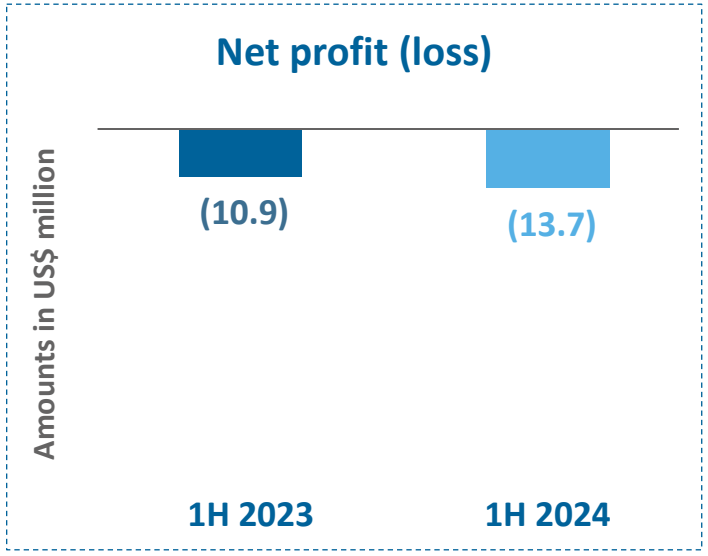
Financial highlights: 1H 2024 vs 1H 2023

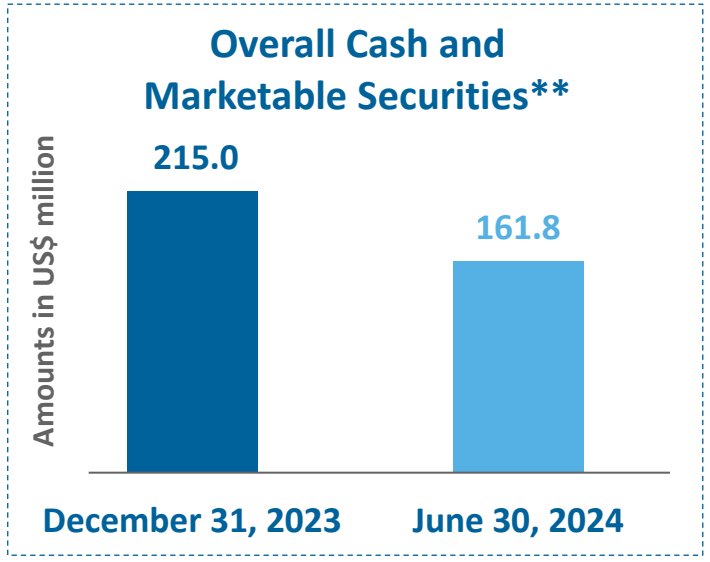






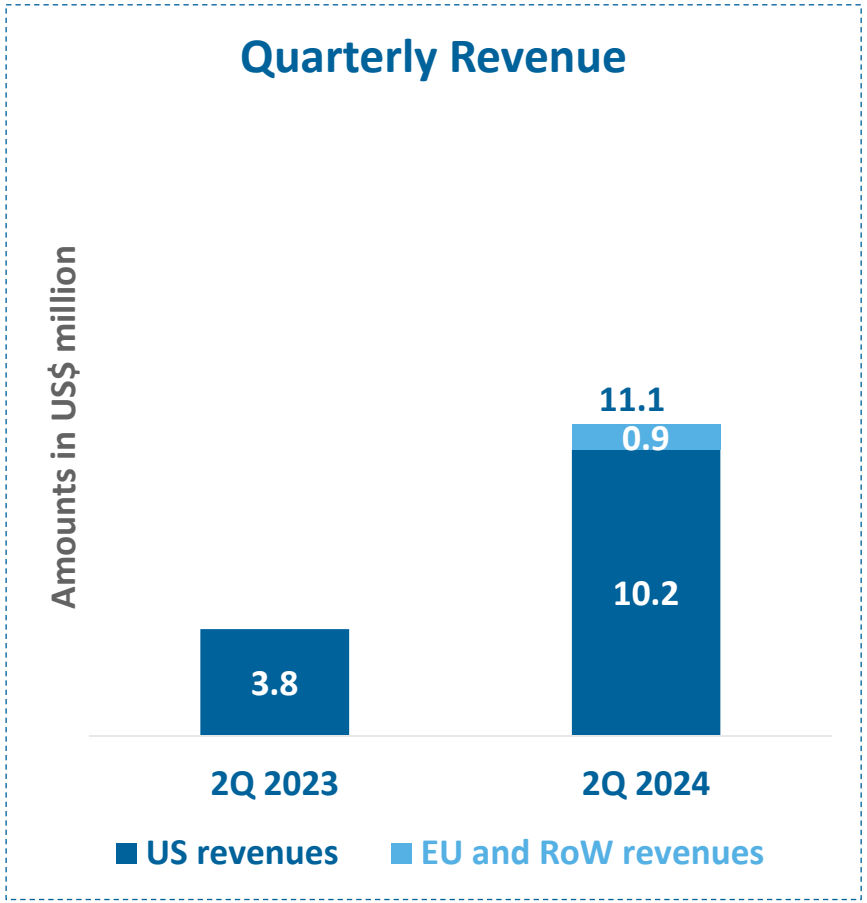


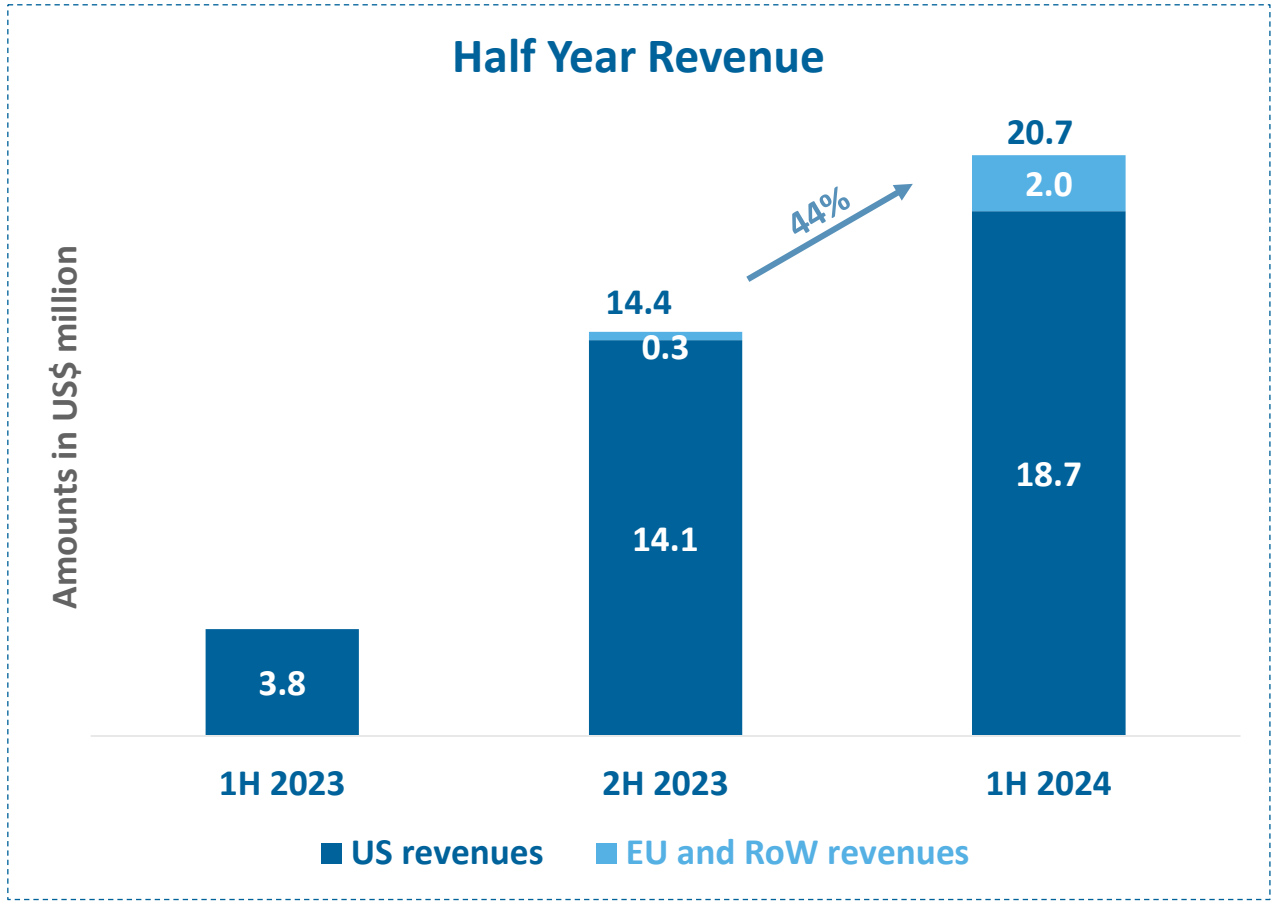




* Operating profit (loss) for 1H 2023 excludes milestone payments for Joenja® (US$10.5 million) and gain on sale of Priority Review Voucher to Novartis (US$21.1 million).
** US$30.1 million of the US$53.2 million decrease in overall cash and marketable securities is due to convertible bond refinancing.

Joenja® revenue breakdown





2024 Financial guidance

	FY 2024 Revenue Guidance	% Growth vs. FY 2023
Total Revenues	US$280 - 295 million	14-20%

- Joenja® significant driver of revenue growth, continued RUCONEST® growth
- Joenja® revenue assumptions:
  - Continued growth in patients on paid therapy
  - Continued high adherence (compliance) rates ~85%
  - U.S. Pricing: 30-day supply $47,220, Annual cost (WAC) $566,640, GTN Discount ~15%
- 2H 2024 OpEx – adjustments / savings due to EMA delay

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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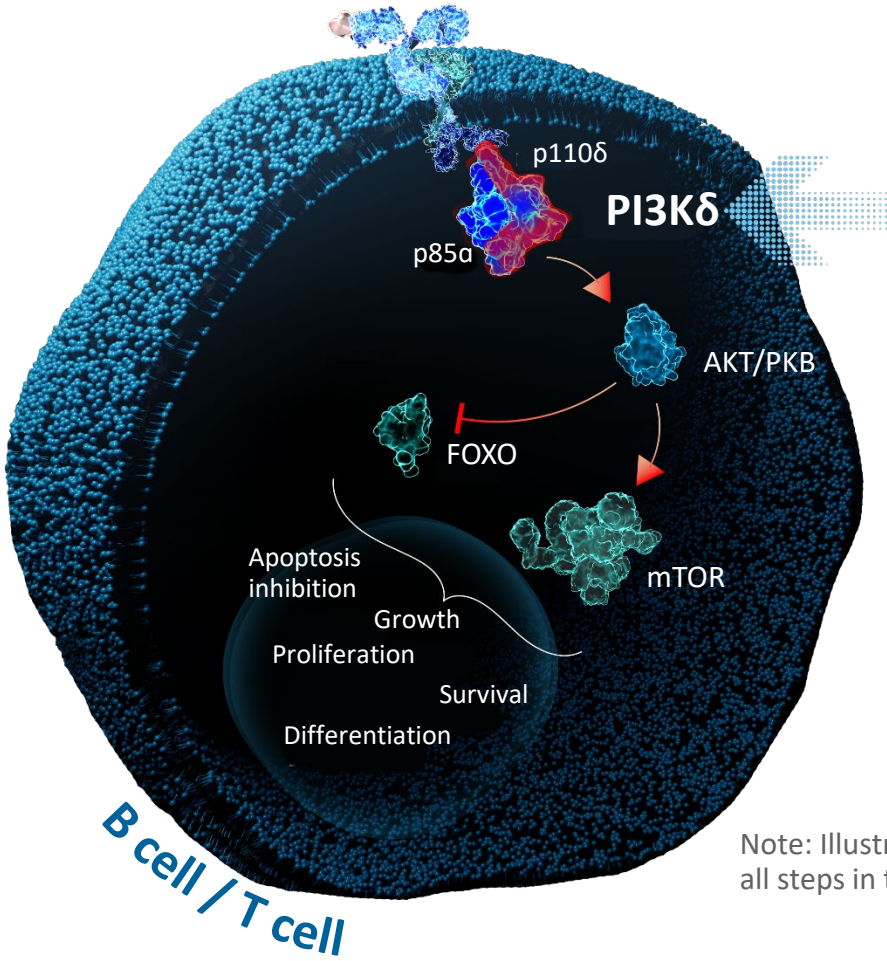
Appendix

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

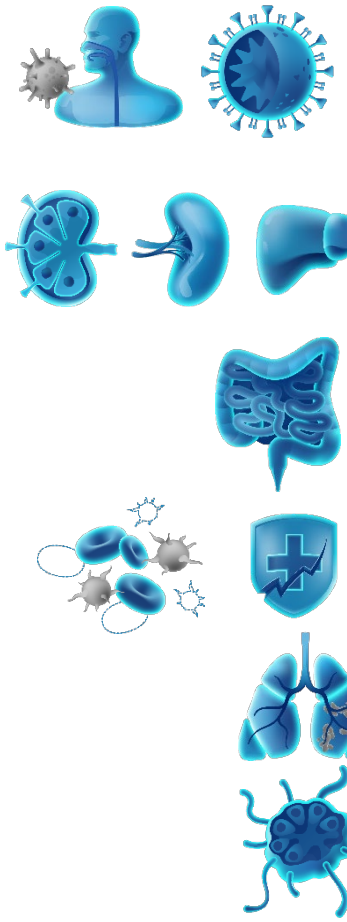
Hyperactive PI3Kδ results in dysregulated B and T cell development[1-3]



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.

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

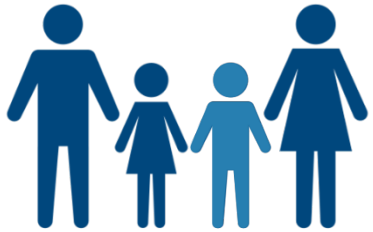
Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS)

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

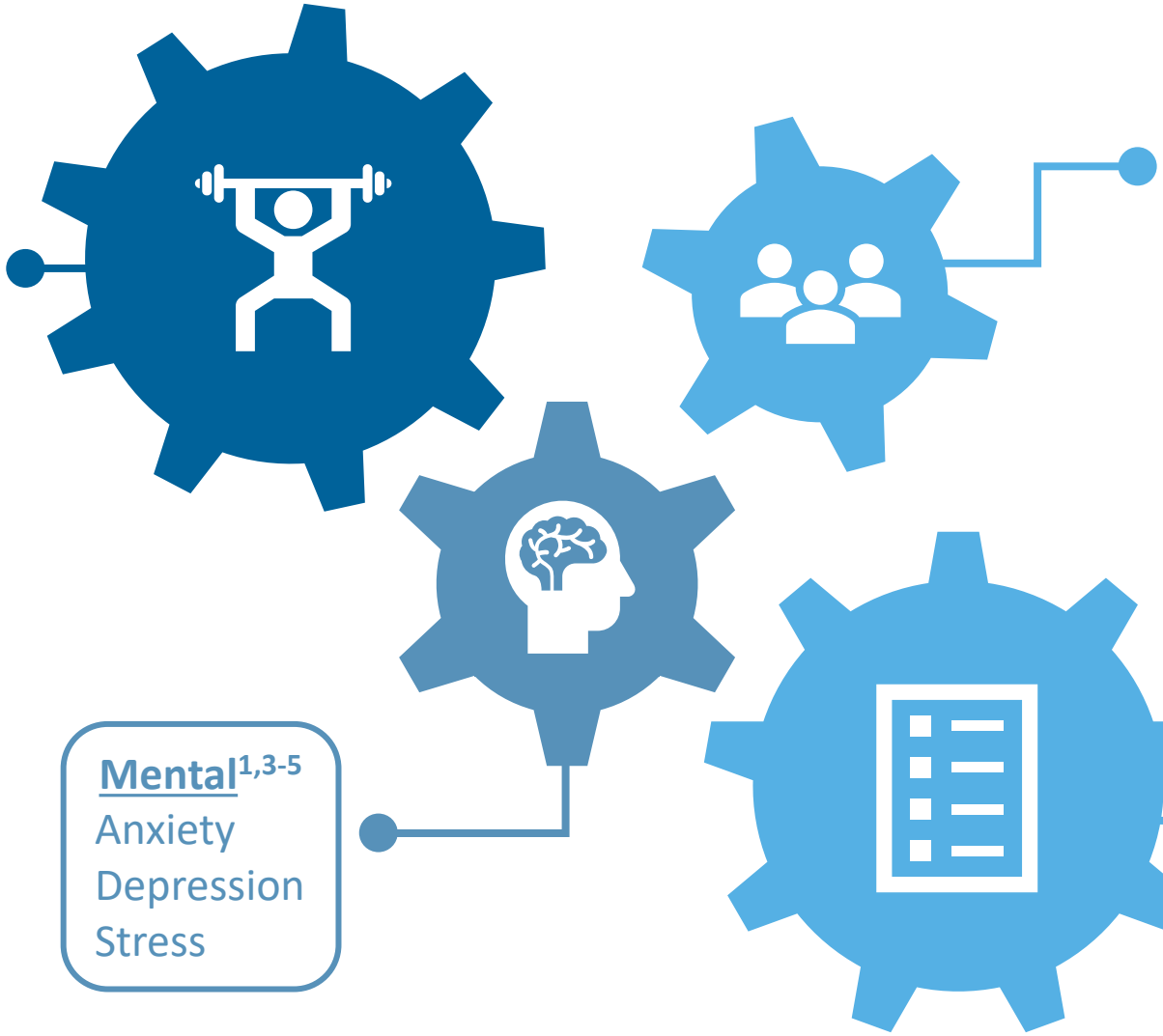
Without an indicated treatment specifically for APDS, physicians could only manage symptoms

*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

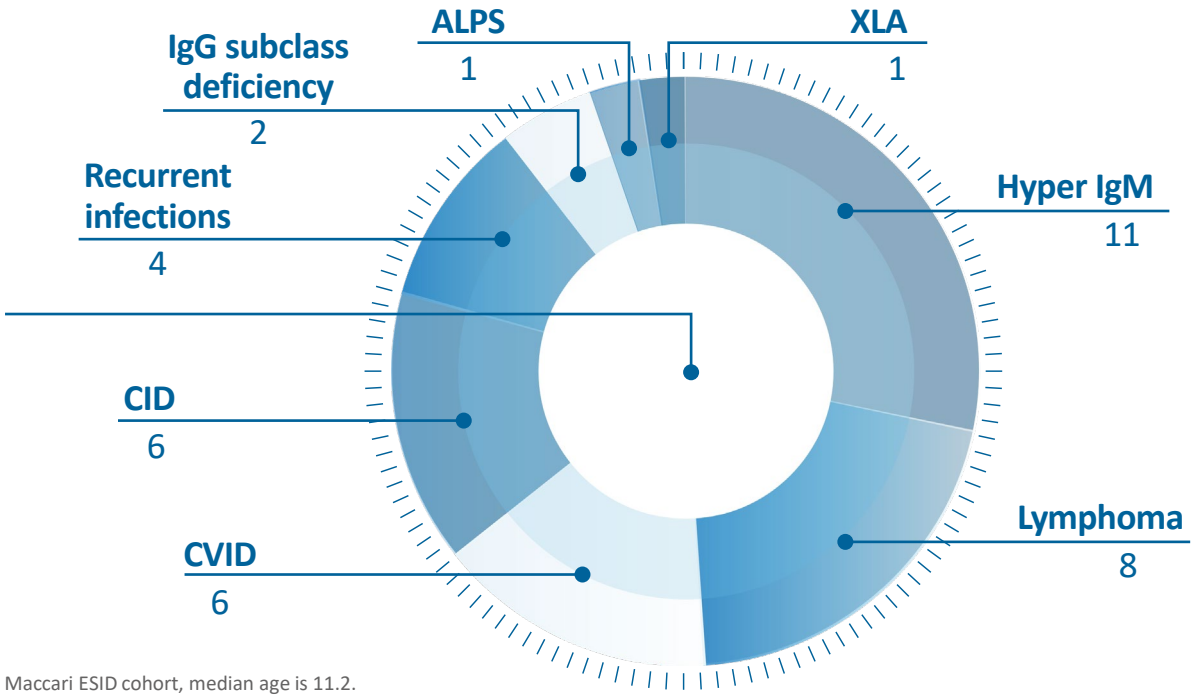
Timeline of the most common pathologies* seen in APDS[1-4]

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]



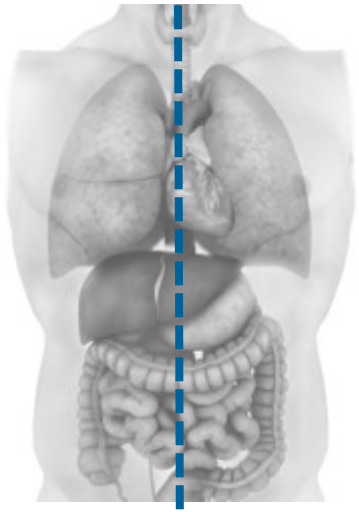
Improved identification of symptoms, increased genetic testing, and earlier diagnosis are needed

*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

Pharming®

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

- Nonrandomized, open-label, dose-escalating
- 6 patients with APDS
- 12 weeks
- 10 mg, 30 mg, 70 mg bid (4 weeks each dose)
- 70 mg bid selected for Part 2

Pivotal Trial - Part 2: Efficacy & Safety Evaluation[3]

- Randomized, triple-blinded, placebo-controlled
- 31 patients with APDS (21 Joenja®, 10 placebo)
- 12 weeks
- 70 mg bid
- Co-primary efficacy end points
  - Change from baseline in log^{10}-transformed SPD of index lesions
    - Also assessed as % change
  - Change from baseline in percentage of naïve B cells out of total B cells
- Secondary and exploratory end points
- Safety

Open-label extension study[4,5]

- Nonrandomized, open-label, long-term study
- 35 patients with APDS from Parts 1 and 2
- 2 patients with APDS previously treated with investigational PI3Kδ inhibitors
- Ongoing
- 70 mg bid
- Long-term safety, tolerability, efficacy, and pharmacokinetics

bid, twice a day; PI3Kδ, phosphoinositide 3-kinase delta; SPD, sum of product diameters

1. Rao VK, et al. *Blood*. 2017;130(21):2307-2316. 2. NCT02435173. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02435173. Updated May 6, 2015. Accessed March 13, 2023. 3. Rao VK, et al. *Blood*. 2023;141(9):971-983.
4. NCT02859727. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02859727. Updated October 31, 2022. Accessed March 3, 2023. 5. Data on file. Pharming Healthcare Inc; 2022.

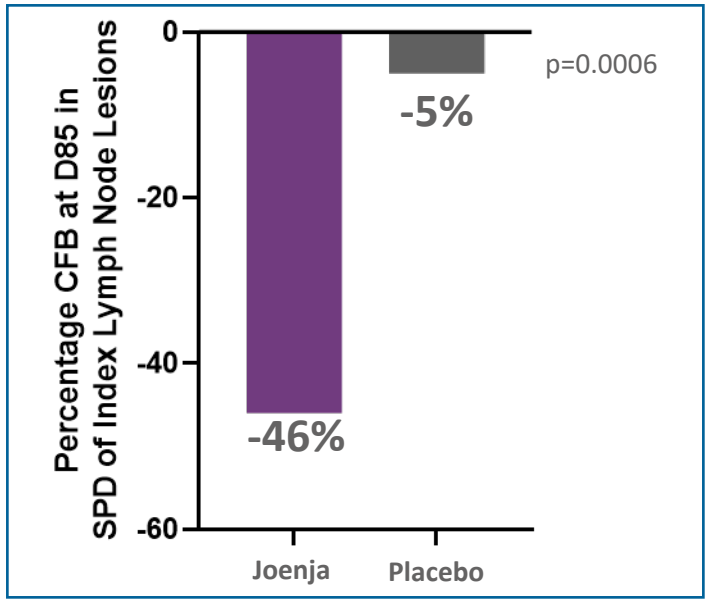
Joenja® addresses the underlying cause of APDS to help restore immune balance – Phase 3 co-primary endpoints

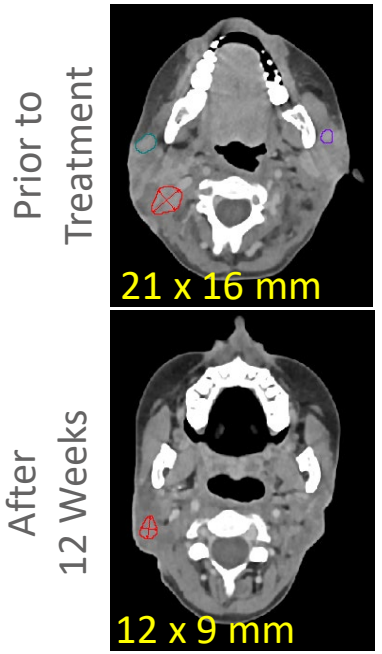
At 12 weeks Joenja® decreased lymphadenopathy and increased naïve B cells

Immune Dysregulation

Change from baseline in index nodes*

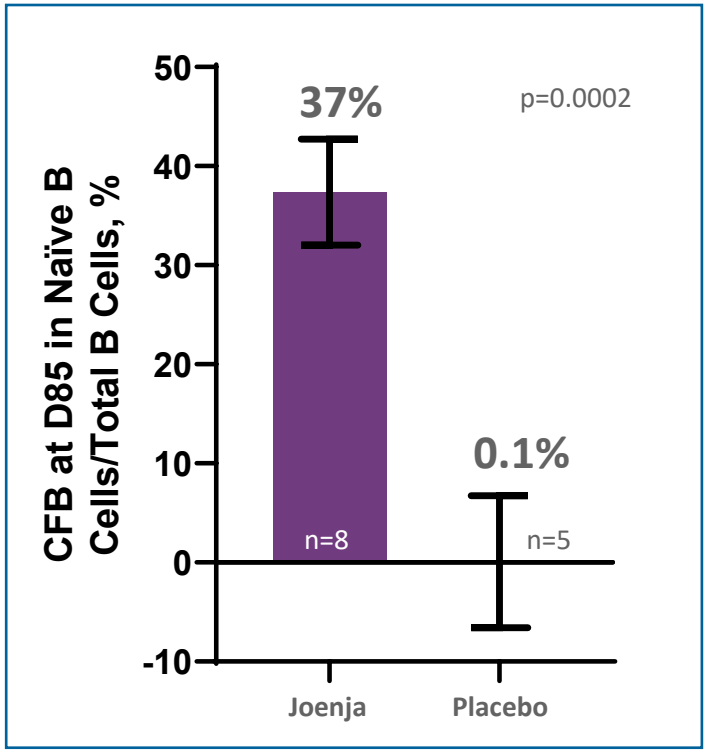
Log_{10}-transformed SPD of index lesions	Joenja (n=18)	Placebo (n=8)
Baseline mean (SD)	3.03 (0.42)	3.05 (0.39)
Change from baseline, LS mean (SE)	-0.27 (0.04)	-0.02 (0.05)
Difference vs placebo (95% CI)		-0.25 (-0.38, -0.12)





Immune Deficiency

Change from baseline in naïve B cells†



Data were analyzed using an ANCOVA model with treatment as a fixed effect and baseline as a covariate. Use of glucocorticoids and IRT at baseline were both included as categorical (Yes/No) covariates. Baseline is defined as the arithmetic mean of the baseline and D1 values when both are available, and if either baseline or the D1 value is missing, the existing value is used. P-value is 2-sided. Least square means are graphed. Error bars are standard error of the mean.

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

†Out of 27 patients in the PD analysis set, 13 patients met the analysis requirements, including having a percentage of <48% of naïve B cells at baseline, to form the B-PD analysis set.

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

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

Joenja® significantly reduced splenomegaly

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

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

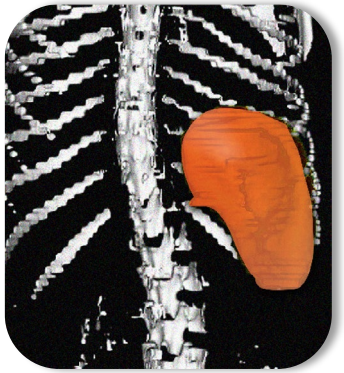
at week 12

27%

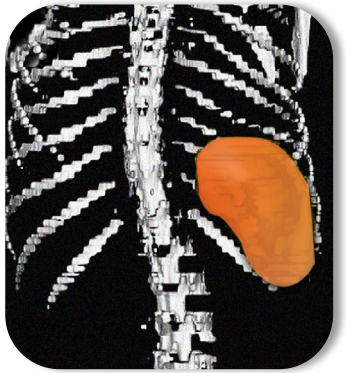
reduction in 3D spleen volume*

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

Prior to treatment:
491 mL



At week 12:
314 mL



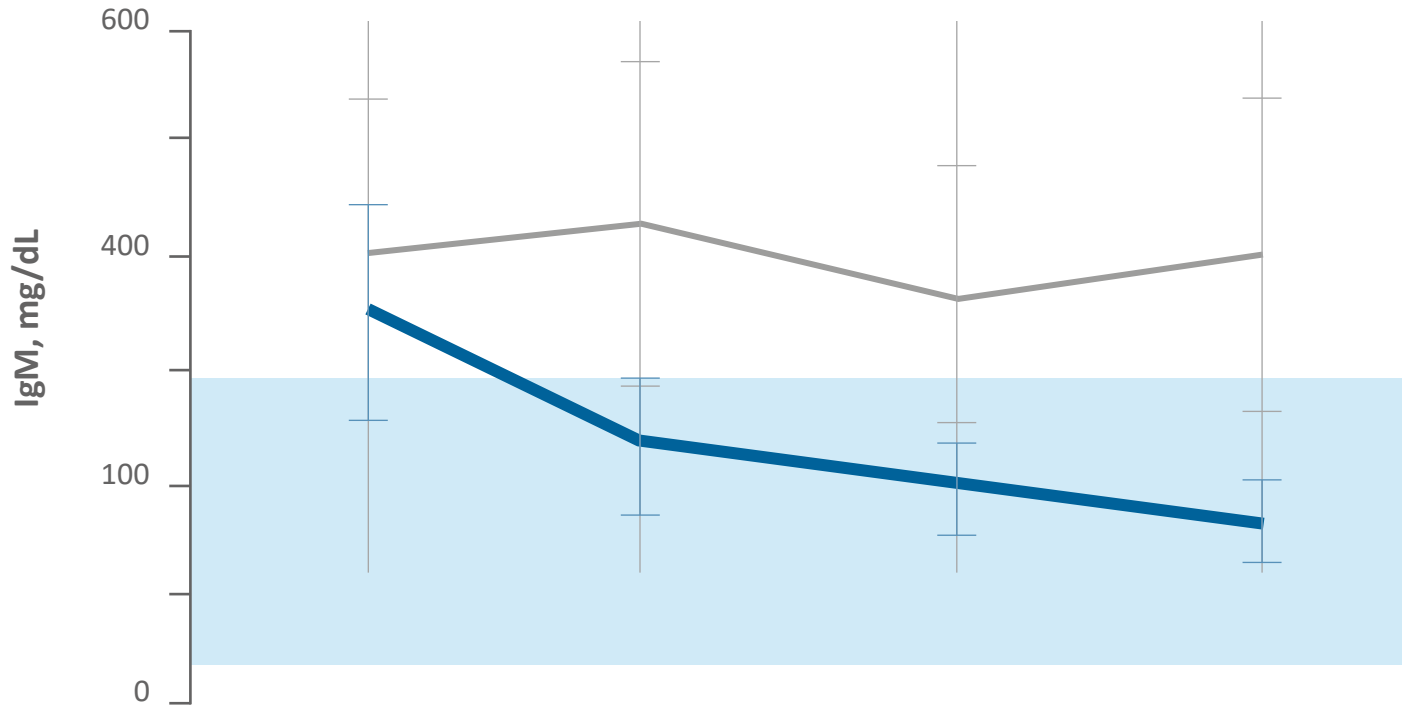
Actual patient images of a 17-year-old male. As individual results vary, images may not be representative of all patients.

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

*In the PD analysis set, the mean (SD) percentage change from baseline to week 12 in 3D spleen volume (mm^3) was -26.68% (12.137) with Joenja® (n=19) and -1.37% (24.238) with placebo (n=9). The ANCOVA model was used with treatment as a fixed effect and log_{10}-transformed baseline as a covariate for index and non-index lesions. The use of both glucocorticoids and IV Ig at baseline was included as categorical (yes/no) covariates.
This analysis excluded 2 patients in each treatment group. In the Joenja® group, 1 patient with a complete index lesion response was excluded, and 3 patients were excluded for no non-index lesion at baseline.
PD, pharmacodynamics.

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

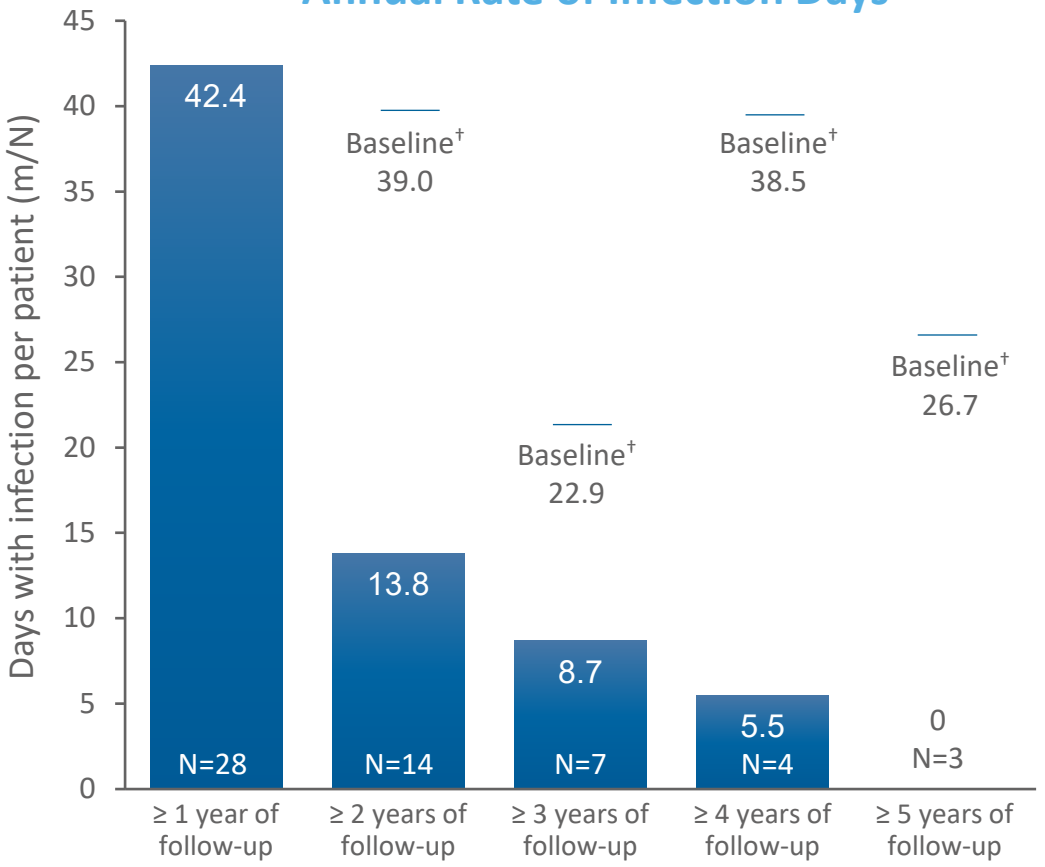
Across all trials[2]

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

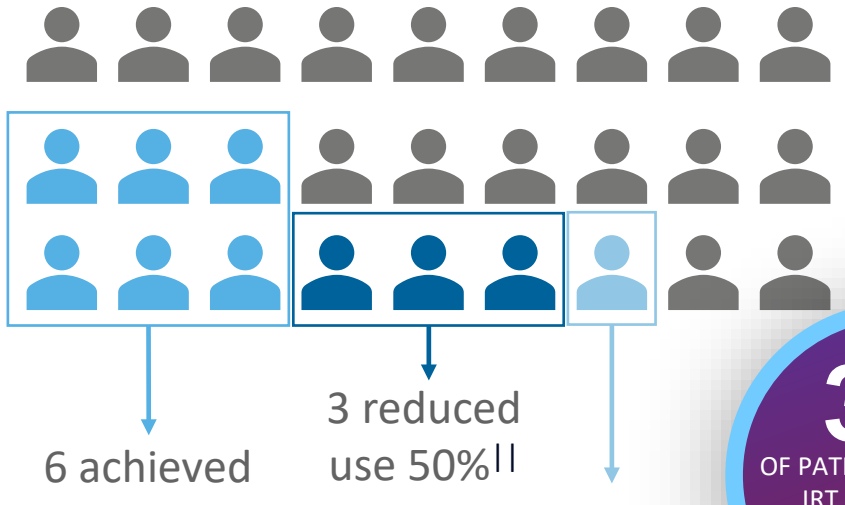
Open-label extension interim analysis of days spent with infections and IRT reduction

Annual Rate of Infection Days*



Physician-reported IRT Reduction‡

Of 27 patients receiving IRT:



6 achieved IRT freedom§

3 reduced use 50%‖

1 reduced use 30%

37% OF PATIENTS RECEIVING IRT REDUCED OR DISCONTINUED DOSE

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

Although safety was the primary objective of the open-label study, this post hoc analysis from the open-label study was not powered to provide any statistical significance of efficacy and therefore no conclusions should be drawn.

*Infections that developed during the study were reported as adverse events. Investigators were requested to inquire about signs and symptoms of infections at each visit, with a particular focus on bacterial enterocolitis. Patients were not provided an infection diary to document infections occurring between visits. One patient was excluded from the analysis due to an incorrect year that was recorded for an infection.
†Baseline infections are each group's year 1 annual rate of infections. N values changed because patients were in the OLE for different lengths of time. ‡Data on concomitant medication usage was reported at each patient visit. §One patient had a subsequent one-time dose. ‖One patient achieved IRT freedom for 3 months but subsequently restarted IRT.
IRT, immunoglobulin replacement therapy; **m**, number of infection days; **N**, number of patients in follow-up category.
Rao VK, et al. Poster presented at: *64th Annual American Society of Hematology Annual Meeting*; December 10-13, 2022; New Orleans, LA.
Please see Important Safety Information and full Prescribing Information available at joenja.com

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.