



Pharming Group N.V.

Jefferies Global Healthcare
Conference

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

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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



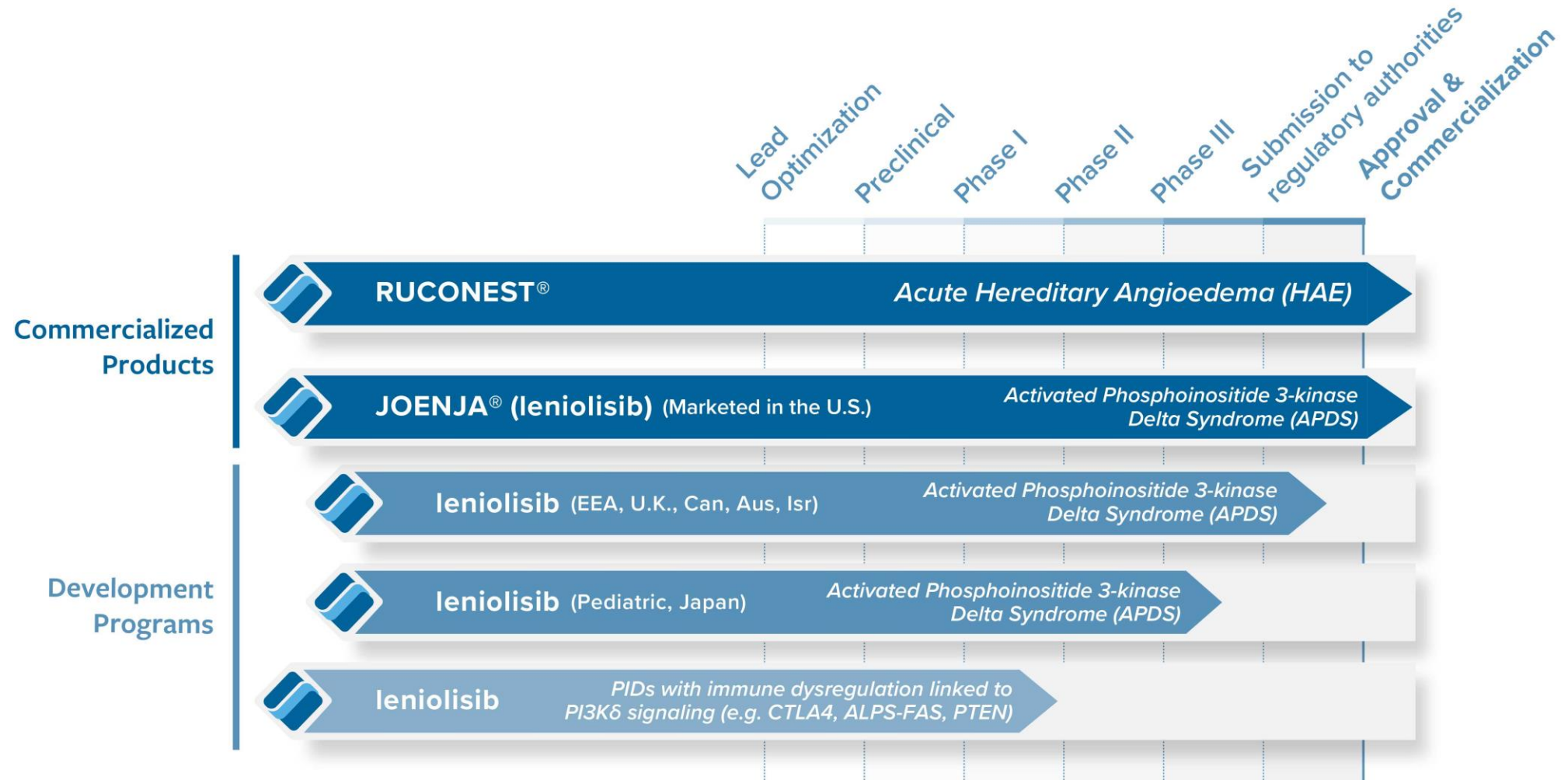
Advance internal projects and rare disease in-licensing and acquisition strategy

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

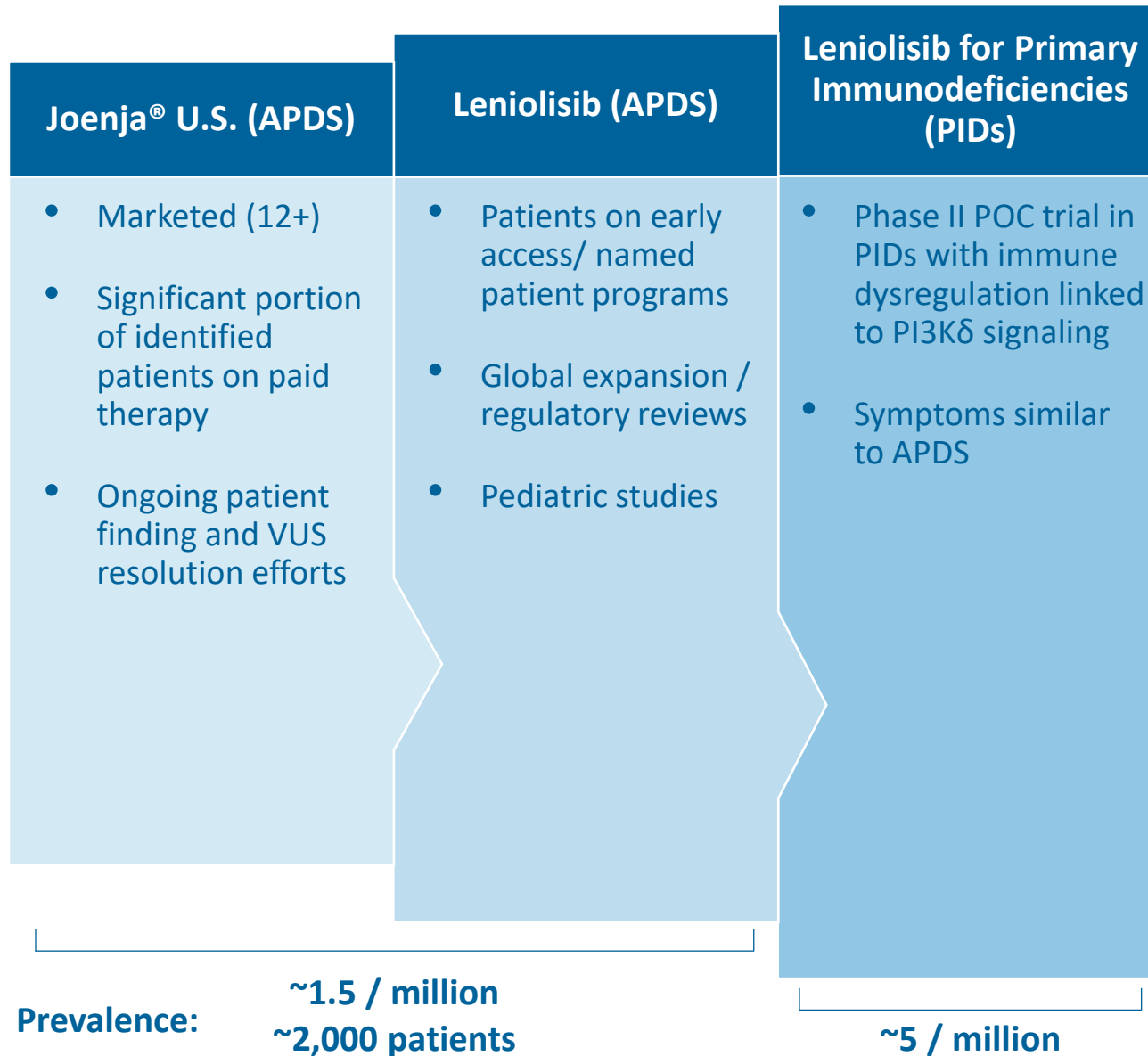
2024 Total Revenue Guidance - \$280 – \$295M (14 – 20% growth)

Driven by Joenja®

Pipeline – multiple commercial stage rare disease products



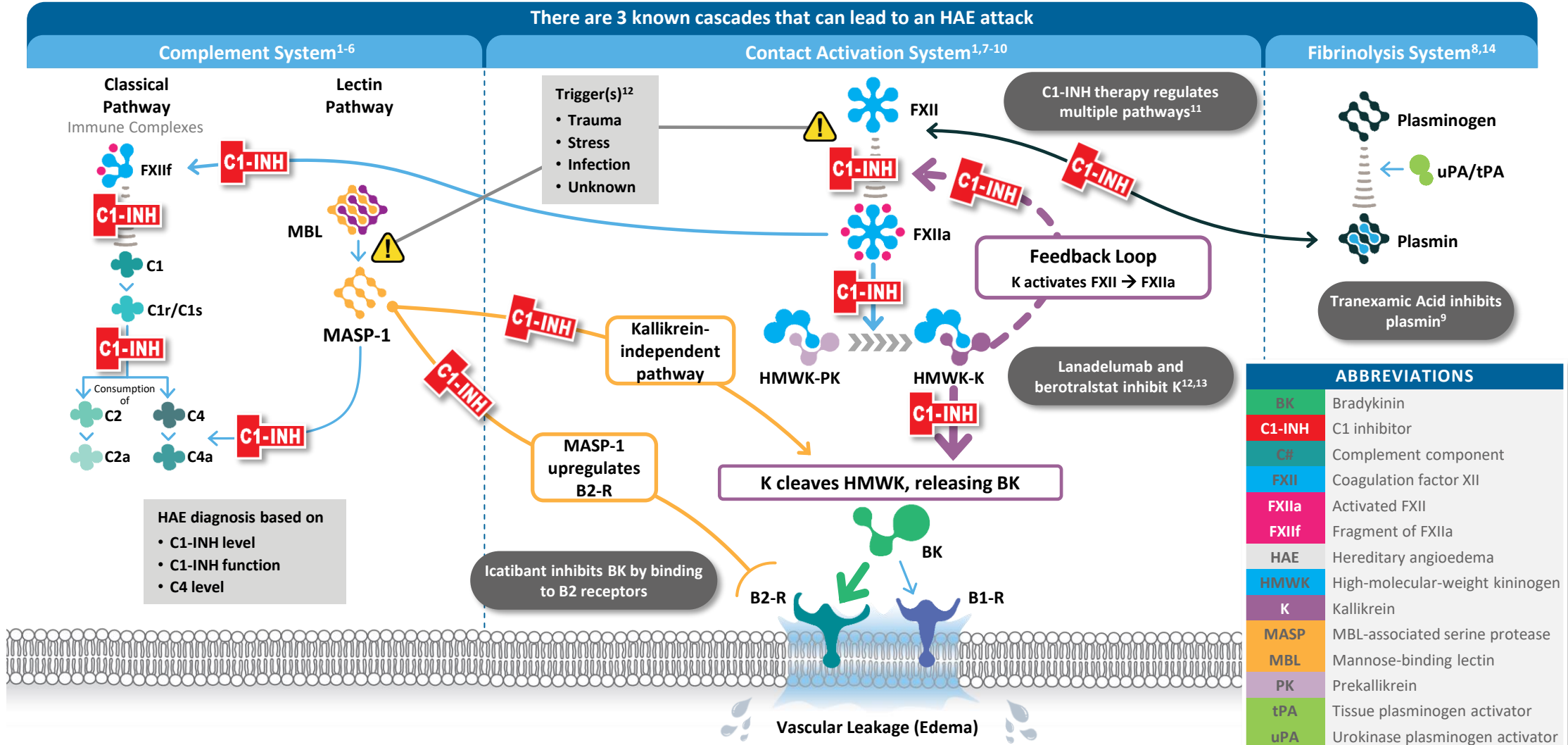
Joenja[®] (leniolisib) franchise – multi-year growth potential





RUCONEST®

C1-INH targets the root cause of HAE



ABBREVIATIONS	
BK	Bradykinin
C1-INH	C1 inhibitor
C#	Complement component
FXII	Coagulation factor XII
FXIIa	Activated FXII
FXIIf	Fragment of FXIIa
HAE	Hereditary angioedema
HMWK	High-molecular-weight kininogen
K	Kallikrein
MASP	MBL-associated serine protease
MBL	Mannose-binding lectin
PK	Prekallikrein
tPA	Tissue plasminogen activator
uPA	Urokinase plasminogen activator

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



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 days²



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



Joenja[®] (leniolisib)

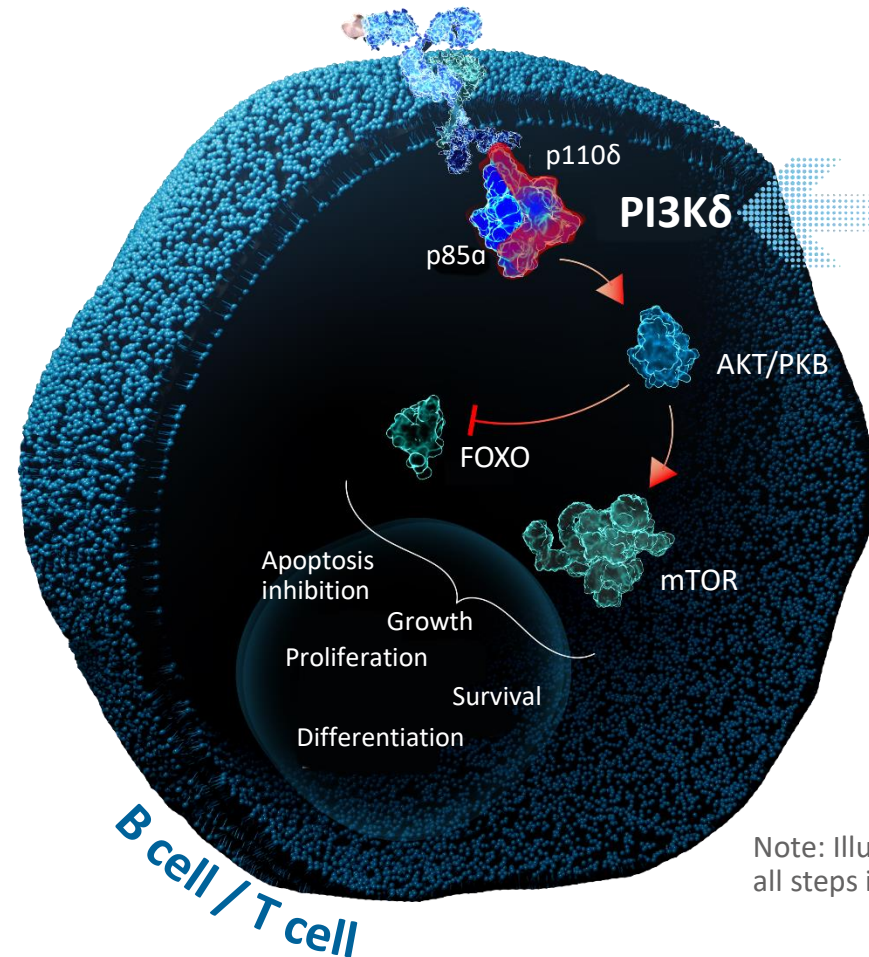
APDS is a rare, primary immunodeficiency (PID)

Genetic defect leads to PI3K δ hyperactivity

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

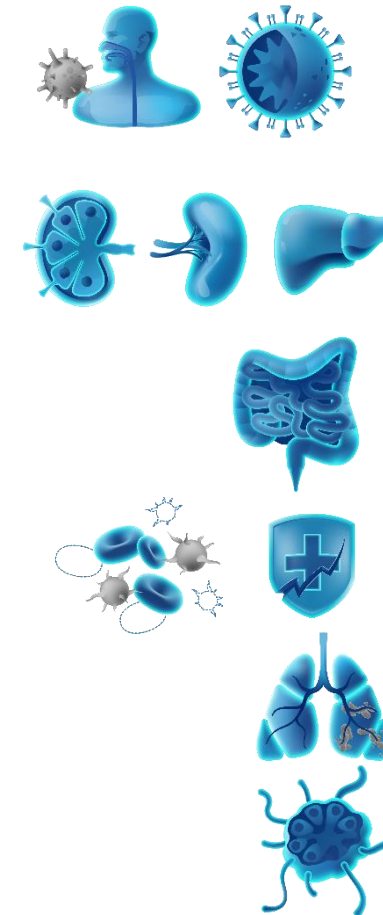


Immune imbalance leads to diverse signs and symptoms^{1,4-6}



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.

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 (PI3K δ) syndrome (APDS) in adult and pediatric patients 12 years of age and older

In a randomized placebo-controlled trial of patients with APDS

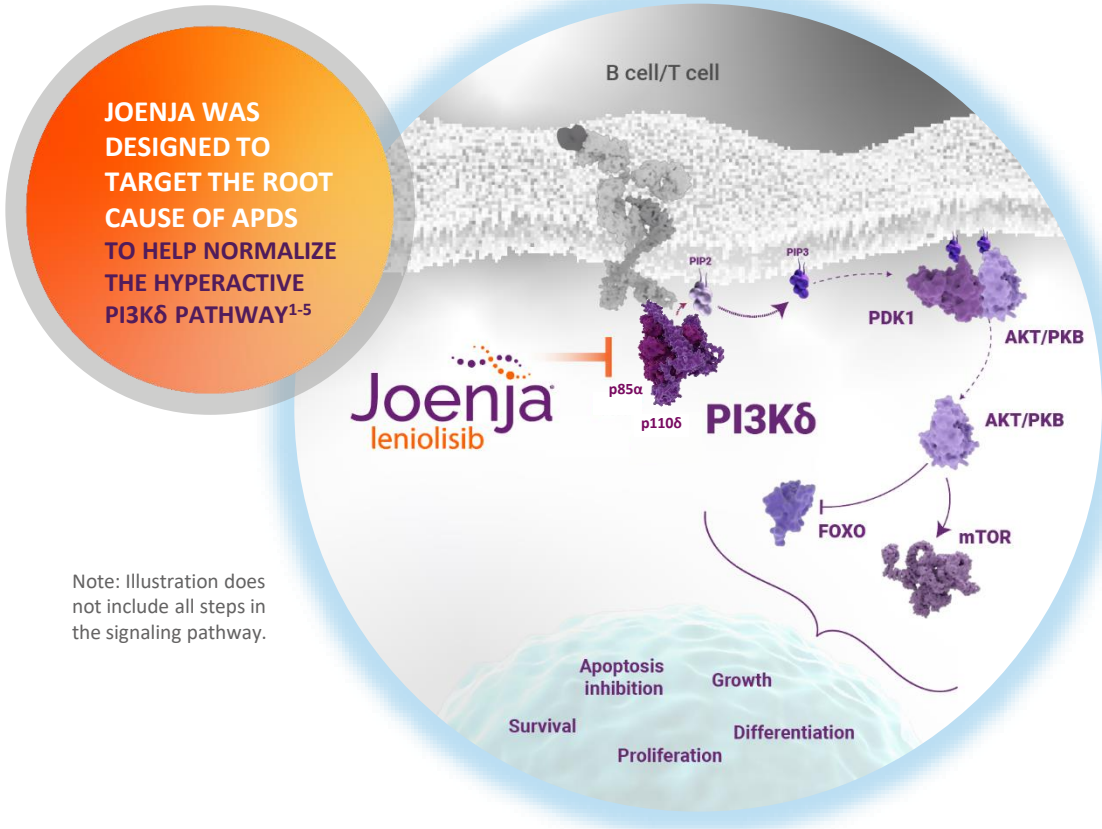
- Joenja[®] met both primary end points with significant efficacy results
- Demonstrated significant improvement in other secondary and exploratory parameters



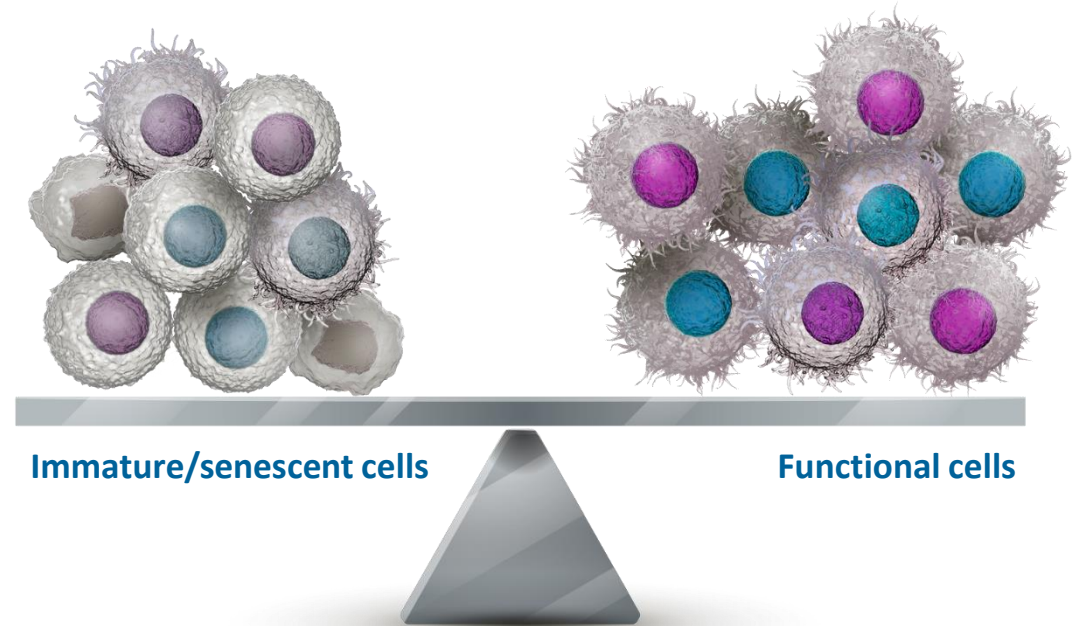
There were no drug-related serious adverse events or study withdrawals in Joenja[®] trials

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



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.




Medical education to raise awareness of APDS and share leniolisib data

- ◆ Conferences and congresses
- ◆ Abstracts
- ◆ Publications



Genetic testing

- ◆ Sponsored, no-cost testing program 
- ◆ 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[®] (leniolisib) franchise – multi-year growth potential



Joenja [®] U.S. (APDS)	Leniolisib (APDS)	Leniolisib for Primary Immunodeficiencies (PIDs)
<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> Global expansion / regulatory reviews Pediatric studies Found >840 patients globally 138 patients on therapy (access programs and clinical studies) 	<ul style="list-style-type: none"> Phase II POC trial in PIDs with immune dysregulation linked to PI3Kδ signaling Similar to APDS
<p>Prevalence: ~1.5 / million ~2,000 patients</p>		<p>~5 / million</p>

- ❖ 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



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



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



Pediatric study for 4 to 11 years
Enrollment completed



Expanded Access and Named Patient Programs



Israel marketing authorization received April 30, 2024



U.K., CAN, AUS submissions under regulatory review
Approvals in 2024-25* **



Pediatric study for 1 to 6 years ongoing
First patient dosed November 2023, enrollment continuing as planned



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

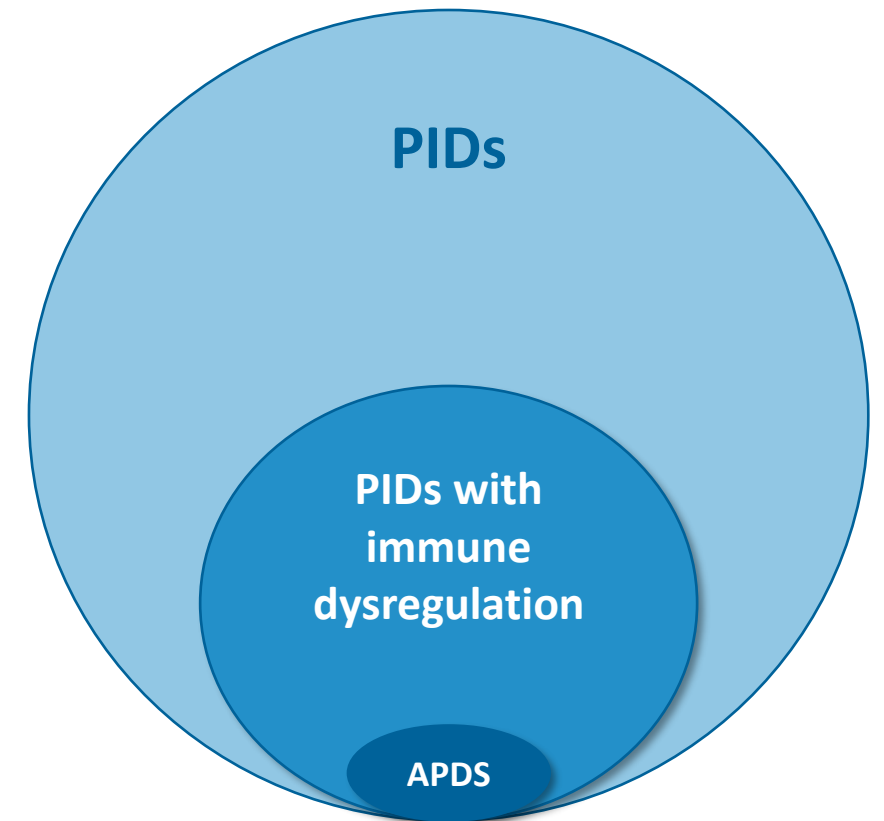
* In the U.K., Pharming filed an MAA on March 12, 2024 through the International Recognition Procedure (IRP) on the basis of FDA approval. The MAA was validated on April 17, 2024. The MHRA has 110 days from the date the IRP submission is validated, with an optional clock stop at Day 70, to review and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

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

PIDs are a broad group of disorders¹ 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 autoimmunity²

APDS is an example of a PID with immune dysregulation

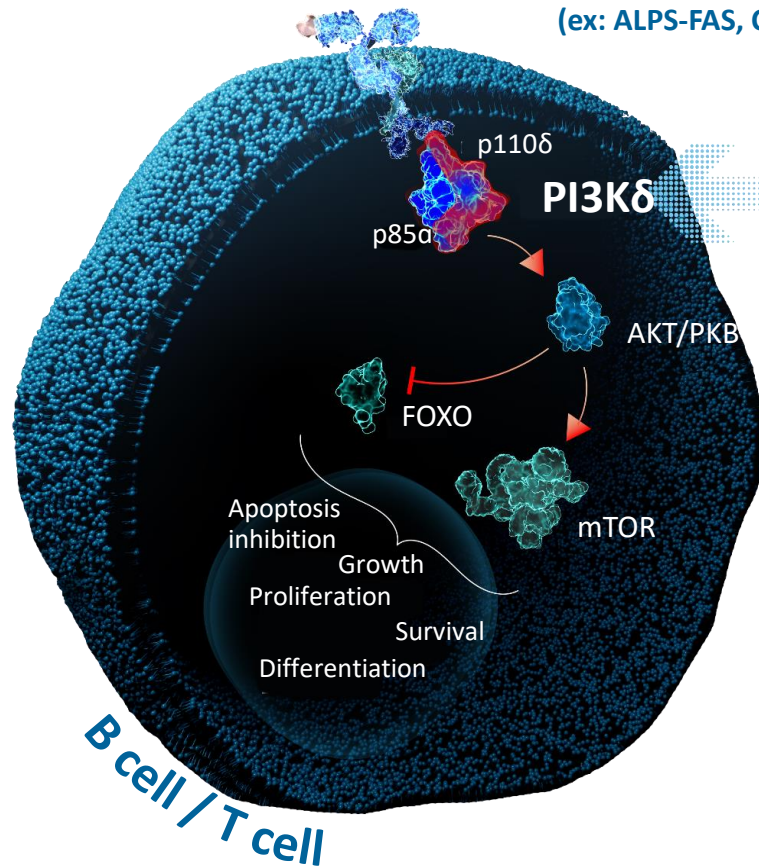


Not to scale with population sizes

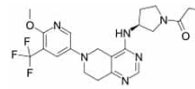
1. Bousfiha et al 2022 IUIS categorization
2. Chan and Torgerson 2020 Curr Opin Allergy Clin Immunol 20(6): 582-590

Given importance of PI3K δ in B & T cells, immune dysregulation in PIDs can occur via alterations in PI3K δ signaling

Altered PI3K δ 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.

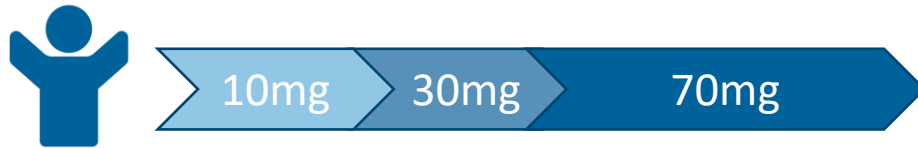
Clinical manifestations, disease onset and severity similar to APDS ⁵⁻⁸

- 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; PI3K δ , 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, Schreiber G, Westdorp H, Ligtenberg M, Netea-Maier R, Netea MG, de Vries IJM, Hoogerbrugge N. Transl Oncol. 2019;12(2):361-367

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



- Patients with PIDs linked to PI3K δ signaling, e.g. ALPS-FAS¹, CTLA4 haploinsufficiency², PTEN deficiency³
- Primary: Safety & Tolerability
- Secondary/Exploratory: PK/PD, efficacy measures
- 10/30/70 mg: 4/4/12 wks treatment, respectively
- Pick Best Dose regimen for Ph3



National Institute of
Allergy and
Infectious Diseases

Lead Investigator: Gulbu Uzel, M.D., Senior Research Physician

Co-Investigator: V. Koneti Rao, M.D., FRCPA, Senior Research Physician

Primary Immune Deficiency Clinic (ALPS Clinic)

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

Epidemiology of PIDs linked to PI3K signaling suggests treatable population of ~5/million¹

Patients identified to date included in table below

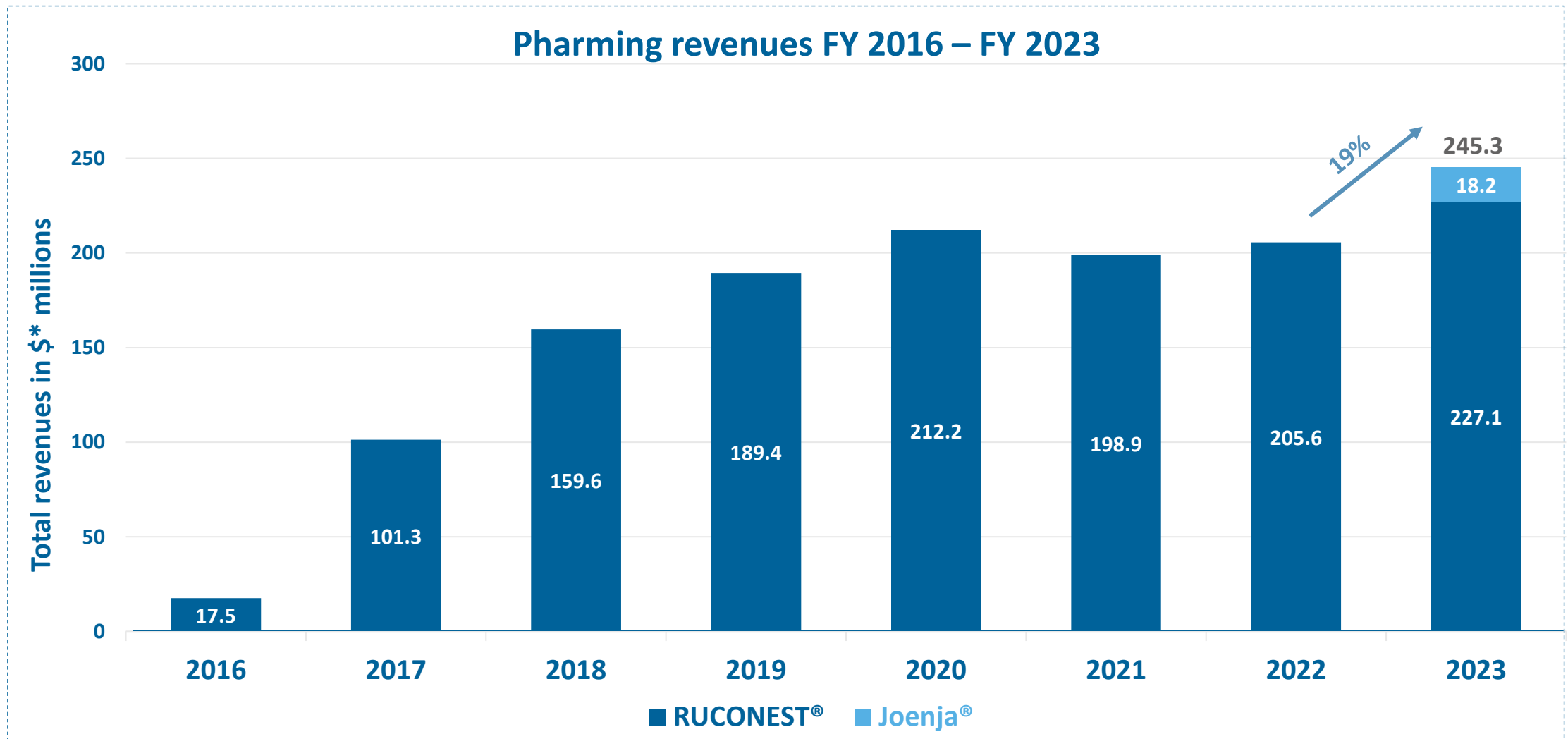
Genetic PID Type	Publication/cohort/registry	Cohort Size
ALPS-FAS	NIH protocol cohort	~500
	ESID registry ²	236
	Price et al 2014 ³	150
CTLA4	Egg et al 2022 ⁴	173
	Schwab et al 2018 ⁵	133
	NIH protocol cohort	~100
	ESID registry ²	38
PTEN	All PTEN PID patients reported across publications	~88 ⁶

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 CTLA4 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.



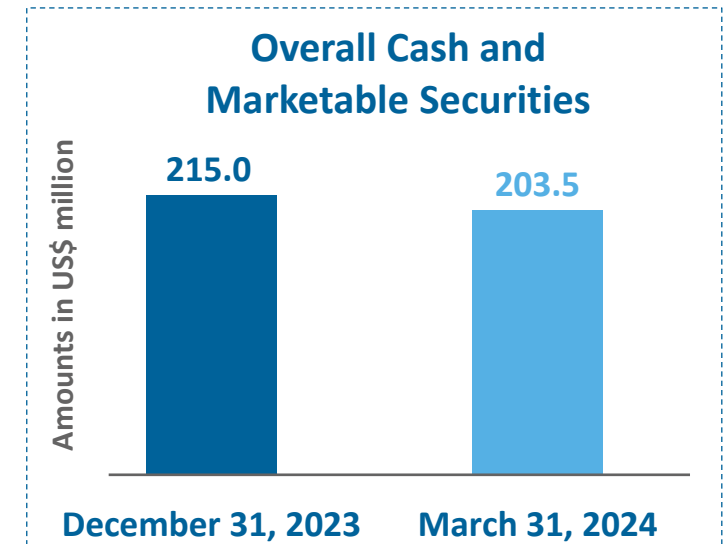
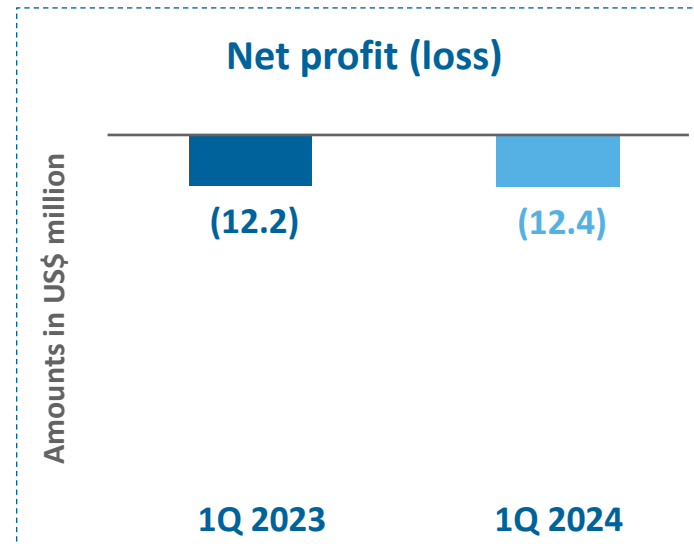
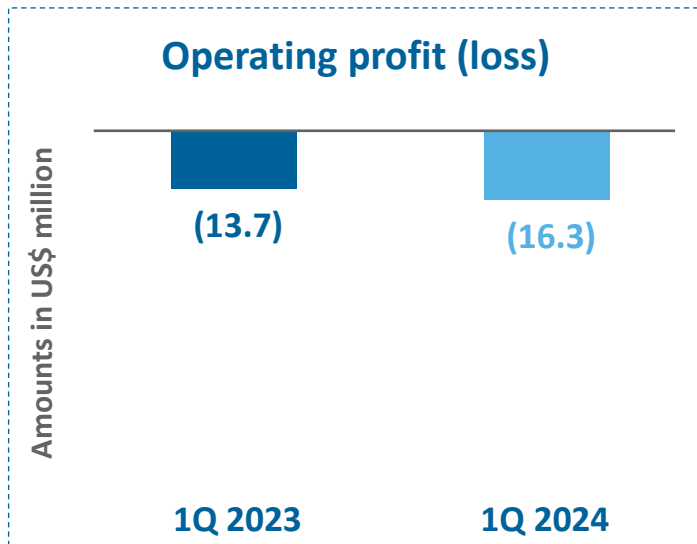
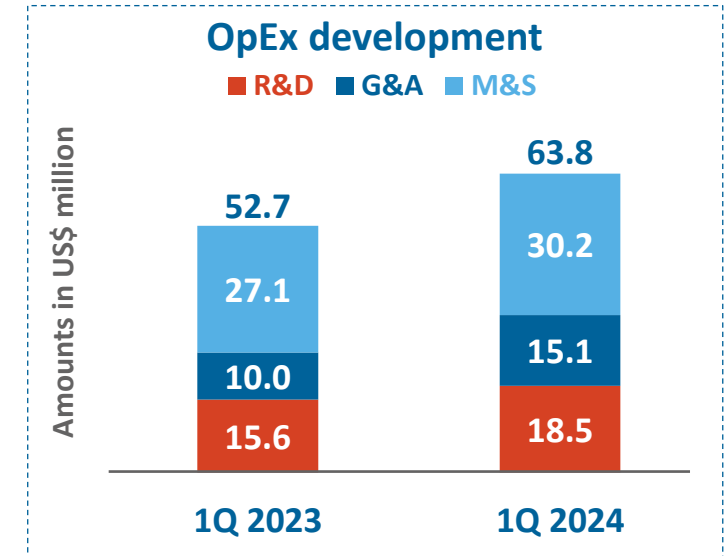
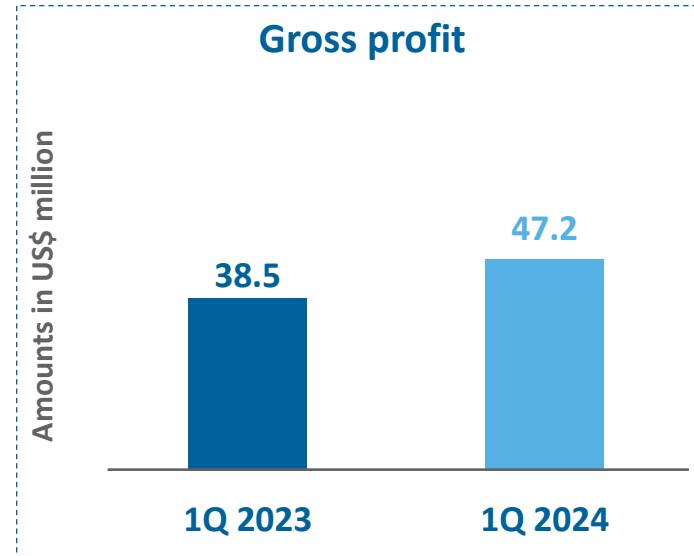
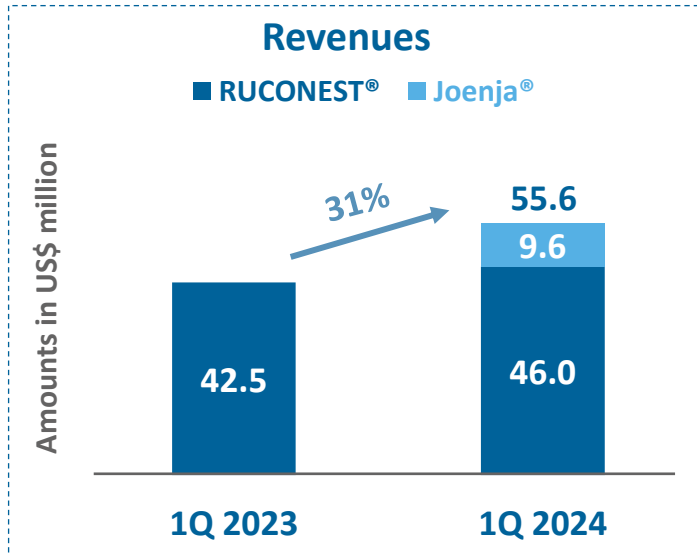
Financials and Outlook

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



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 PI3K δ 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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