Pharming Group N.V.

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

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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
  3Q24 US$63.6M (+6% vs. '23)
  9M24 US$172.6M (+12% vs. '23)
- 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

- Revenue – U.S. and NPP
  3Q24 US$11.2M (+73% vs. '23)
  9M24 US$31.9M (+210% vs. '23)
- Strong focus on patient finding
- U.K., Israel approvals
- Regulatory reviews ongoing in EUR, CAN, AUS
- Pediatric and Japan clinical trials

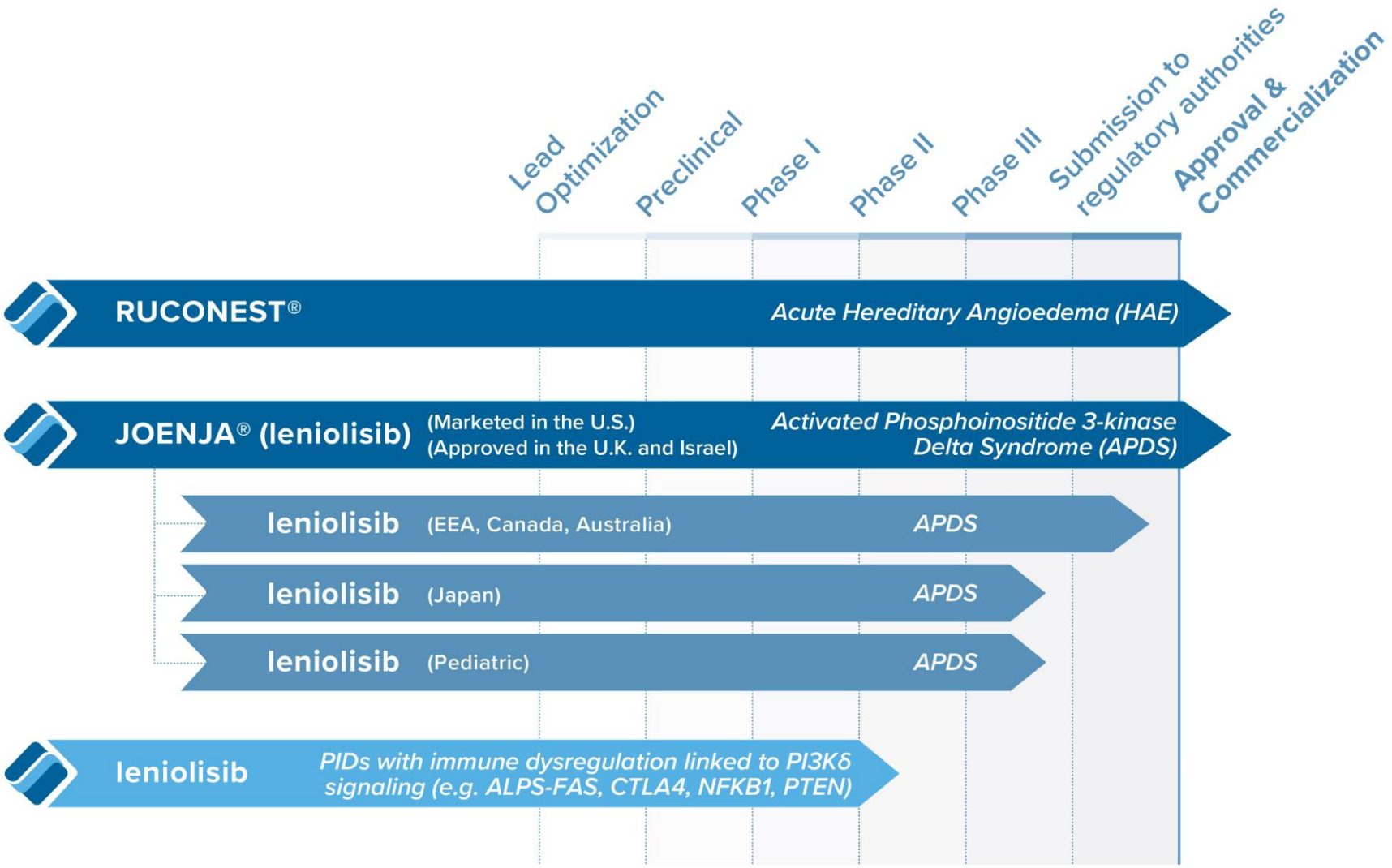
Ongoing pipeline development and management of rare disease assets

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

- Leniolisib development for PIDs with immune dysregulation beyond APDS – Started 1st Ph II
- 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



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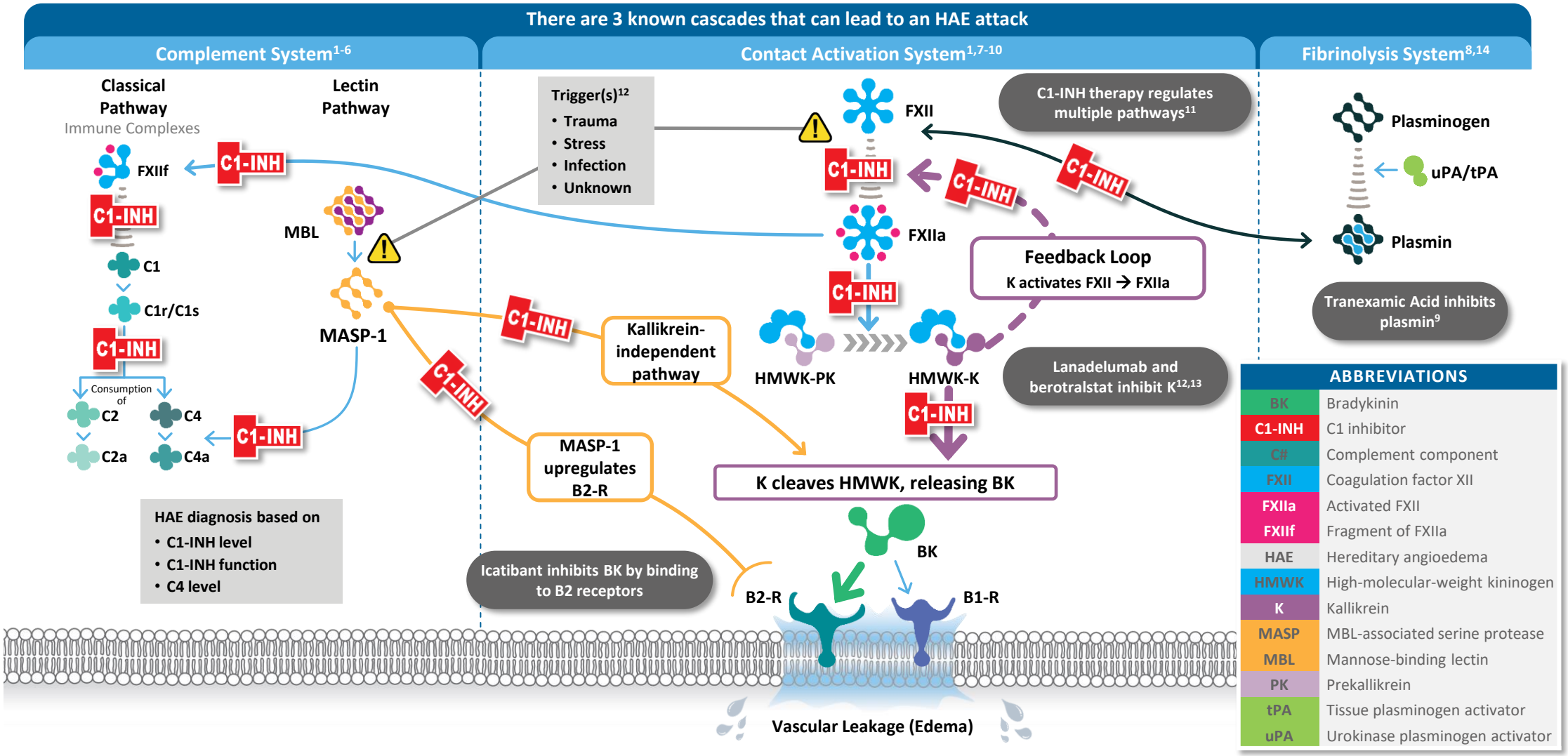
RUCONEST®

C1-INH targets the root cause of HAE

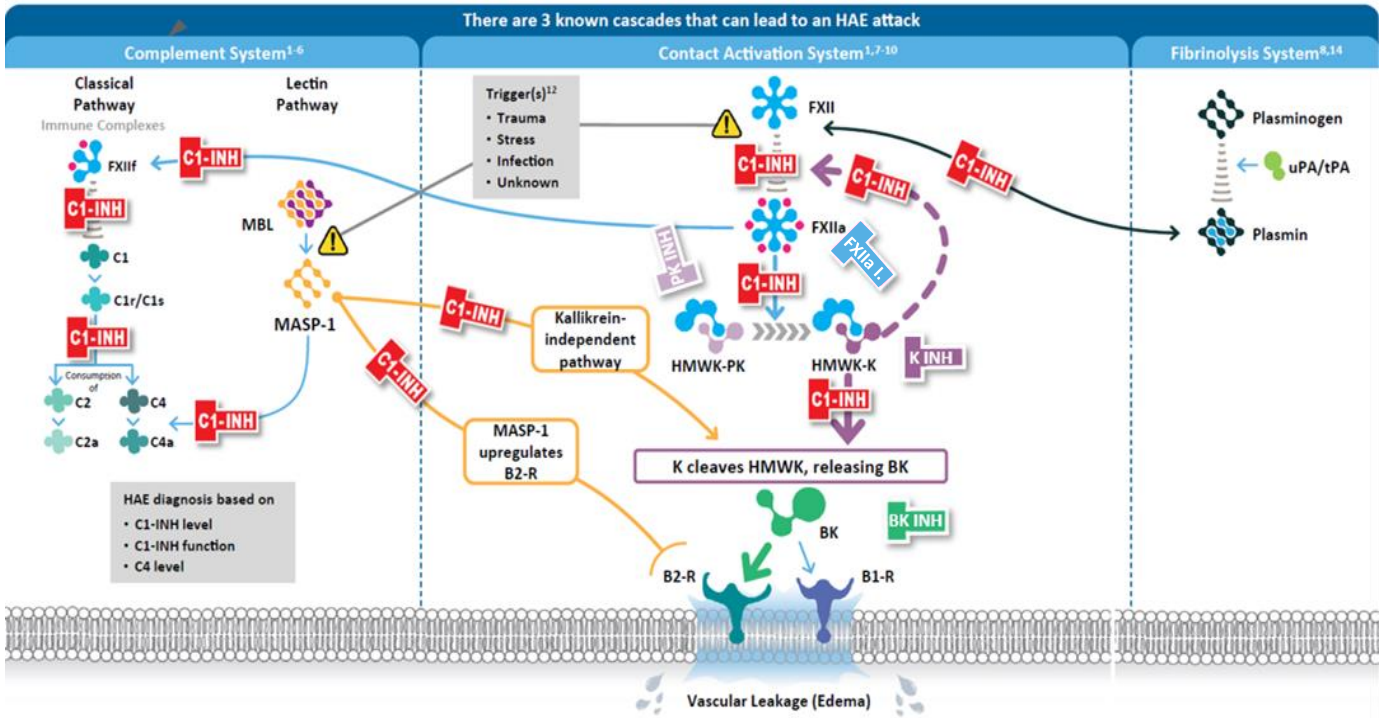


Adapted from a clinical cascade developed in partnership with Dr. Allen Kaplan. This is a current scientific understanding of the cascades. Clinical implications are unknown.

C1-INH targets the root cause of HAE
Addresses patient needs unmet by other therapies

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

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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
~100 enrollments in 3Q24

Performing well in leading U.S. revenue indicators: patients on therapy, vials shipped, physicians prescribing (786, +57 vs. 2023)

Revenue:
FY23 US$227.1M (+10%)
9M24 US$172.6M (+12%)

Strong growth in 2024, well positioned 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® (leniolisib) – strong execution and growth opportunity

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Joenja® U.S. (APDS)	Leniolisib (APDS)	Leniolisib for Primary Immunodeficiencies (PIDs)
• Marketed (12+) • Found >230 of ~500 patients • 93 patients on paid therapy + 5 pending • >30 diagnosed patients (12+) not yet enrolled and >60 pediatric • Growth potential from patient finding and VUS efforts	• Found >870 patients globally • Global expansion / regulatory reviews • Pediatric studies / label expansion (>25% patients) • 164 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**

~7 / million

- Revenues:
  - U.S. commercial sales
  - Europe / RoW access program
- 3Q24 revenue US$11.3M
- 9M24 revenue US$31.9M
- U.S. Pricing
  - 30-day supply $47,220
  - Annual cost (WAC) $566,640
- Global expansion:
  - Europe, U.K., Japan, Asia Pacific, Middle East, Latin America and Canada

Hiding in plain sight: Patient finding strategy

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 (>1,200 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® – geographic / pediatric / indication expansion

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

U.K. marketing authorization received September 25, 2024

Japan clinical study: Patient enrollment is now complete
PMDA filing mid-2025

Expanded Access and Named Patient Programs

Israel marketing authorization received April 30, 2024

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

Pediatric studies
4 to 11 years - Enrollment complete
1 to 6 years - Enrollment continuing
Filing to begin 2H 2025

Initiated Phase II trial for PIDs with immune dysregulation linked to PI3Kδ signaling

* Anticipate regulatory action in 2025 for Australia

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

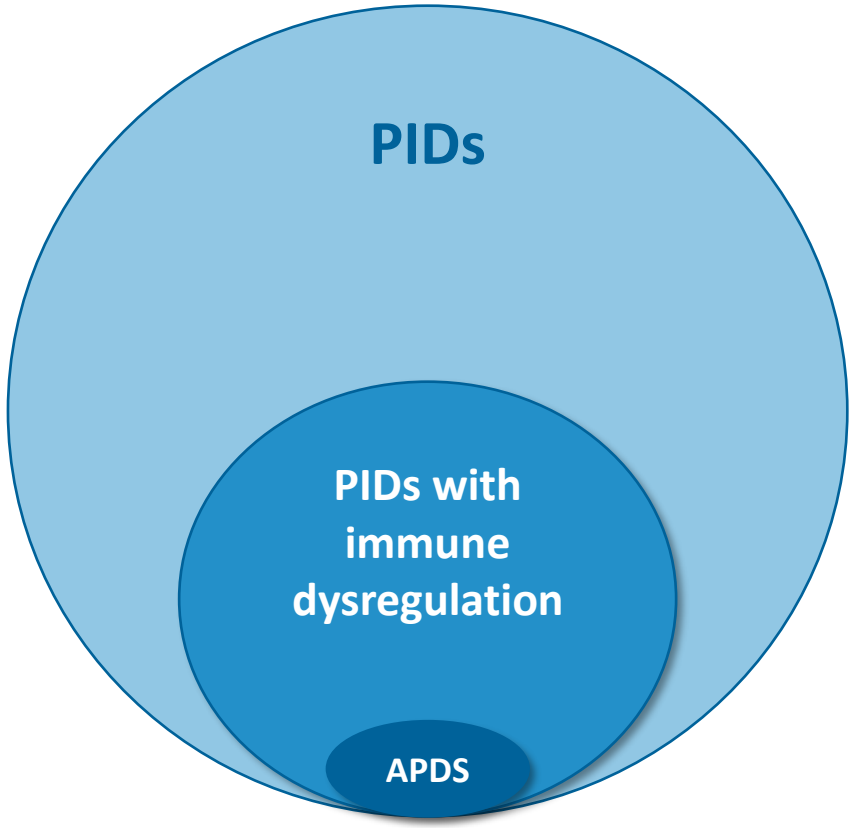
- **Pharming developing leniolisib for PIDs with immune dysregulation beyond APDS**

PIDs with immune dysregulation linked to PI3Kδ signaling

- Multiple PIDs with alterations in PI3Kδ signaling (including ALPS-FAS, CTLA4 haploinsufficiency, NFKB1 haploinsufficiency and PTEN deficiency)
- Clinical manifestations, disease onset and severity similar to APDS
- No approved therapies
- Prevalence ~7/million (approximately five times that of APDS)
- Phase II proof of concept clinical trial started October 2024

Next indication

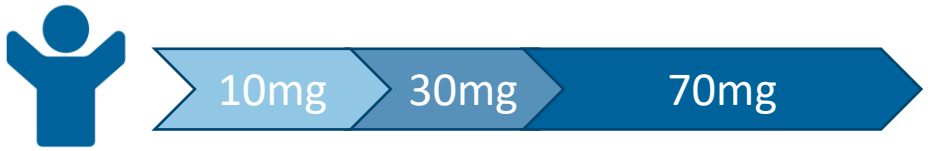
- Obtaining regulatory feedback on proposed clinical development plan



Not to scale with population sizes

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], NFKB1 haploinsufficiency[3], PTEN deficiency[4] (treatable population ~7/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

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. Bride K & Teachey D. F1000Res. 2017;6:1928. ; Rao VK & Oliveria JB. Blood 2011; 118(22):5741-51.
2. Kuehn HS, et al. Science 2014; 345:1623-27. ; Schwab C, et al. J Allergy Clin Immunol. 2018;142(6):1932-1946.
3. Lorenzini T, et al. J Allergy Clin Immunol. 2020:146:901-11.
4. Eissing M, et al. Transl Oncol. 2019;12(2):361-367. ; Tsujita, et al. J Allergy Clin Immunol. 2016;138(6):1872-80.

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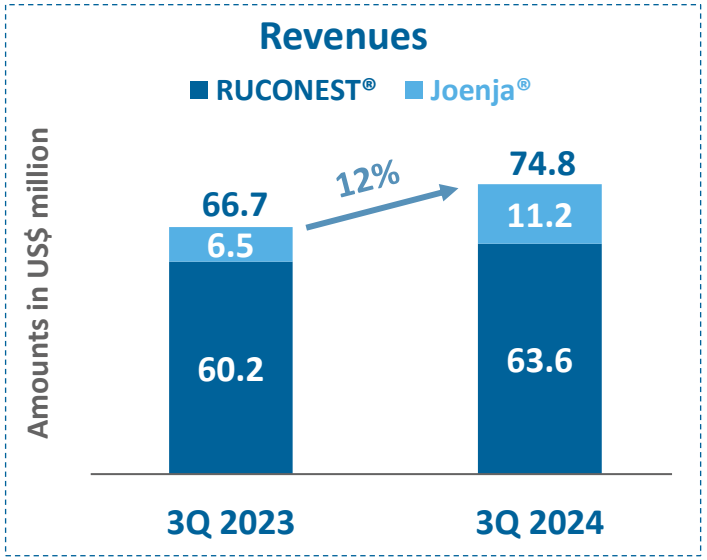
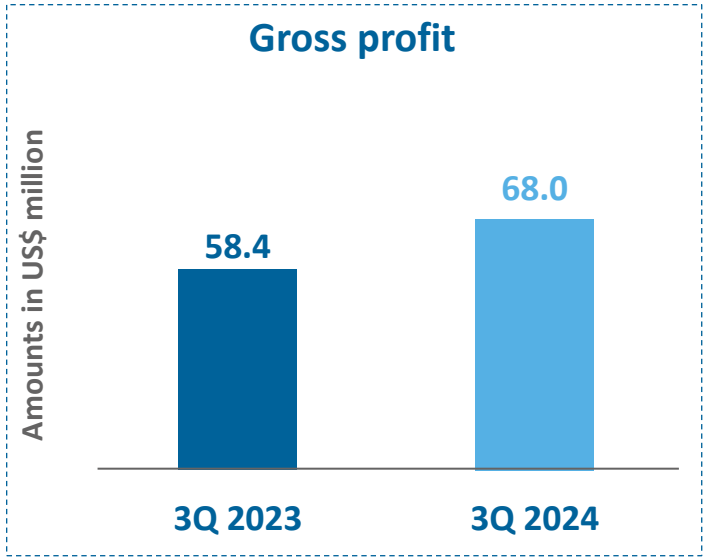
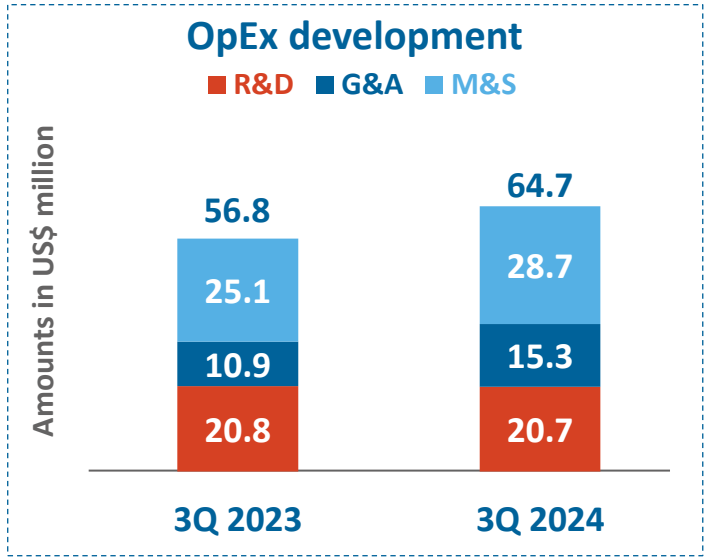
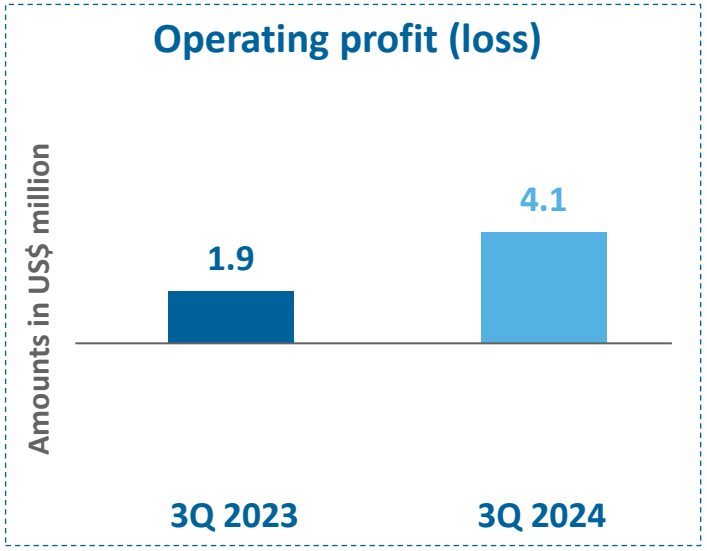
Financials and Outlook

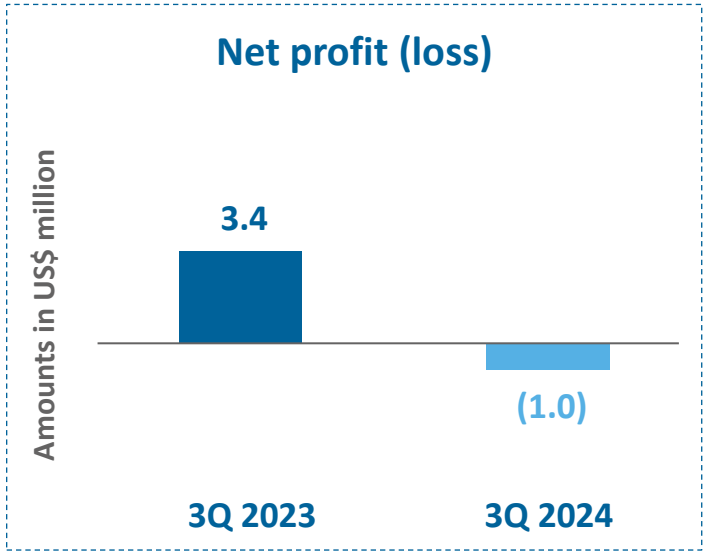
Financial highlights: 3Q 2024 vs 3Q 2023

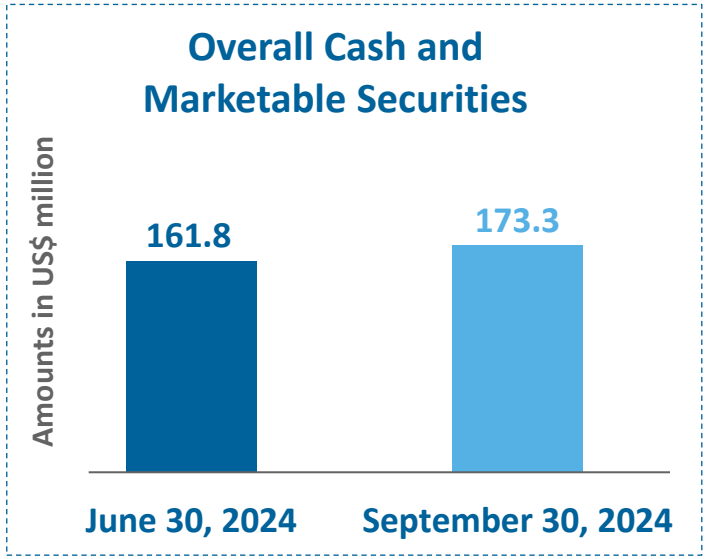




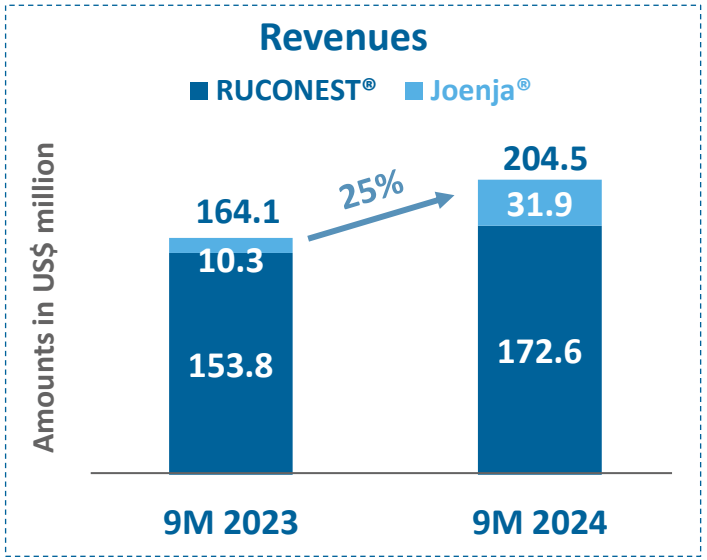


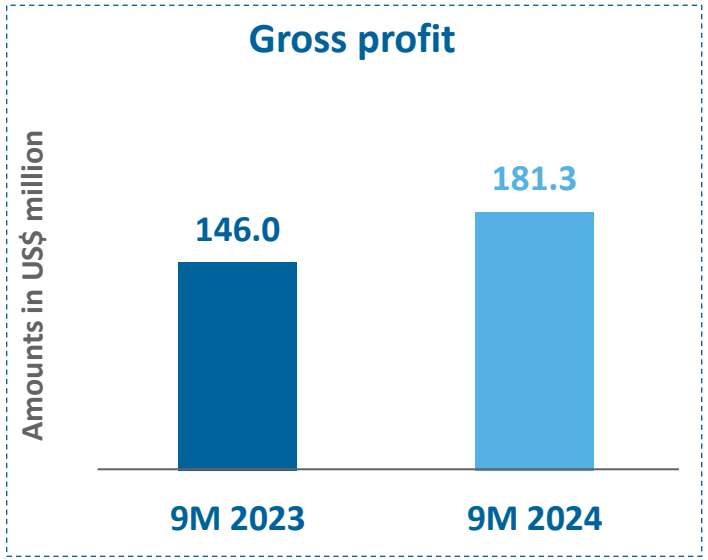


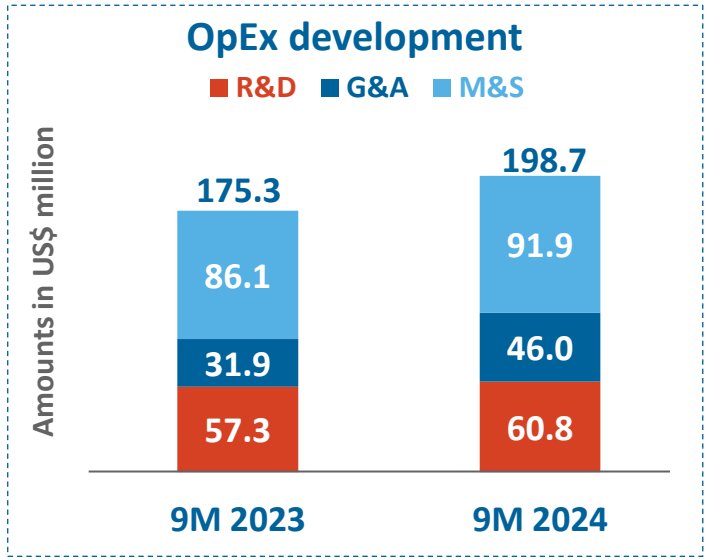


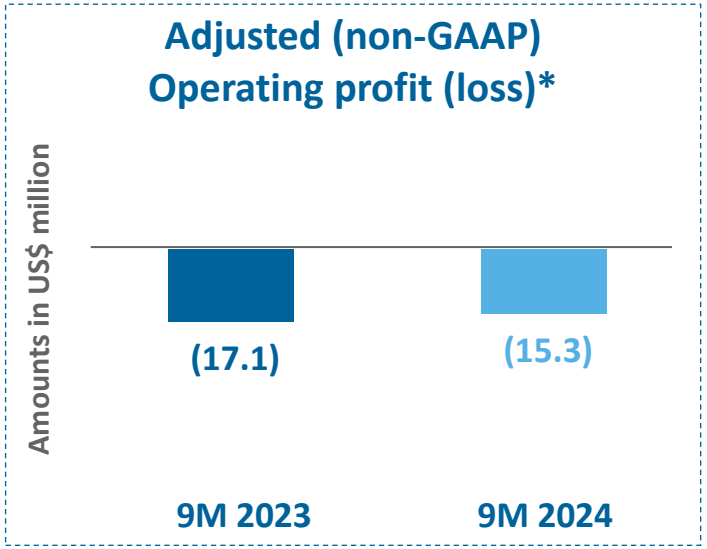


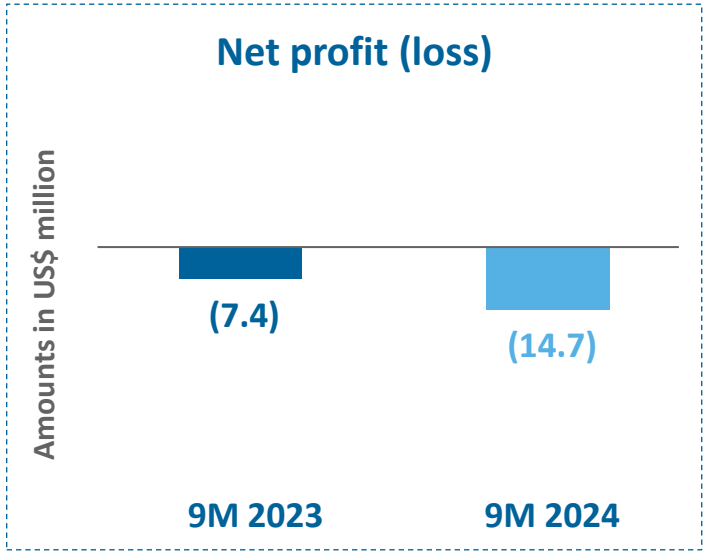
Financial highlights: 9M 2024 vs 9M 2023











* Operating profit (loss) for 9M 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$30.4 million of the US$41.6 million decrease in overall cash and marketable securities is due to convertible bond refinancing.

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 (monthly) adherence (compliance) rates >85%
  - U.S. Pricing: 30-day supply $47,220, Annual cost (WAC) $566,640, GTN Discount ~15%
- OpEx adjustments to continue in 4Q

Pharming 2024 Outlook

- Total revenues between US$280 and US$295 million (14% to 20% growth).
- 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 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, Canada and Australia.
- Advancing the Phase 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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