













Sijmen de Vries, MD
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## **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 and technical developments. In light of these risks and uncertainties, and other risks and uncertainties that are described in Pharming's 2022 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2022, 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 forwardlooking 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.







Introduction

## Building a leading global rare disease biopharma company







Ongoing pipeline development and management of rare disease assets

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

- ◆ FY23 revenue US\$227.1M
- ◆ 10% revenue growth vs. low single digit growth guidance
- Revenue acceleration increase in patients and prescribers
- Patients reliant on RUCONEST® despite increased therapy options

Successful commercialization of Joenja® (leniolisib) – first and only FDA approved treatment for APDS

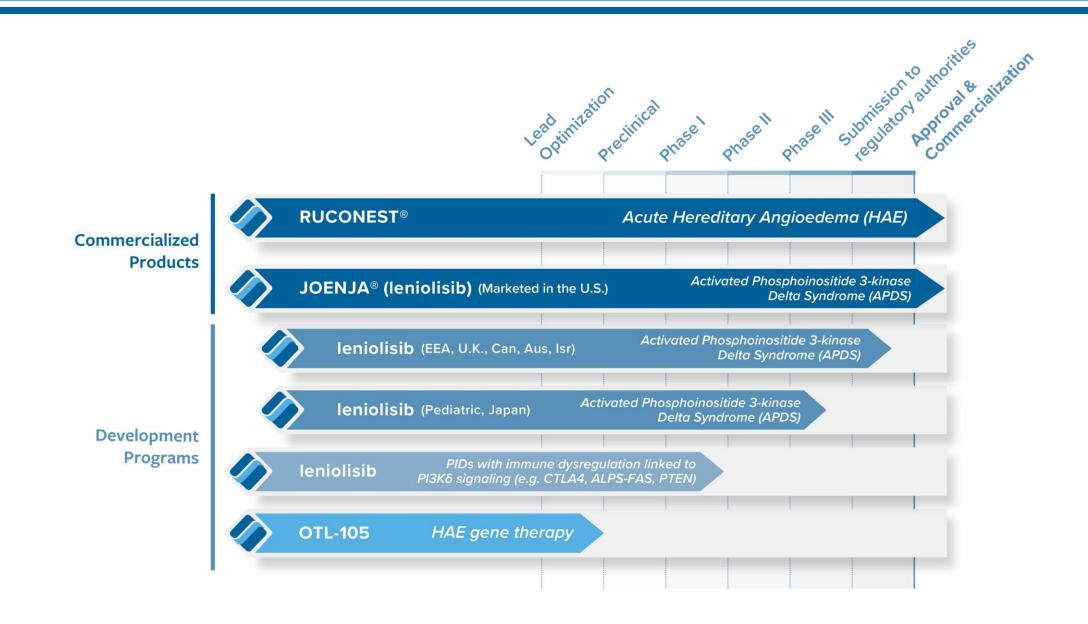
- ◆ Joenja® U.S launch April 2023 FY23 revenue US\$18.2M
- Regulatory reviews ongoing in EUR, CAN, AUS, ISR; U.K. (filed)
- Pediatric and Japan clinical trials ongoing
- Strong focus on patient finding

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

- ▶ Leniolisib development for PIDs with immune dysregulation beyond APDS Ph2 start 2Q24
- Partnership focus on early to late-stage clinical programs in immunology, hematology, respiratory and gastroenterology

## Pipeline – multiple commercial stage rare disease products







## **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 days<sup>2</sup>



Strong U.S. in-market demand – New patient enrollments up 25% FY23 vs. FY22, >70 each quarter



Performing well in leading revenue indicators in the U.S.: active patients, vials shipped, # physicians prescribing



Revenue: FY23 US\$227.1M (+10%) 4Q23 US\$73.3M (+34%)



Continued growth in 2024, strong positioning vs. acute orals in late-stage development

## **Strong commitment to HAE community**





**Strong patient organization support** since 2000



More than 729 U.S. physicians (and growing) prescribing RUCONEST®

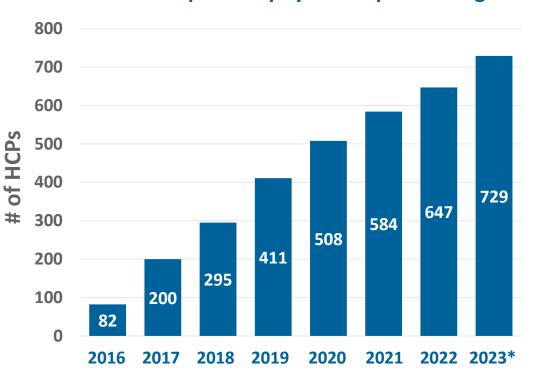


>2,000 patients with HAE have been prescribed RUCONEST®





#### # of unique U.S. physicians prescribing



\*Data thru December 31, 2023

## Joenja® U.S. launch: strong commercial execution





Strong commercial execution 9 months into U.S. launch



Continue to enroll patients and add patients on paid therapy in 4Q23 92 enrollments, of which 81 patients on paid therapy at end 4Q23



APDS Assist program ensures eligible patients have access to therapy



FY23 revenue US\$18.2M, including US\$7.9M in 4Q23



Significant focus on genetic family testing



Validation studies to confirm which variants of uncertain significance (VUS) should be classified as APDS to complete in 4Q24, focused on >1100 patients identified in the U.S. with VUSs









Anurag Relan, MD
Chief Medical Officer

APDS
Joenja® (leniolisib)
Second indication

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





# Activated phosphoinositide 3-kinase delta (PI3K $\delta$ ) 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

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

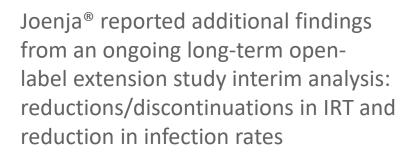


Joenja® (leniolisib) is a prescription medicine that is used to treat activated phosphoinositide 3-kinase delta (PI3K $\delta$ ) syndrome (APDS) in adult and pediatric patients 12 years of age and older

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



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® – looking beyond FDA approval





**Europe – awaiting CHMP opinion on MAA\*** 



UK – submitted MAA to MHRA on March 12, 2024\*\*



Japan clinical study: Patient enrollment is now complete

PMDA filing following completion of appropriate clinical trials



CAN, AUS, ISR submissions under regulatory review

Approvals in 2024\*\*\*



Pediatric study for 4 to 11 years

**Enrollment nearing completion** 



Pediatric study for 1 to 6 years ongoing

First patient dosed November 2023, enrollment continuing as planned



**Expanded Access and Named Patient Programs** 



Initiate leniolisib development for PIDs with immune dysregulation (Phase 2 trial)

<sup>\*</sup> Received CHMP Day 180 second list of outstanding issues in November 2023. CHMP consulted Ad-hoc Expert Group (AEG) at end November 2023 meeting. Assuming positive outcome of CHMP review, EMA approval ~2 months later.

\*\* Pharming filed an MAA through the International Recognition Procedure (IRP) on the basis of FDA approval. MHRA would have 110 days – with an option to enforce a 60-day clock stop, if needed - from the date the IRP submission is

validated, to review and issue a decision.

## Hiding in plain sight: Patient finding strategy





# Medical education to raise awareness of APDS and share leniolisib data

- Conferences and congresses
- Abstracts
- Publications





**MMUNODEFICIENCIES** 

CONGRESS



& Immunology



Sponsored, no-cost testing program



- Genetic counselors to assist with testing and reviewing results
- Partnering with genetic testing companies to identify previously and newly diagnosed APDS patients



## **Family testing**

- Inherited disease\* but most APDS patients do not have diagnosed family members
- Patients may not be aware of genetics or have access to specialty physicians
- Cooperating with clinicians to encourage family testing
- Patients can request a genetic test through partner Genome Medical (if suspect APDS for themselves or family members)
- Reduces barrier for easier testing of those suspected with APDS

## Helping diagnose APDS patients: Variant of Uncertain Significance (VUS) resolution



# Genetic testing frequently leads to inconclusive results - previously unseen genetic variants:



Patients have clinical symptoms compatible with APDS, but genetic variant test is inconclusive



Frustrating for patients and clinicians

Need to determine if Variant of Uncertain Significance (VUS) causes APDS

### Pharming initiatives/partnerships to resolve VUSs



#### **Variant Curation**

- ClinGen expert panels develop gene/disease specific thresholds and criteria for classifying variants
- Partnership with Genomenon to develop Genomic Landscape (comprehensive, systematic review of all published variant data)



### **Functional testing**

- Improve access to directly measure PI3K pathway activity in patient blood samples
- Sharing of results via public databases (ClinVar)



## Multiplexed assays of variant effect (MAVE)

- Test nearly all possible variants in a single experiment
- Generate variant effect map, including variants already found and those not yet found (proactive)

## Recent medical conference presentations (selected)







 A Real-world Comparison of Health Care Resource Utilization and Health Care Costs Among Patients With Activated PI3K-Delta Syndrome Versus a Control Cohort of Patients Without Activated PI3K-Delta Syndrome in the United States



- ACAAI American College of Allergy, Asthma & Immunology (November 2023)
  - Mortality in Patients With Activated Phosphoinositide 3-Kinase Delta Syndrome, a Systematic Literature Review



- **♦ IPIC International Primary Immunodeficiencies Congress (November 2023)** 
  - Results of a second interim analysis of an ongoing single-arm open-label extension study of leniolisib in activated PI3K delta syndrome: long-term efficacy and safety through to March 2023.
  - Complicated course of activated PI3K delta syndrome-1 ameliorated by leniolisib: a case study.
  - Gastrointestinal manifestations in patients with activated PI3K delta syndrome (APDS) treated with leniolisib.
  - Assessing long-term treatment with leniolisib and its effects on bronchiectasis in patients with activated PI3K delta syndrome (APDS).



- AAAAI American Academy of Allergy, Asthma & Immunology (February 2024)
  - Clinical and Genetic Findings of Individuals Tested via the navigateAPDS Sponsored Genetic Testing Program

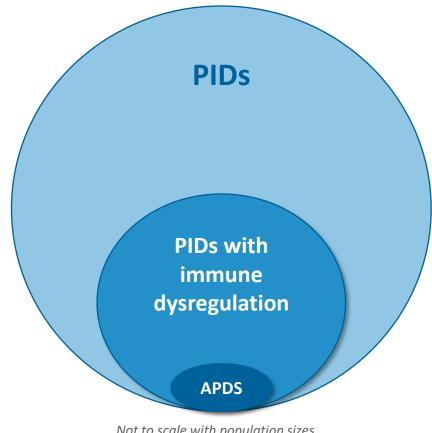
## Primary Immunodeficiencies (PIDs) with immune dysregulation



### PIDs are a broad group of disorders<sup>1</sup> with key features:

- Genetic basis, i.e., not secondarily caused by another disease 'Inborn Errors of Immunity' (IEI) is used interchangeably with PID
- An increased risk of infection may be the predominant manifestation, due to poor immune system function
- PID patients may have a predominance of immune dysregulation, for example: lymphoproliferation and autoimmunity<sup>2</sup>

APDS is an example of a PID with immune dysregulation

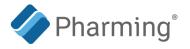


Not to scale with population sizes

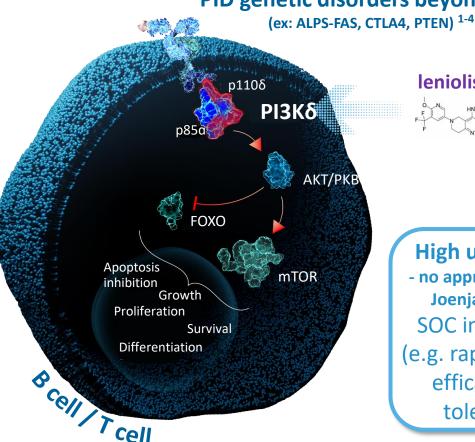
Bousfiha et al 2022 IUIS categorization

Chan and Torgerson 2020 Curr Opin Allergy Clin Immunol 20(6): 582-590

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



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



## **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

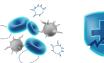
Note: Illustration does not include all steps in the signaling pathway.

### 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





- Sinopulmonary
- Herpesvirus



#### Lymphoma

Infections

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

## Leniolisib development for PIDs with immune dysregulation



- Based on APDS experience, leniolisib has potential to be an effective & tolerable chronic treatment approach for PIDs with immune dysregulation
- Leniolisib, by reducing PI3Kδ activity, should help rebalance immune dysregulation in PIDs, positively impacting clinical manifestations including lymphoproliferation and autoimmunity
- Initial development in PID genetic disorders with immune dysregulation linked to PI3Kδ signaling in lymphocytes with similar clinical phenotypes to APDS, e.g. ALPS-FAS¹, CTLA4 haploinsufficiency², PTEN deficiency³
  - Epidemiology suggests <u>prevalence of ~5/million</u><sup>4</sup>
  - FDA review / feedback received on clinical trial plans
- Phase 2 proof of concept clinical trial final stages of preparations to commence trial

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

<sup>2.</sup> 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

<sup>3.</sup> 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

<sup>4.</sup> Size based on estimate of 5 patients per million (based on Pharming literature review, KOL feedback and review of patient registries)

## PIDs linked to PI3Kδ signaling – Phase 2 study design



Phase 2 proof of concept clinical trial – single arm, openlabel, dose range-finding study (N=12)



- Patients with PIDs linked to PI3Kδ signaling, e.g. ALPS-FAS, CTLA4 haploinsufficiency, PTEN deficiency
- 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



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)







Jeroen Wakkerman Chief Financial Officer

**Financials** 

## Financial highlights: 4Q 2023 vs 4Q 2022



TOTAL REVENUES 4Q 2022

US\$54.6 million



TOTAL REVENUES 4Q 2023

US\$81.2 million



GROSS PROFIT 4Q 2022

US\$48.3 million



GROSS PROFIT 4Q 2023

US\$74.1 million



OPERATING COSTS 4Q 2022

US\$(57.4)million



OPERATING COSTS 4Q 2023

**US\$(73.6) million** 



OPERATING PROFIT (LOSS) 4Q 2022

US\$(10.2) million



OPERATING PROFIT (LOSS)
4Q 2023

**US\$1.1 million** 



NET PROFIT (LOSS) 4Q 2022

US\$(14.6) million



NET PROFIT (LOSS) 4Q 2023

US\$(2.7) million

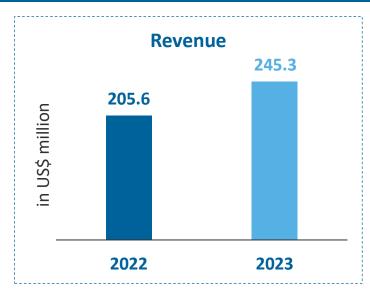




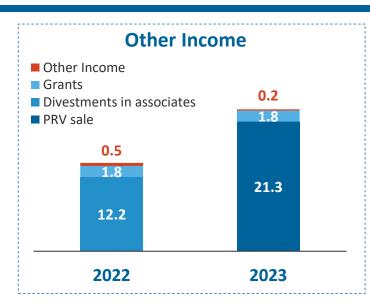
Cash and cash equivalents, together with restricted cash and marketable securities, increased from US\$208.7M at the end of 2022 to US\$215.0M at the end of 2023

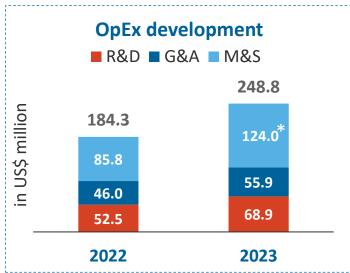
## Financial highlights: FY 2023 vs FY 2022









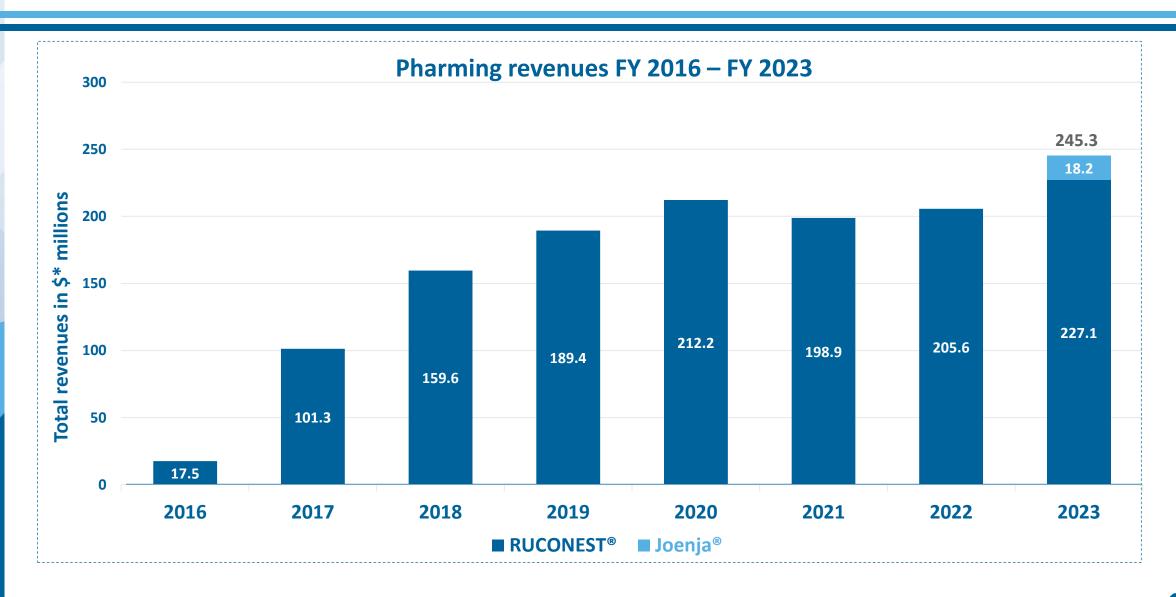






## **RUCONEST®** and Joenja® driving revenue growth



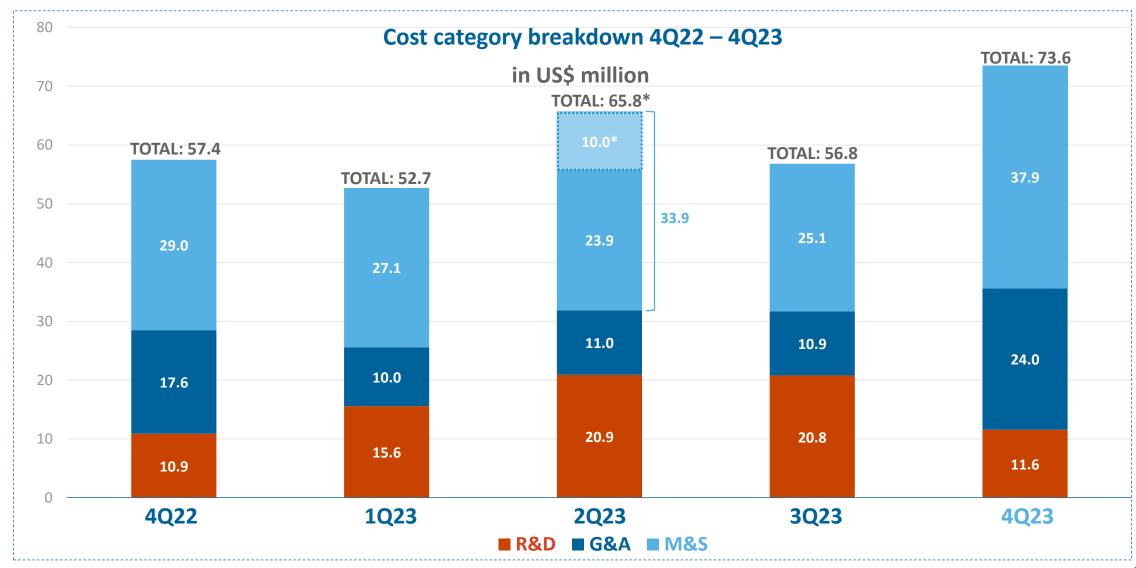


<sup>•</sup> From FY 2016 – FY 2020 Pharming Group reported earnings in EUR. Revenues during this time frame have been converted to USD. In 2021, Pharming Group began reporting earnings in USD.

<sup>- 4</sup>Q 2020 and 1Q 2021 quarterly fluctuations and volatility from COVID-19.

## Investment in Joenja® launch and leniolisib development

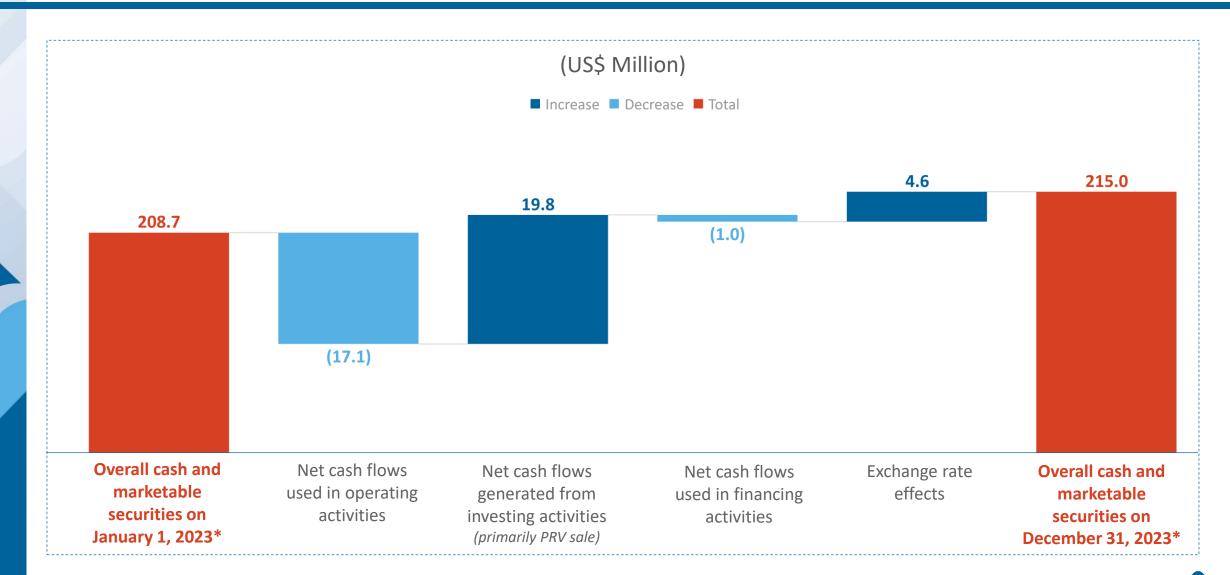




## FY 2023: Cashflow including marketable securities

January 1, 2023 – December 31, 2023





## **2024** Revenue guidance



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

#### **Assumptions**

- Quarterly fluctuations expected
- ♦ Joenja® significant driver of revenue growth, continued RUCONEST® growth
- Joenja® assumptions:
- Continued growth in patients on paid therapy
- U.S. Pricing: 30-day supply \$47,220, Annual cost (WAC) \$566,640

## **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, Australia, and Israel.



Initiate and advance a Ph 2 clinical trial for leniolisib in PIDs with immune dysregulation linked to PI3K $\delta$  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)













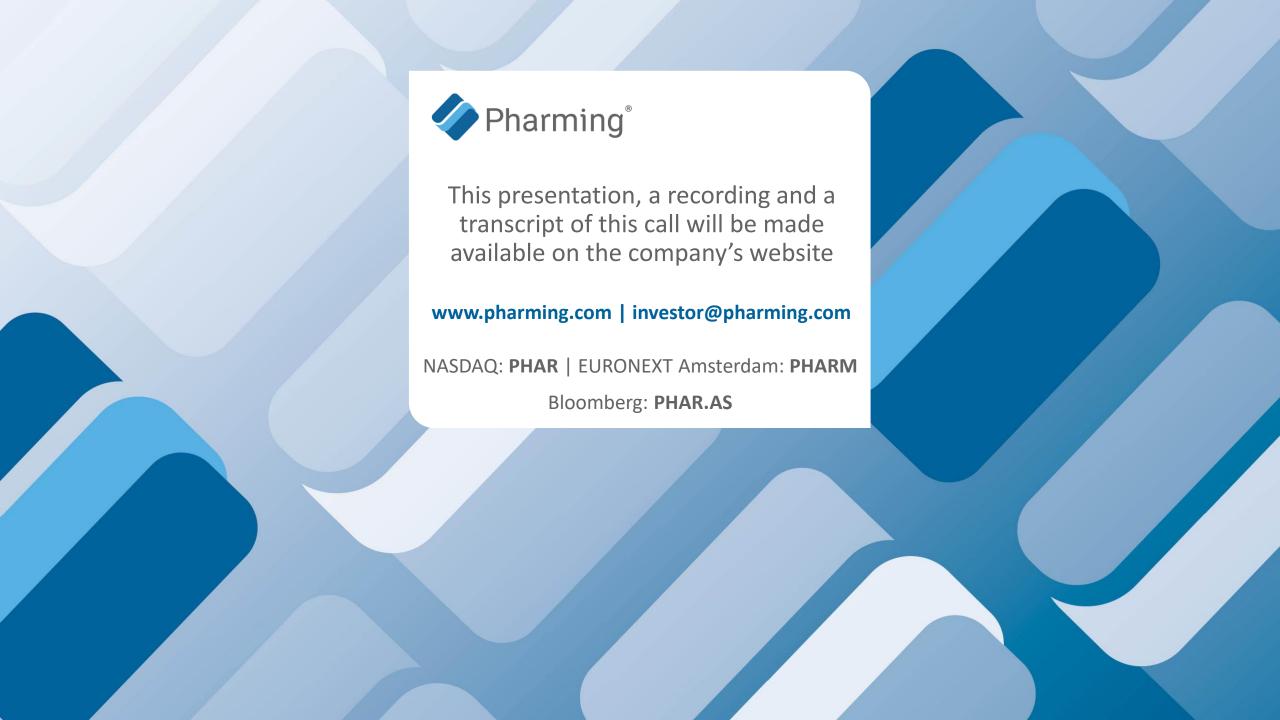


Sijmen de Vries, MD

**Stephen Toor** Chief Executive Officer Chief Commercial Officer

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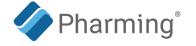


## **Statement of profit and loss**



Amounts in US\$ '000	2023	2022
Revenues	245,316	205,622
Costs of sales	(25,212)	(17,562)
Gross profit	220,104	188,060
Other income	23,349	14,523
Research and development	(68,914)	(52,531)
General and administrative	(55,877)	(46,016)
Marketing and sales	(124,049)	(85,803)
Other Operating Costs	(248,840)	(184,350)
Operating profit (loss)	(5,387)	18,233
Fair value gain (loss) on revaluation	(930)	(1,185)
Other finance income	3,663	4,485
Other finance expenses	(9,069)	(5,463)
Finance result, net	(6,336)	(2,163)
Share of net profits (loss) in associates using the equity method	(289)	(1,083)
Profit (loss) before tax	(12,012)	14,987
Income tax expense	1,893	(1,313)
Profit (loss) for the year	(10,119)	13,674
Basic earnings per share (US\$)	(0.015)	0.021
Diluted earnings per share (US\$)	(0.015)	0.019

## **Balance sheet – assets**



Amounts in US\$ '000	2023	2022
Non-current assets		
Intangible assets	71,267	75,121
Property, plant and equipment	9,689	10,392
Right-of-use assets	23,777	28,753
Long-term prepayments	92	228
Deferred tax assets	28,332	22,973
Investment accounted for using the equity method	2,285	2,501
Investments in equity instruments designated as at FVTOCI	2,020	403
Investment in debt instruments designated as at FVTPL	6,093	6,827
Restricted cash	1,528	1,099
Total non-current assets	145,083	148,297
Current assets		
Inventories	56,760	42,326
Trade and other receivables	46,157	27,619
Restricted cash	222	213
Marketable securities	151,683	_
Cash and cash equivalents	61,519	207,342
Total current assets	316,341	277,500
Total assets	461,424	425,797

## **Balance sheet – liabilities**



Amounts in US\$ '000	2023	2022
Share capital	7,669	7,509
Share premium	478,431	462,297
Other reserves	(2,080)	(8,737)
Accumulated deficit	(264,834)	(256,431)
Shareholders' equity	219,186	204,638
Non-current liabilities		
Convertible bonds	136,598	131,618
Lease liabilities	29,507	29,843
Total non-current liabilities	166,105	161,461
Current liabilities		
Convertible bonds	1,824	1,768
Trade and other payables	70,693	54,465
Lease liabilities	3,616	3,465
Total current liabilities	76,133	59,698
Total equity and liabilities	461,424	425,797

## Cash flow (1/2)



Amounts in \$'000	2023	2022
Profit (loss) before tax	(12,012)	14,987
Adjustments to reconcile net profit (loss) to net cash used in operating activities:		
Depreciation, amortization, impairment of non-current assets	15,925	13,188
Equity settled share based payments	9,251	6,392
Gain on disposal of investment in associate	0	(12,242)
Fair value gain (loss) on revaluation	930	1,185
Gain on disposal from PRV sale	(21,279)	0
Other finance income	(3,663)	(4,485)
Other finance expenses	9,069	5,463
Share of net profits in associates using the equity method	289	1,083
Other	(1,080)	(1,576)
Operating cash flows before changes in working capital	(2,570)	23,995
Changes in working capital:		
Inventories	(14,434)	(15,016)
Trade and other receivables	(18,538)	2,364
Payables and other current liabilities	16,228	11,992
Restricted cash	(438)	273
Total changes in working capital	(17,182)	(387)

## Cash flow (2/2)



Amounts in \$'000	2023	2022
Interest received (paid)	2,883	85
Income taxes received (paid)	(655)	(1,235)
Net cash flows generated from (used in) operating activities	(17,524)	22,458
Capital expenditure for property, plant and equipment	(1,437)	(1,376)
Proceeds on PRV sale	21,279	0
Investment intangible assets	(27)	(601)
Proceed from sale of Investment associate	0	7,300
Purchases of marketable securities	(382,014)	0
Proceeds from sale of marketable securities	232,811	0
Net cash flows generated from (used in) investing activities	(129,388)	5,323
Payment of lease liabilities	(5,126)	(3,311)
Interests on loans and leases	(4,046)	(3,952)
Settlement of share based compensation awards	8,133	2,281
Net cash flows generated from (used in) financing activities	(1,039)	(4,982)
Increase (decrease) of cash	(147,951)	22,799
Exchange rate effects	2,128	(7,381)
Cash and cash equivalents at 1 January	207,342	191,924
Total cash and cash equivalents at December 31	61,519	207,342