



**Pharming Group N.V.**

# Corporate Overview

**January 2023**

NASDAQ: **PHAR** | Euronext Amsterdam: **PHARM**



*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 2021 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2021, 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 press release 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 press release and are based on information available to Pharming as of the date of this release. 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.*



**One commercialized asset:**  
**RUCONEST® (rhC1INH)** for the  
treatment of acute hereditary  
angioedema (HAE)



**Commercialization reach:**  
active in over 30 markets,  
including the US, the EEA, the  
UK and MENA



**Anticipated regulatory approvals  
& launch of leniolisib, a PI3Kδ  
inhibitor in development for  
APDS, in 2023 (approvals - FDA  
1Q, EMA 1H, MHRA 2H)**



**Development of rare disease  
pipeline and leniolisib/PI3Kδ  
for additional rare disease  
indications**



**Headquarters**  
Leiden, Netherlands (Global)  
Warren, New Jersey (US)



**EURONEXT Amsterdam:**  
PHARM (since 1999)  
**Nasdaq: PHAR (since 2020)**

# Leadership: Executive Committee



**Sijmen de Vries, MD MBA**  
Executive Director &  
Chief Executive Officer



**Jeroen Wakkerman**  
Chief Finance Officer



**Anurag Relan MD**  
Chief Medical Officer



**Mireille Sanders MSc**  
Chief Operations Officer

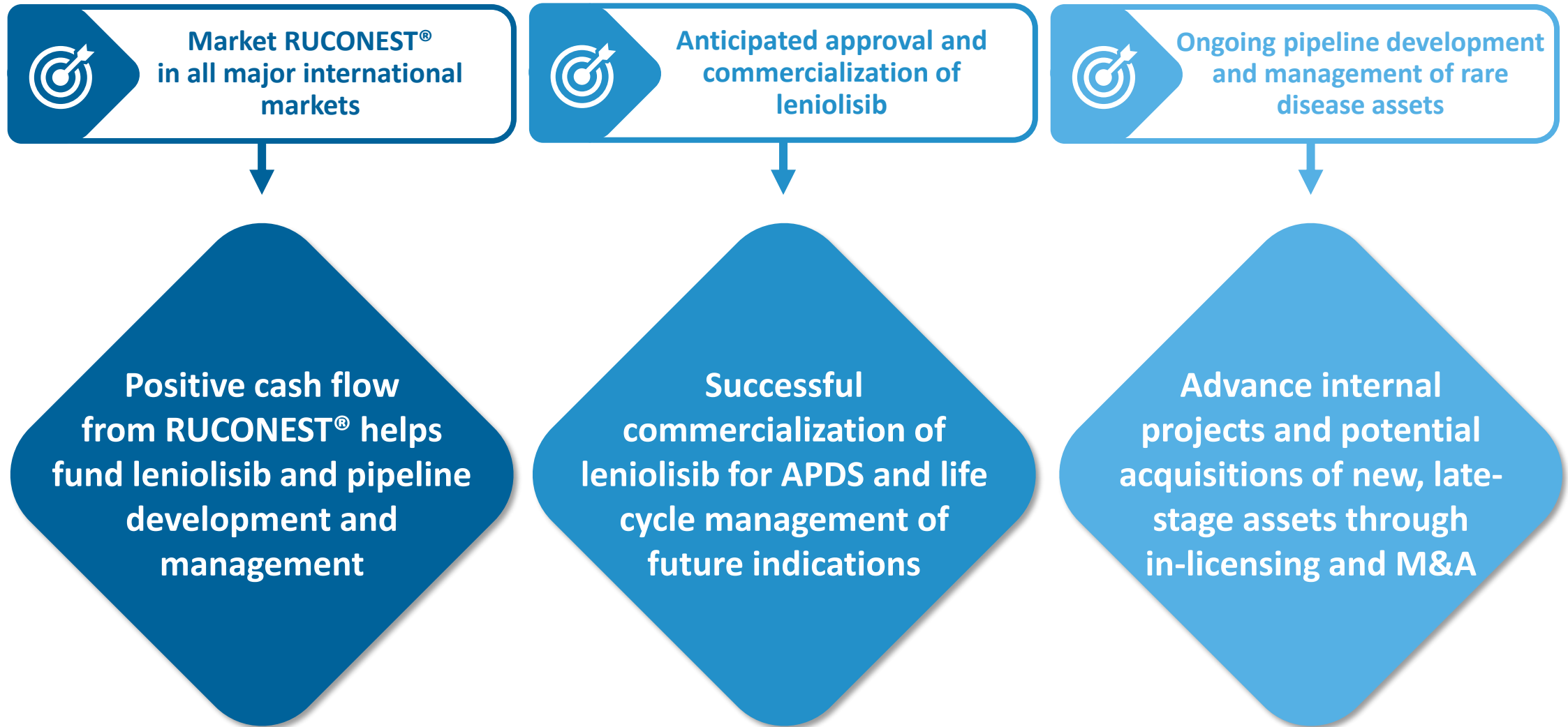


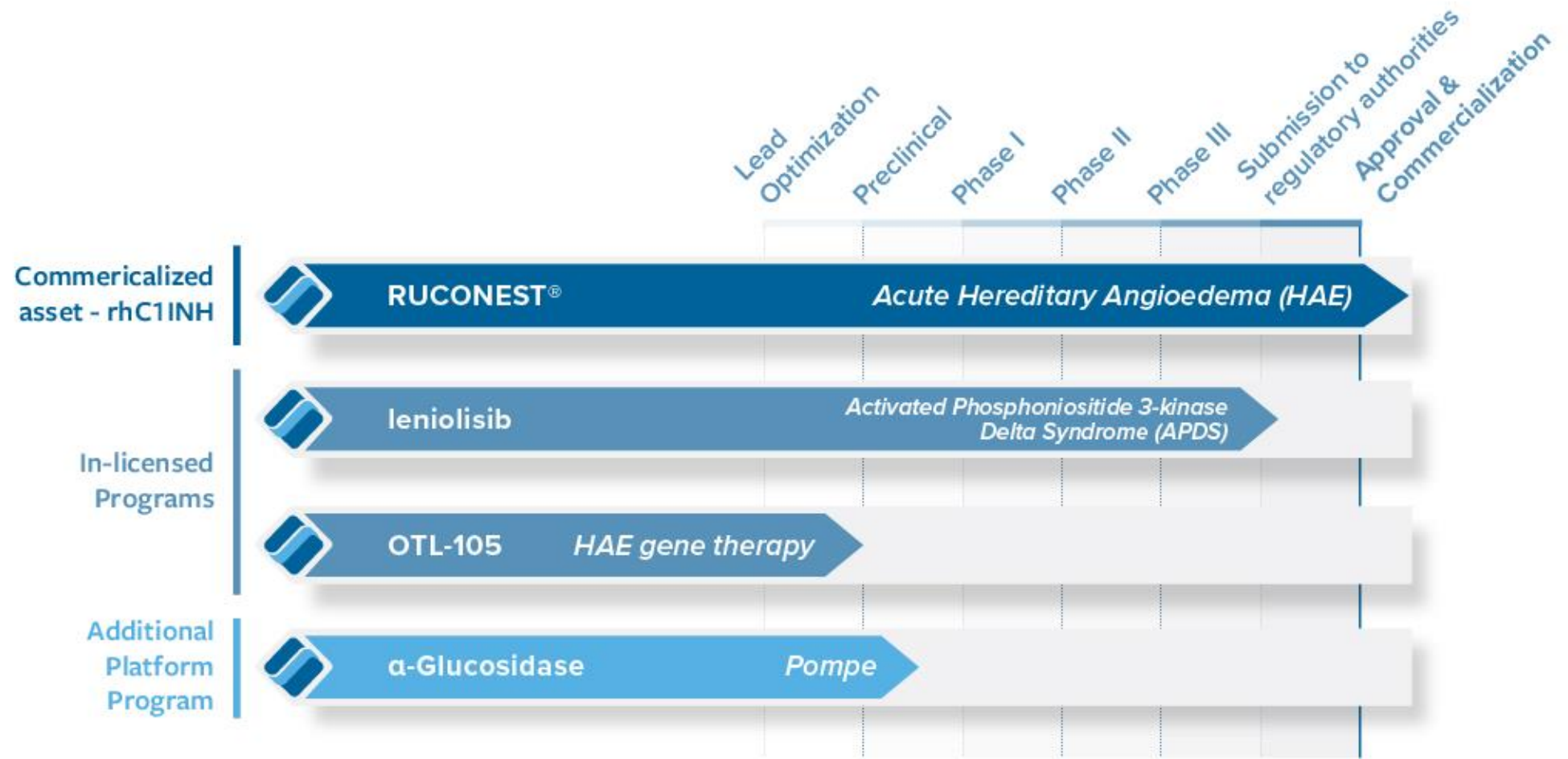
**Ruud van Outersterp**  
Chief Ethics &  
Compliance Officer



**Stephen Toor**  
Chief Commercial Officer &  
President of Pharming  
Healthcare, Inc.







# Strong, rare disease product commercial infrastructure



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



Market access teams



Patient support and reimbursement teams



Disease educators and specialists for APDS and HAE



Medical Affairs teams



High conference penetration & Support for educational KOL speaker programs



Pharming®

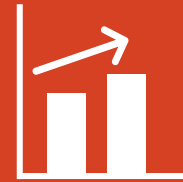
**RUCONEST®**







RUCONEST® sales of US\$198.9 million (FY2021), US\$151.0 million (first 9M of 2022)



Continued single digit growth of revenues expected for 2022



The only recombinant treatment that targets the root cause of HAE by replacing missing or dysfunctional C1-INH



Well-tolerated and effective treatment option for acute hereditary angioedema (HAE) - including breakthrough attacks



Second most prescribed product detailed for acute attacks



97% of acute attacks needed just one dose of RUCONEST®<sup>1</sup>

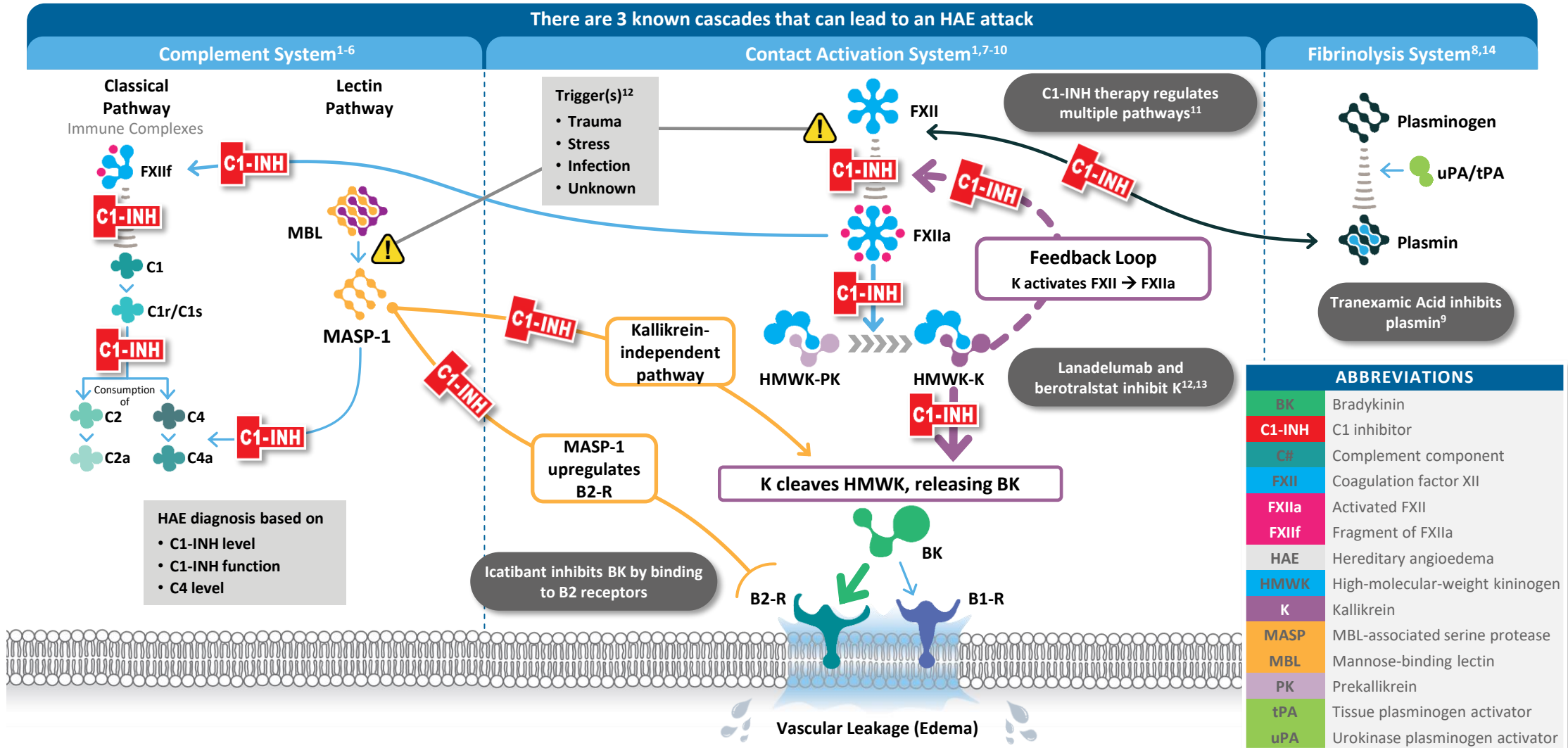


93% of attacks were stopped with RUCONEST® for at least three days<sup>2</sup>



Patients are well managed and feel confident to administer treatment themselves<sup>3</sup>

# Importance of C1-INH in Hereditary Angioedema



ABBREVIATIONS	
BK	Bradykinin
C1-INH	C1 inhibitor
C#	Complement component
FXII	Coagulation factor XII
FXIIa	Activated FXII
FXIIIF	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.



Strong patient organization support since 2000



Over 700 physicians have prescribed RUCONEST® since 2014



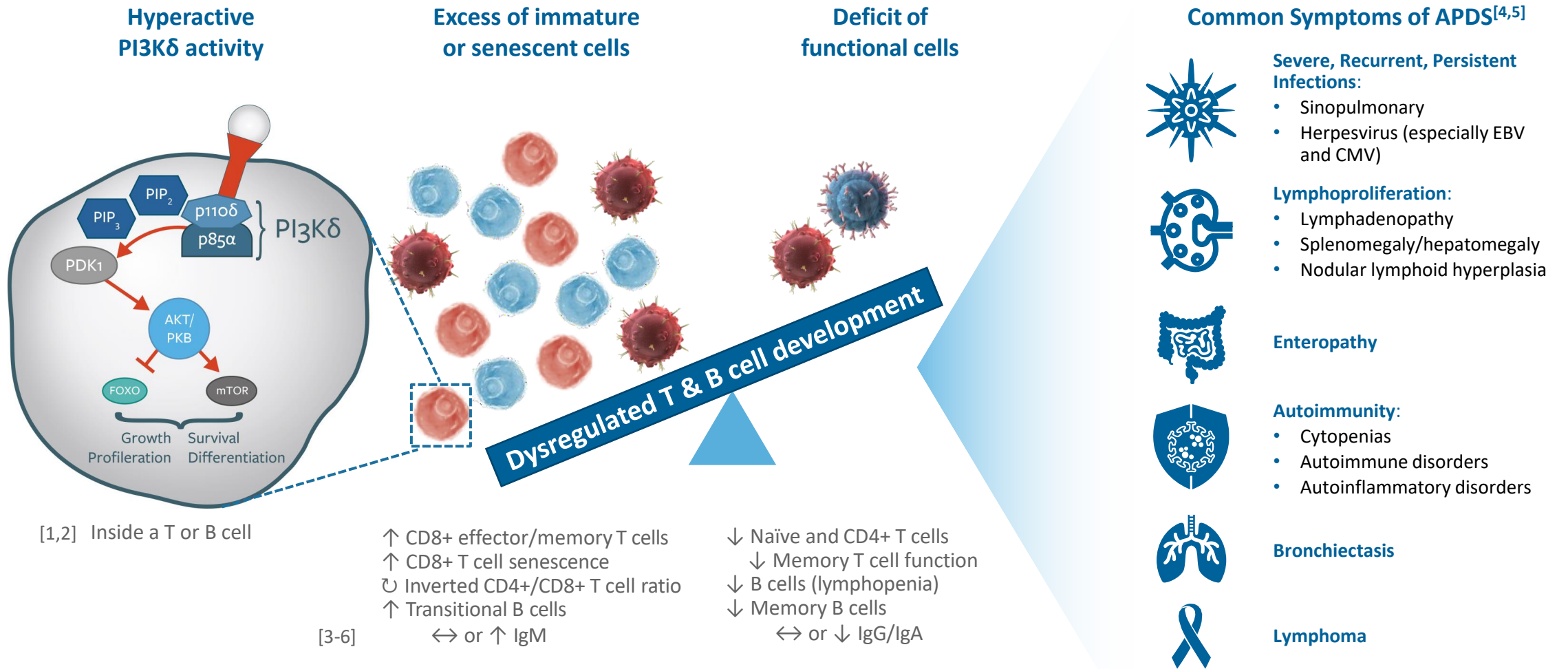
>2,000 patients with HAE have been prescribed RUCONEST®



**leniolisib**

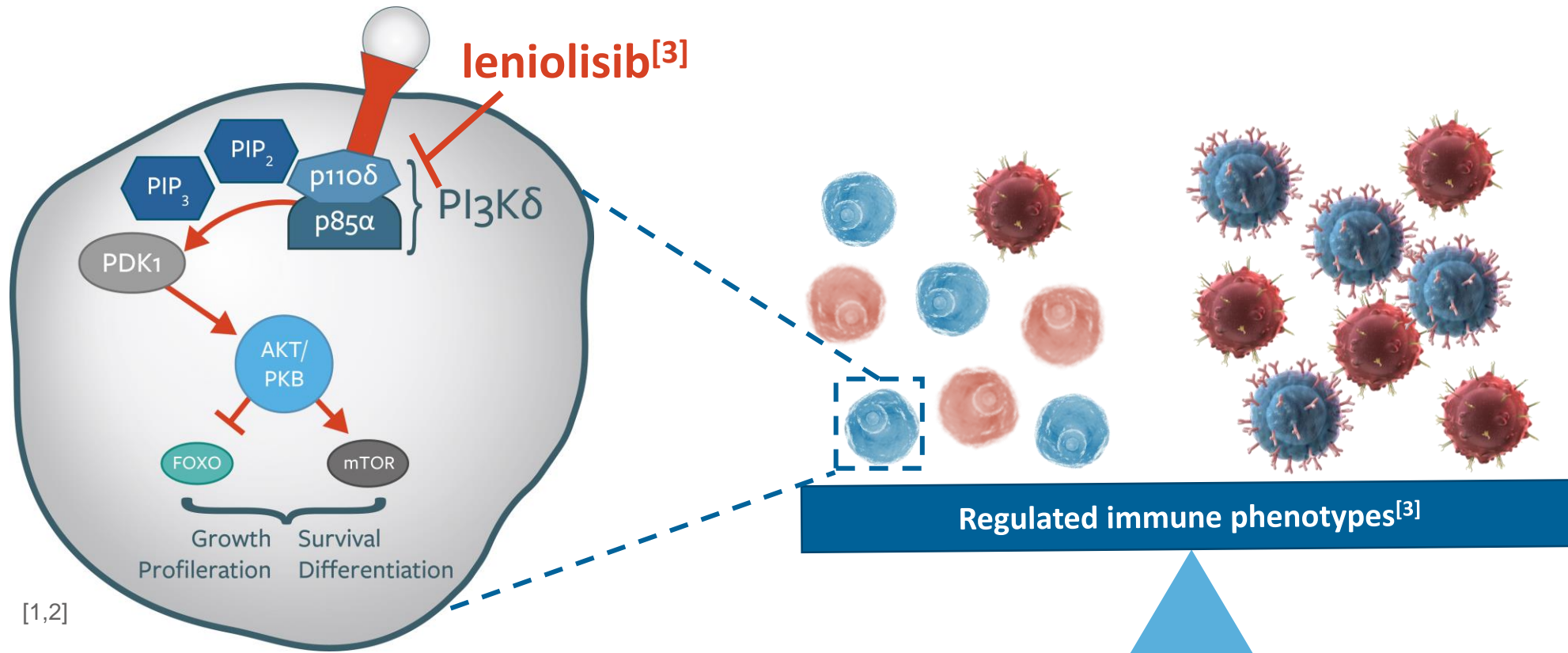


# Genetic defect leads to PI3K $\delta$ hyperactivity, causing APDS symptoms



APDS, activated phosphoinositide 3-kinase  $\delta$  syndrome; CMV, cytomegalovirus; EBV, Epstein-Barr virus; FOXO, forkhead box O; Ig, immunoglobulin; PDK1, phosphoinositide-dependent protein kinase 1; PIP<sub>2</sub>, phosphatidylinositol 4,5-bisphosphate; PIP<sub>3</sub>, phosphatidylinositol 3,4,5-trisphosphate; PI3K $\delta$ , phosphoinositide 3-kinase  $\delta$ ; PKB, protein kinase B.

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. Lucas CL, et al. *Nat Immunol*. 2014;15(1):88-97. 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.

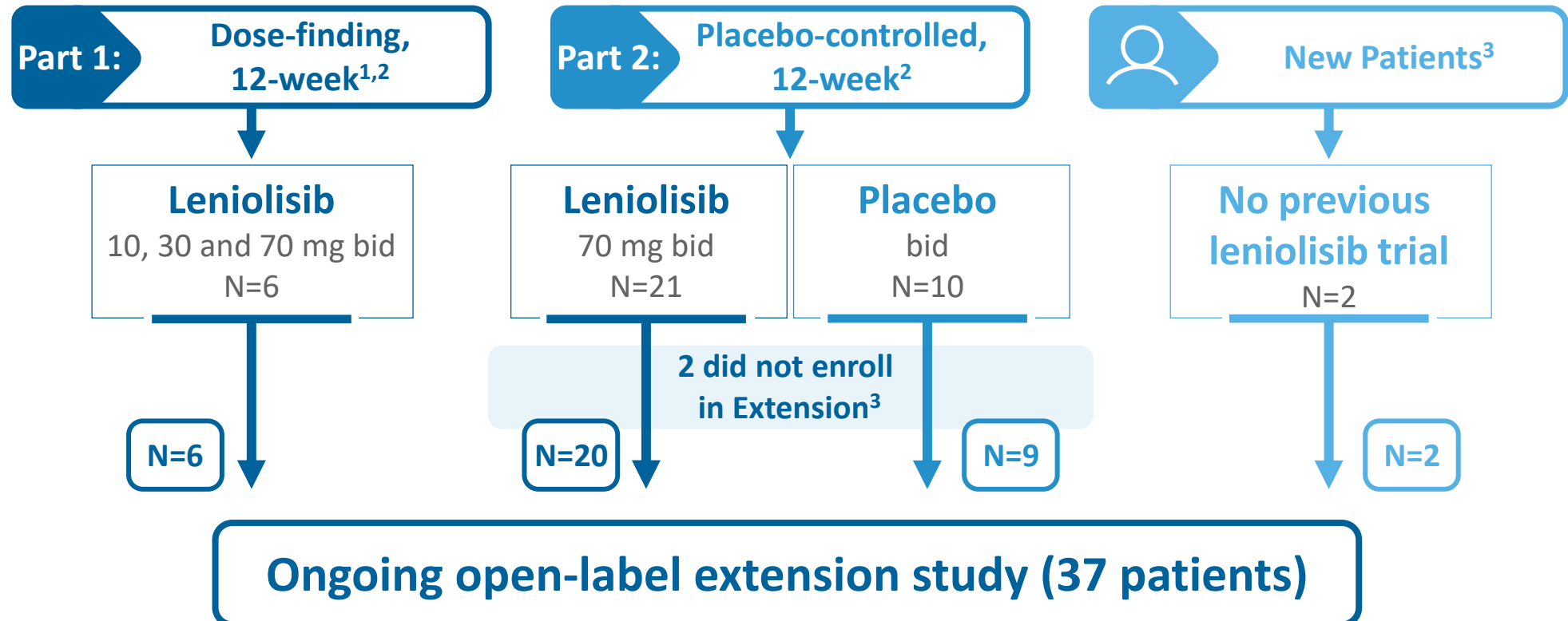


[1,2]

**Leniolisib balances PI3Kδ enzyme activity  
Addressing immune deficiency and dysregulation**

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. Rao VK, et al. *Blood*. 2017;130(21):2307-2316.

## Completed Ph2/3 DBPC Registrational Trial



Data cutoff: December 13, 2021

bid, twice a day.

1. Rao VK, et al. *Blood*. 2017;130(21):2307-2316. 2. NCT02435173. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT02435173>. Updated August 10, 2022. Accessed August 18, 2022.

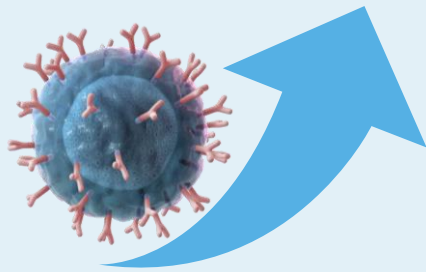
3. Data on file. Pharming Healthcare Inc. 2022. 4. NCT02859727. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT02859727>. Updated July 25, 2022. Accessed August 18, 2022.

# Leniolisib clinical summary – RCT and long-term extension study

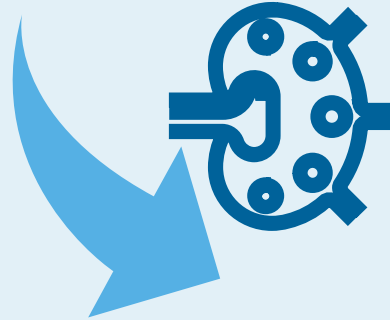
## Highly effective therapy addresses underlying cause of APDS

### Primary Outcomes

Increased  
naïve B cells



Decreased  
lymphadenopathy

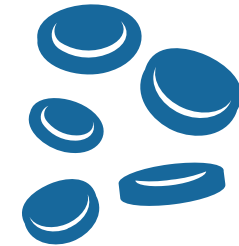


### Other Efficacy Outcomes

Decreased  
spleen size



Improved  
cytopenias



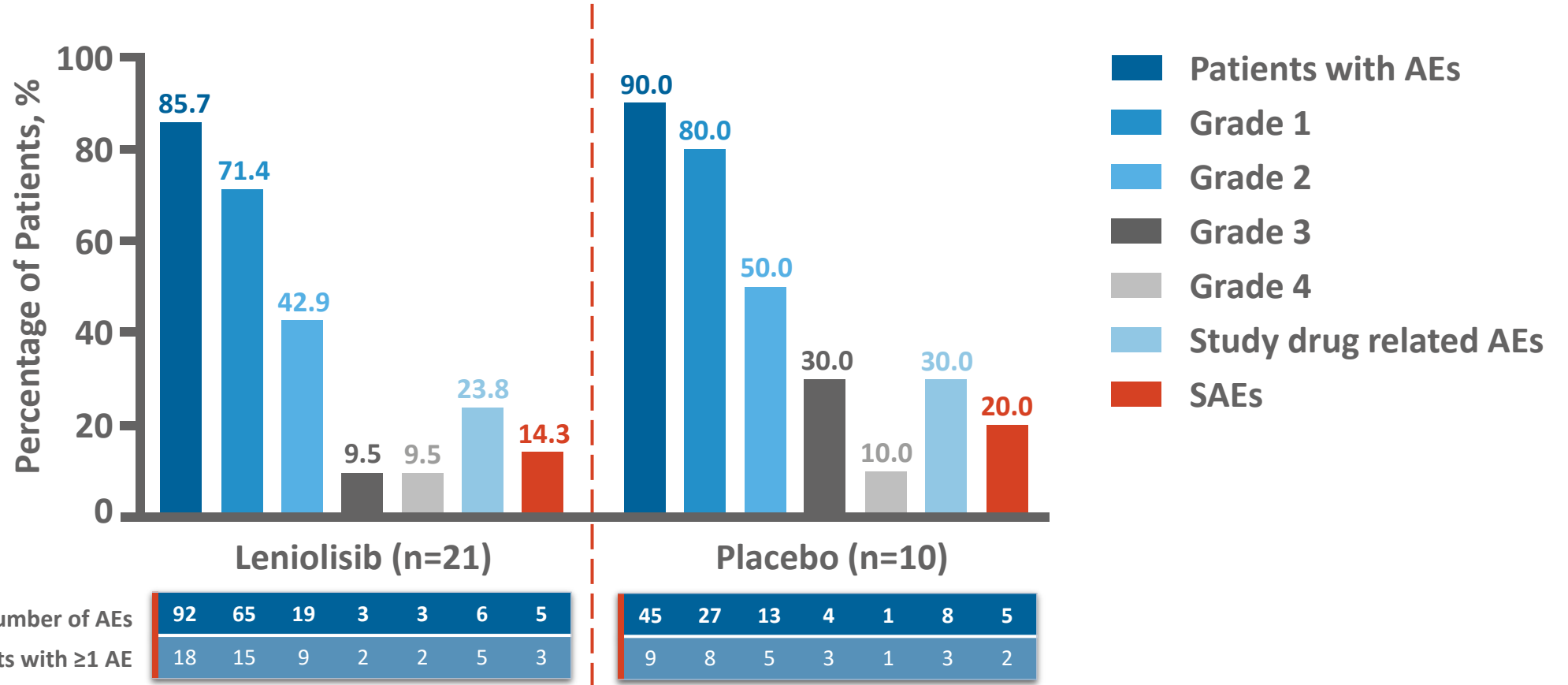
- ◆ Met both primary endpoints ( $p=0.0002$ ,  $p=0.0006$ ) indicating correction of immune dysregulation
- ◆ Long-term leniolisib administration was well-tolerated in patients with APDS (median exposure 2 years)
- ◆ Extension study interim analysis demonstrated durability of efficacy results, including continued improvement in lymphoproliferation and multilineage cytopenias
- ◆ Reductions in infection seen over time along with reductions in immunoglobulin replacement therapy



64th ASH Annual Meeting and Exposition | 2022  
New Orleans, LA



# Safety Data from RCT: Leniolisib was well-tolerated



- ◆ No deaths (grade 5 AEs) were reported
- ◆ No AEs led to discontinuation of study treatment

- ◆ No SAEs were related to study treatment, and the incidence of SAEs was lower in the leniolisib group than the placebo group

CTC were used to determine AE grade. If CTC-AE grading did not exist for an AE, the following definitions were used: 1, mild; 2, moderate; 3, severe; 4, life-threatening; 5, death. AEs, adverse events; CTC, Common Toxicity Criteria; SAEs, serious adverse events. Data on file. Pharming Healthcare Inc. 2022.

Market opportunity with an estimated

**>1,350 patients\***

**(500 US, 675 EU, 190 Japan)**

APDS patients. >500 patients globally identified by Pharming to date

(as of December 2022)

Partnership with **Invitae** – a compressive genetic platform – used to find APDS patients in the US



Disease educators and patient finders – experience in finding patients with rare, ultra-rare diseases

All about **APDS**  
Activated PI3K Delta Syndrome



Strong presence by Pharming and clinical collaborators at well-regarded conferences



\*Size based on population and available literature (1-2 patients per million)

# Regulatory status: on track for 2023 approvals in major markets



USA



EEA



UK



SEP 28  
2022

FDA accepted NDA filing with Priority Review for adults and adolescents aged 12 and older



JAN 6  
2022

Positive EMA decision on Pediatric Investigation Plan (PIP) for leniolisib



APR 6  
2022

MHRA grants PIM designation for patients 1 year to <18 years of age



OCT 1  
2022

ICD-10-CM (US CDC) reimbursement code for APDS took effect



AUG 1  
2022

Announced EMA Accelerated Assessment granted for adults and adolescents ages 12+



1H23

Anticipated MHRA filing



MAR 29  
2023

Prescription Drug User Fee Act (PDUFA) approval date



OCT  
2022

MAA submitted to EMA and validated for Accelerated Assessment



2H23

Anticipated MHRA regulatory approval (will follow ECDRP route)



1H23

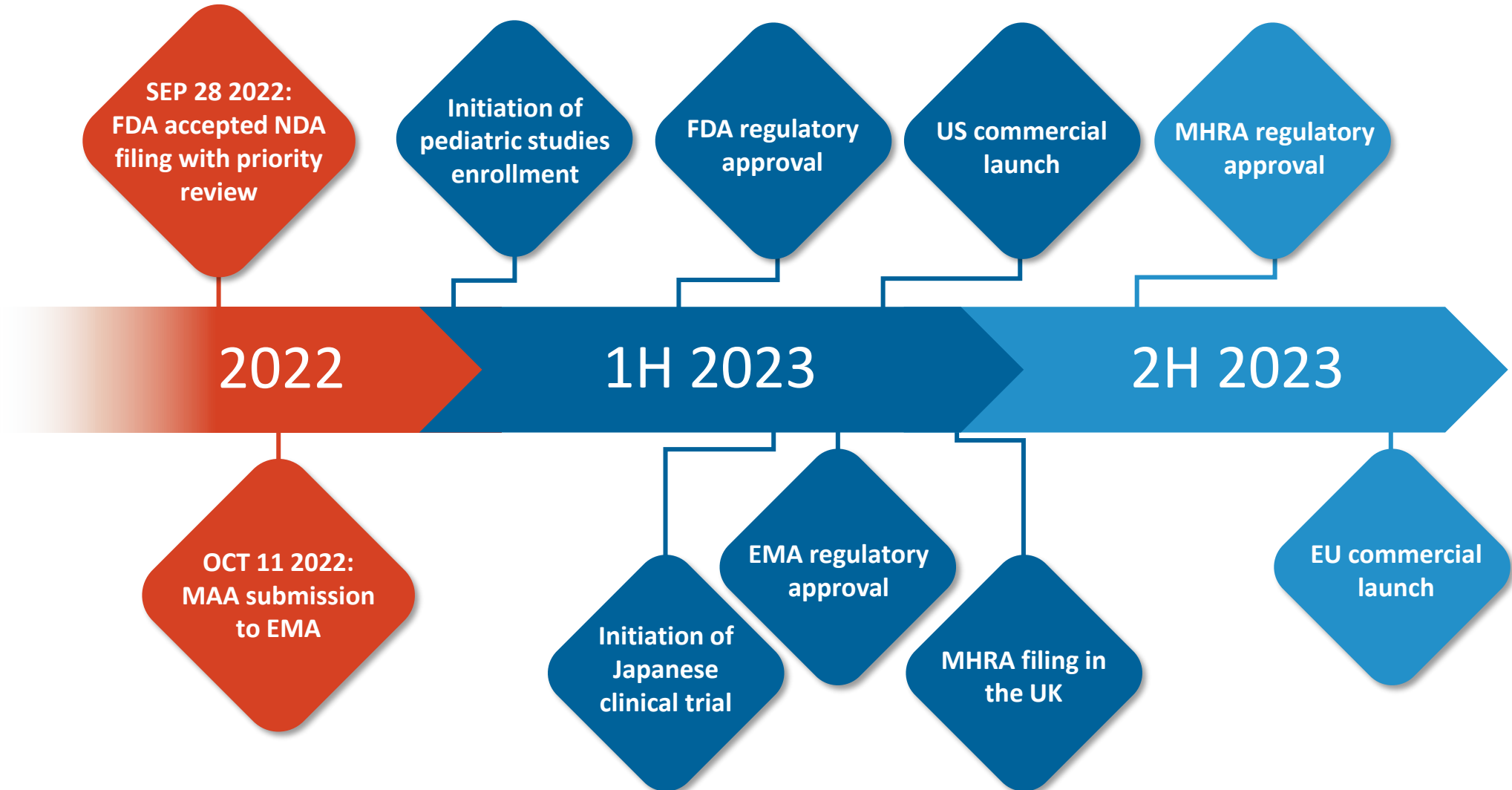
Anticipated approval (1Q23) and commercialization (2Q23) of leniolisib



2023

Anticipated EMA approval (1H23) and commercialization (2H23) of leniolisib

# Anticipated milestones for leniolisib\*

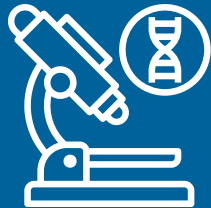


\*These dates are not an assurance of future performance; they are based on current expectations and assumptions regarding the future of our business. Please refer to our Forward-looking Statement on slide 2 of this presentation.



## Progress continues in preclinical studies

### OTL-105



Good progress on developing the lentiviral vector to enhance C1-inhibitor expression, now testing in preclinical HAE disease models



Anticipate providing further updates as we move towards preparing an Investigational New Drug (IND) filing

### POMPE



Study into the development of a next-generation alpha-glucosidase therapy for the treatment of Pompe disease is ongoing



Currently engaged in preclinical studies. As and when results from these preclinical studies become available, we will update the market



# Financials and Outlook





**US\$198.9 million total revenues for FY2021. Revenues for first 9M of 2022 increased by 3% compared to the first 9M 2021**



**Gross profit increased by 7% to US\$139.7 million, driven by growth in revenues, production efficiencies, and favorable tailwind from currency translation effects**



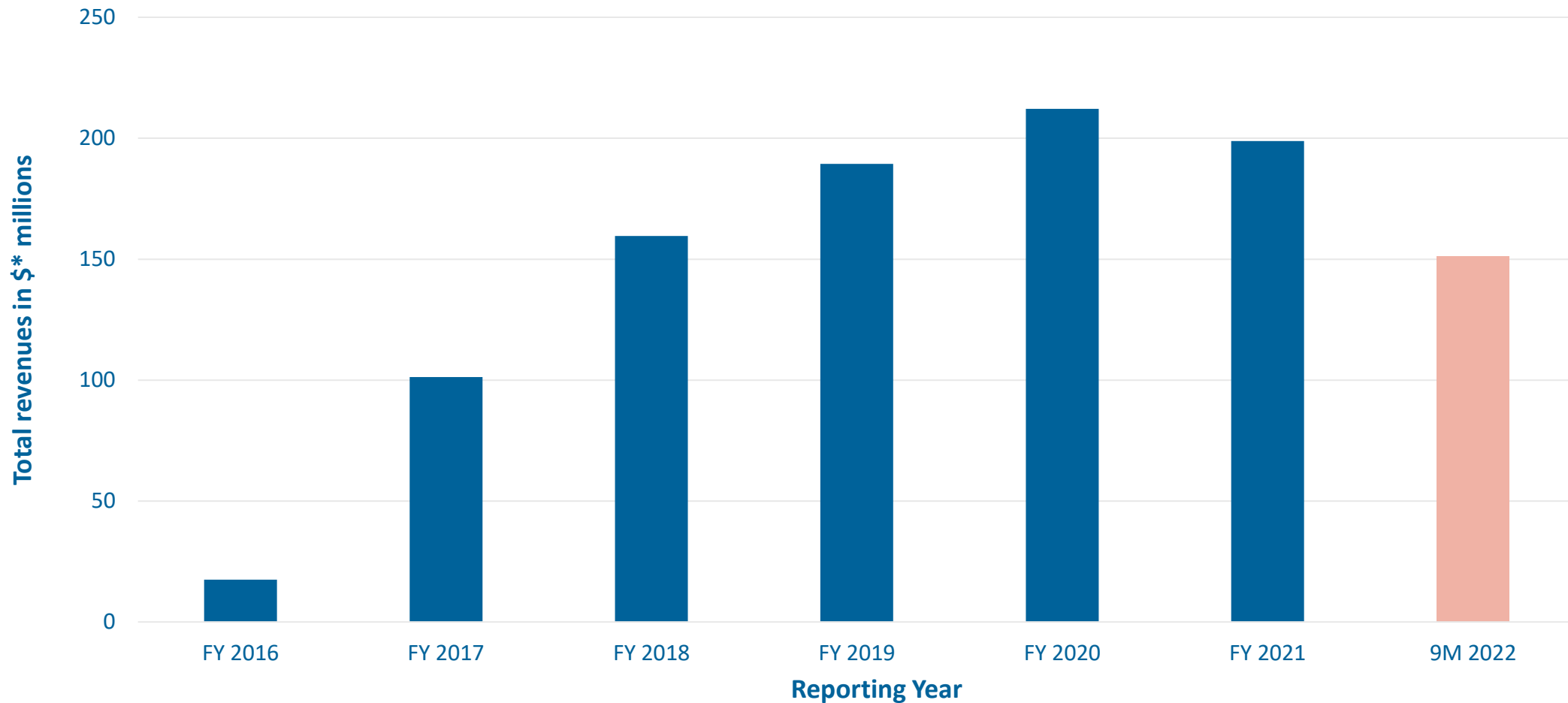
**Net profit increased by 104% compared to first 9M 2021, driven by an increase in Other income**



**Cash and cash equivalents, together with restricted cash, decreased from US\$193.0 million at the end of 2021, to US\$189.9 million at the end of the third quarter 2022.**

# Pharming Group revenues since reacquiring RUCONEST® rights from Valeant Pharmaceuticals

### Pharming revenues FY 2016 - 9M 2022



- 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





Single digit growth Group revenues from RUCONEST® sales in 2022



Commercial approval of leniolisib from FDA in 1Q 2023, with an anticipated launch and commercialization in US in 1H 2023.\*



Positive opinion of leniolisib from the CHMP, followed by issuance of MAA by European Commission end of 1H 2023. Commercial launch in EU markets in 2H 2023.\*



Submit an ECDRP filing for leniolisib to MHRA, after anticipated positive CHMP opinion, MHRA decision expected in 2H 2023.\*



Continue to allocate resources towards the anticipated launch and commercialization of leniolisib and development of pipeline with the view of accelerating future growth



Investment and continued focus on potential acquisitions and in-licensing of new, late-stage development opportunities and assets in rare diseases.

\*subject to positive outcomes of the FDA and EMA reviews



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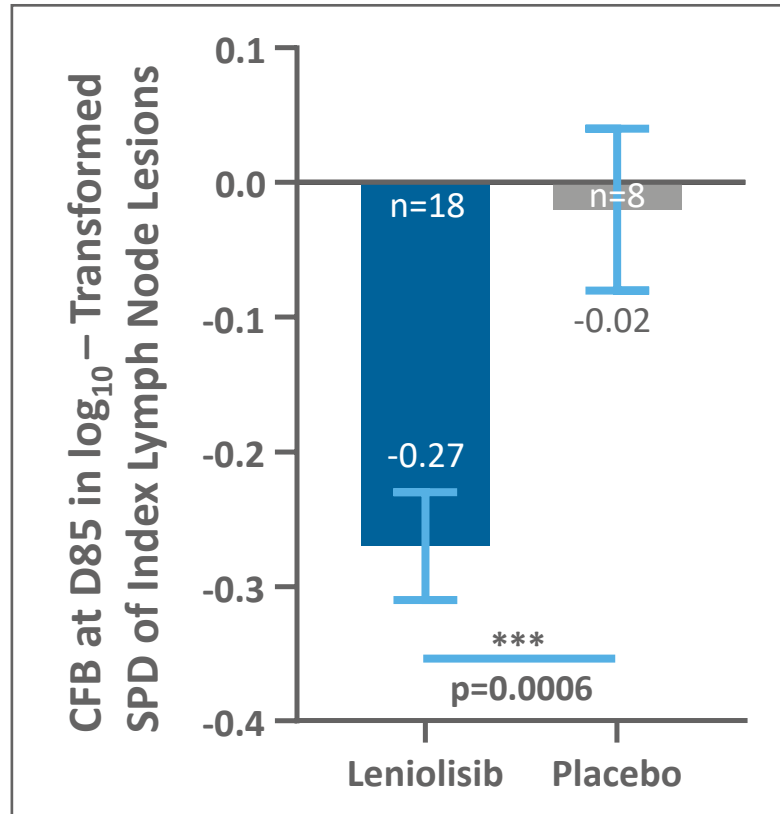
# Appendix

leniolisib clinical trial data



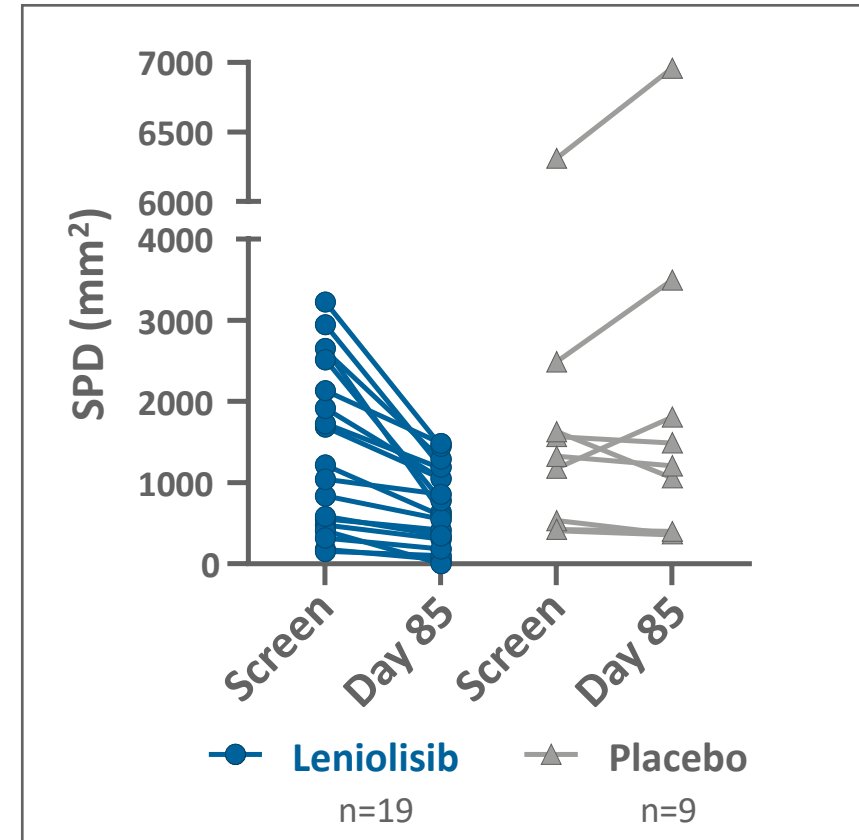
## Primary Outcome Analysis\*

Change from baseline in index lesions



## Individual Index Lesion Sizes

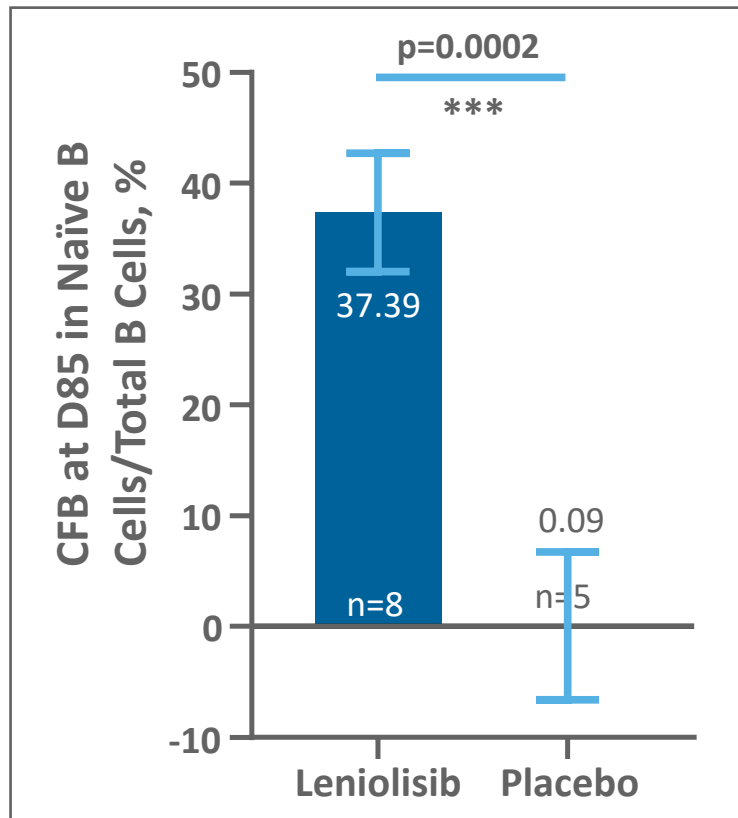
Safety analysis set



\*Data were analyzed using ANCOVA model with treatment as a fixed effect and  $\log_{10}$ -transformed baseline as a covariate. Use of glucocorticoids and IRT at baseline were both included as categorical (Yes/No) covariates. P-value is 2-sided. Least square means are graphed. Error bars are standard error of the mean. 4 patients from the 31 in the safety analysis were excluded from the PD analysis. An additional patient was excluded from the index lesion analysis because the baseline lung index had fully resolved (0 mm) by D85.

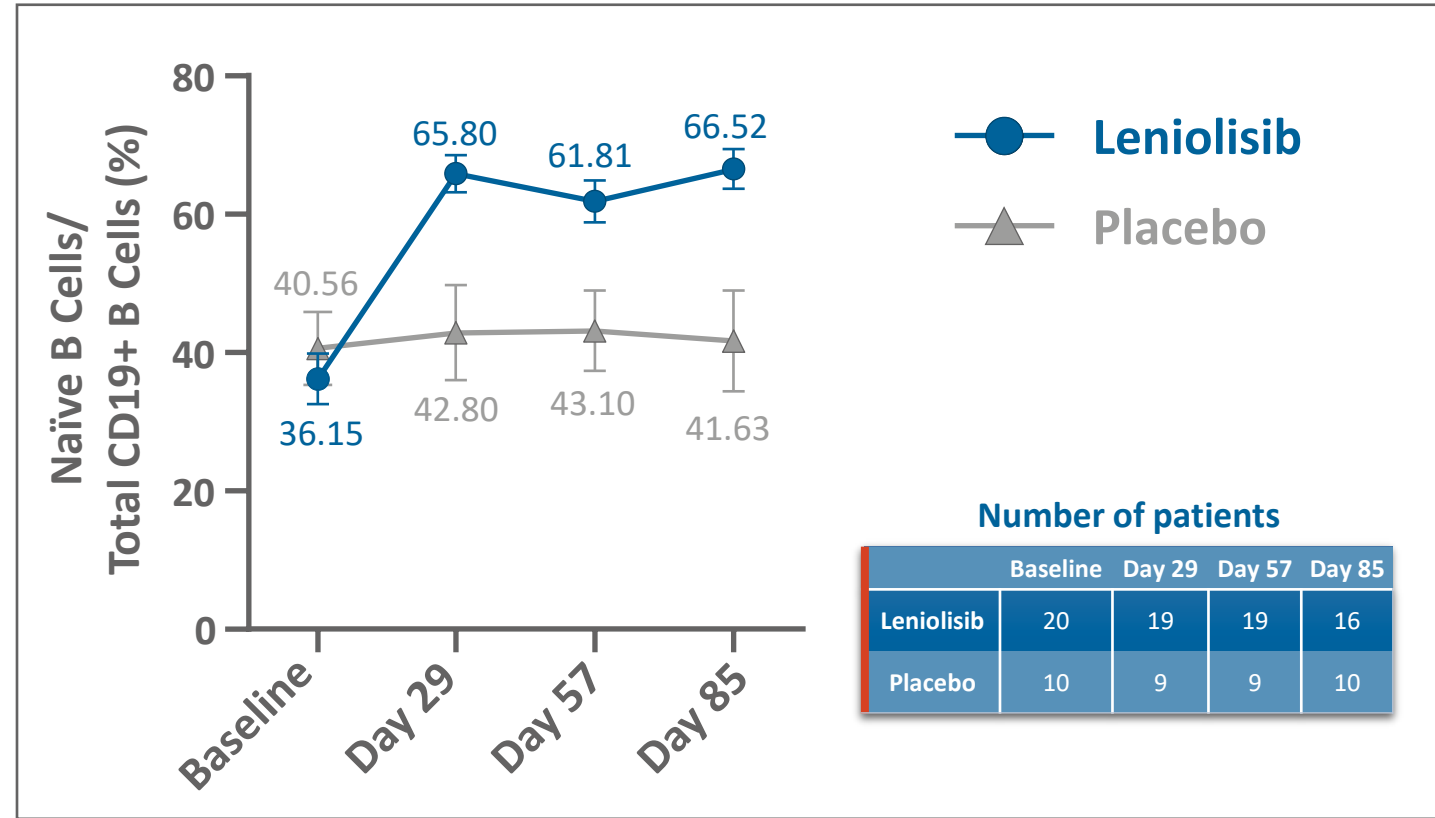
## Primary Outcome Analysis\*

Change from baseline in naïve B cells



## Mean Percentage of Naïve B Cells Over Time

Safety analysis set

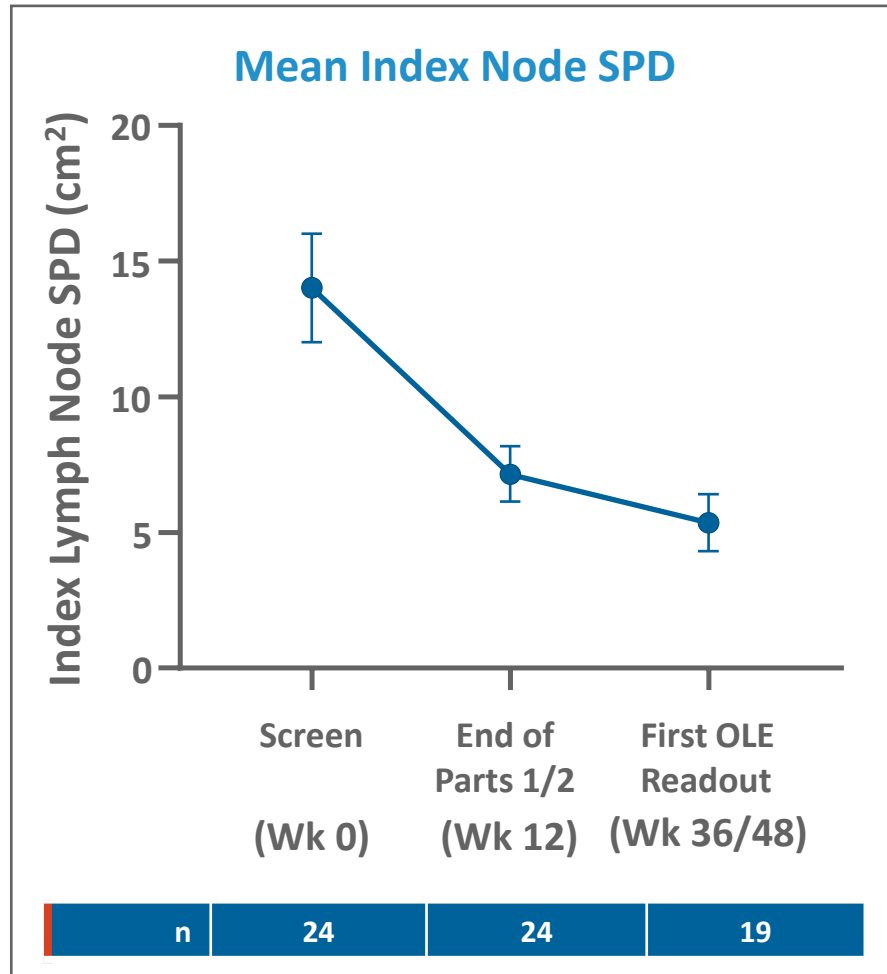


### Number of patients

	Baseline	Day 29	Day 57	Day 85
Leniolisib	20	19	19	16
Placebo	10	9	9	10

\*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 Day 1 values when both are available, and if either baseline or the Day 1 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. 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.

# Leniolisib continued to reduce lymphadenopathy



Part 1 & OLE:  
Leniolisib



SCR: 23 x 8mm

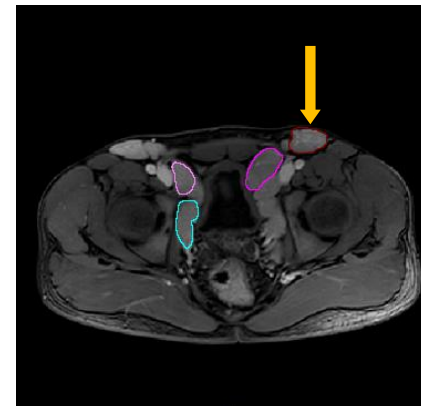


D85: 20 x 7mm

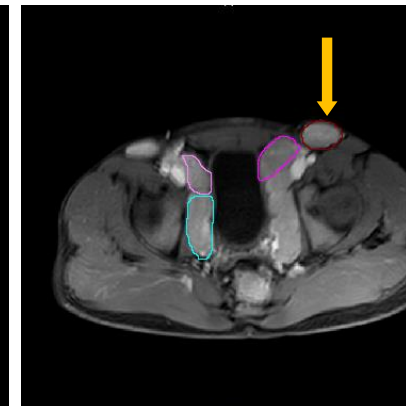


ED252: 16 x 4mm

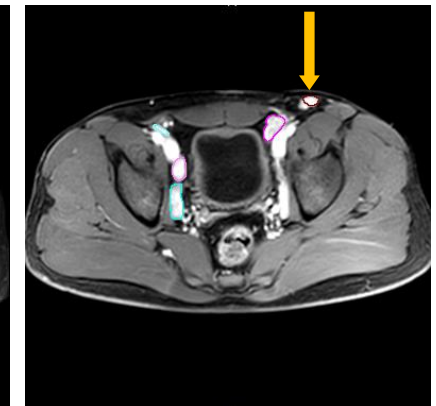
RCT: Placebo



SCR: 35 x 23mm



D85: 37 x 27mm



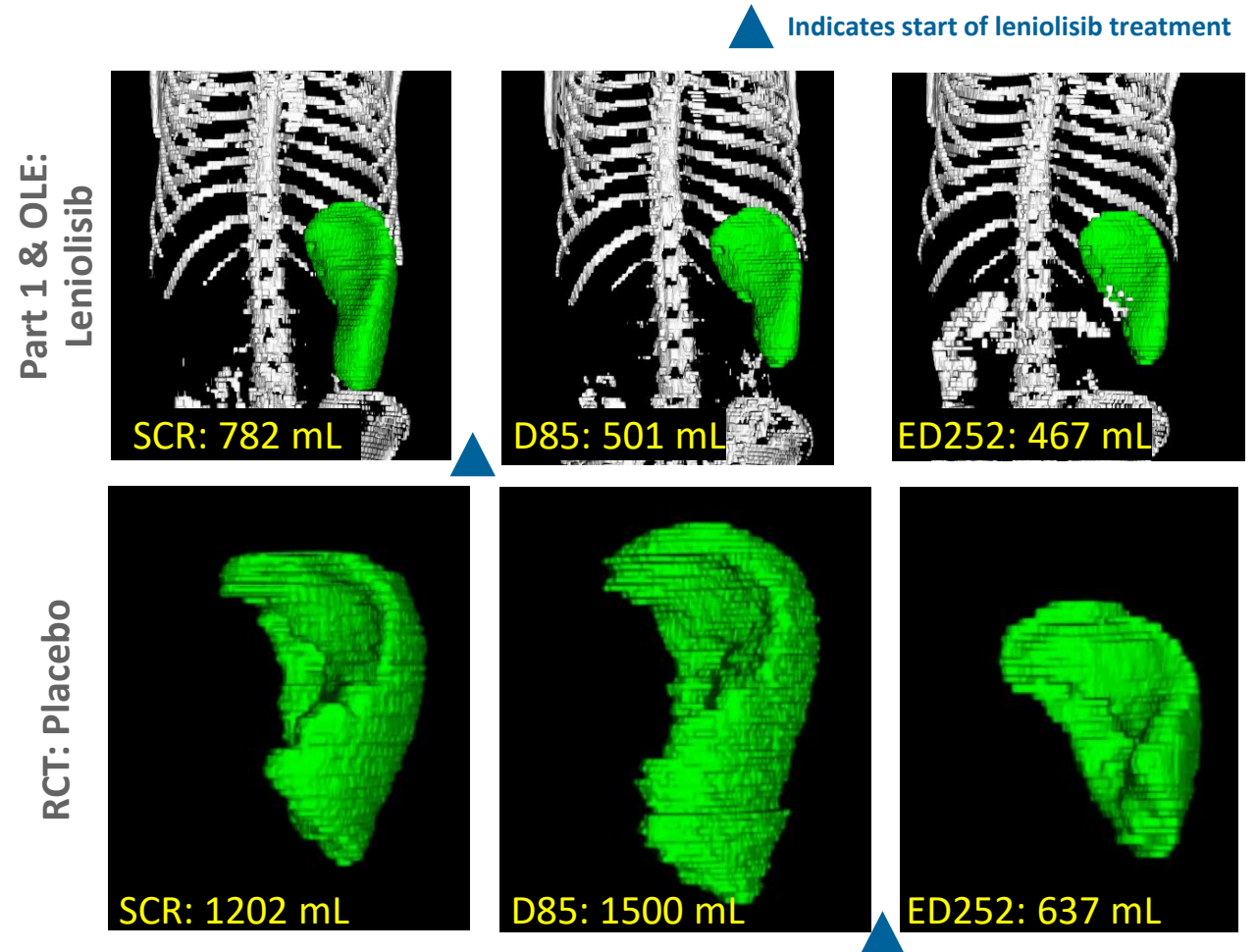
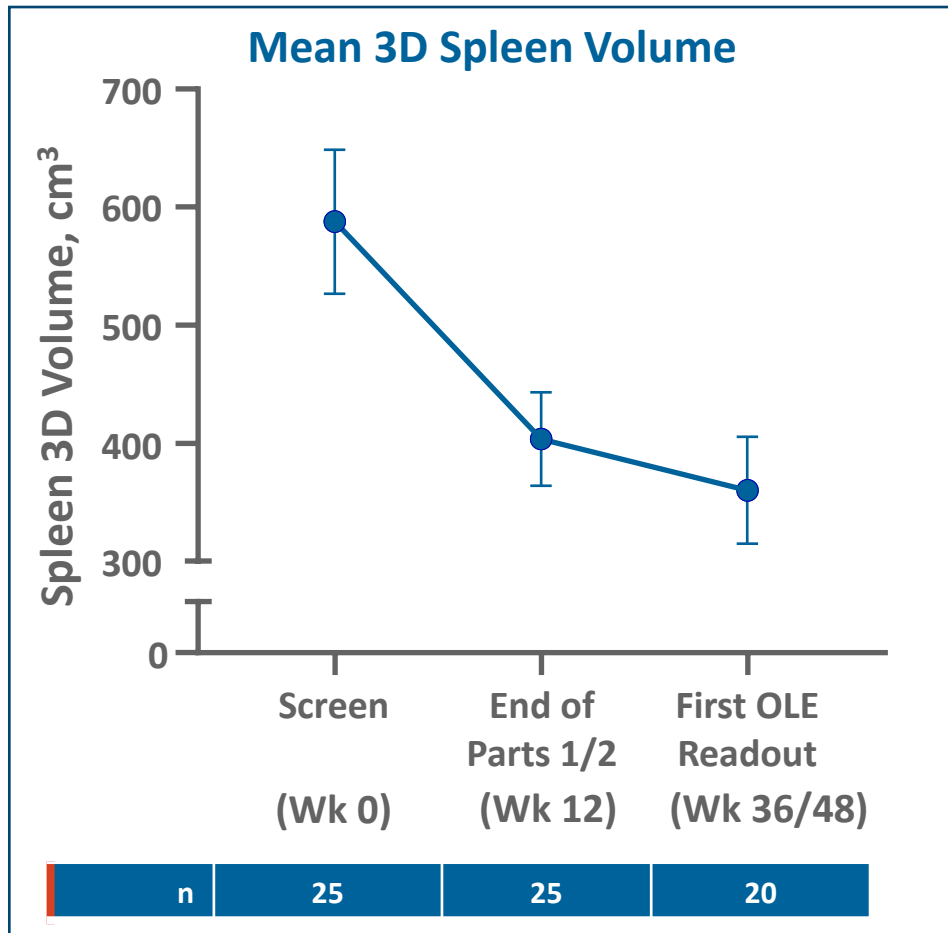
ED252: 15 x 8mm

▲ indicates start of leniolisib treatment

The mean index node graph has been corrected since the original ESID presentation.

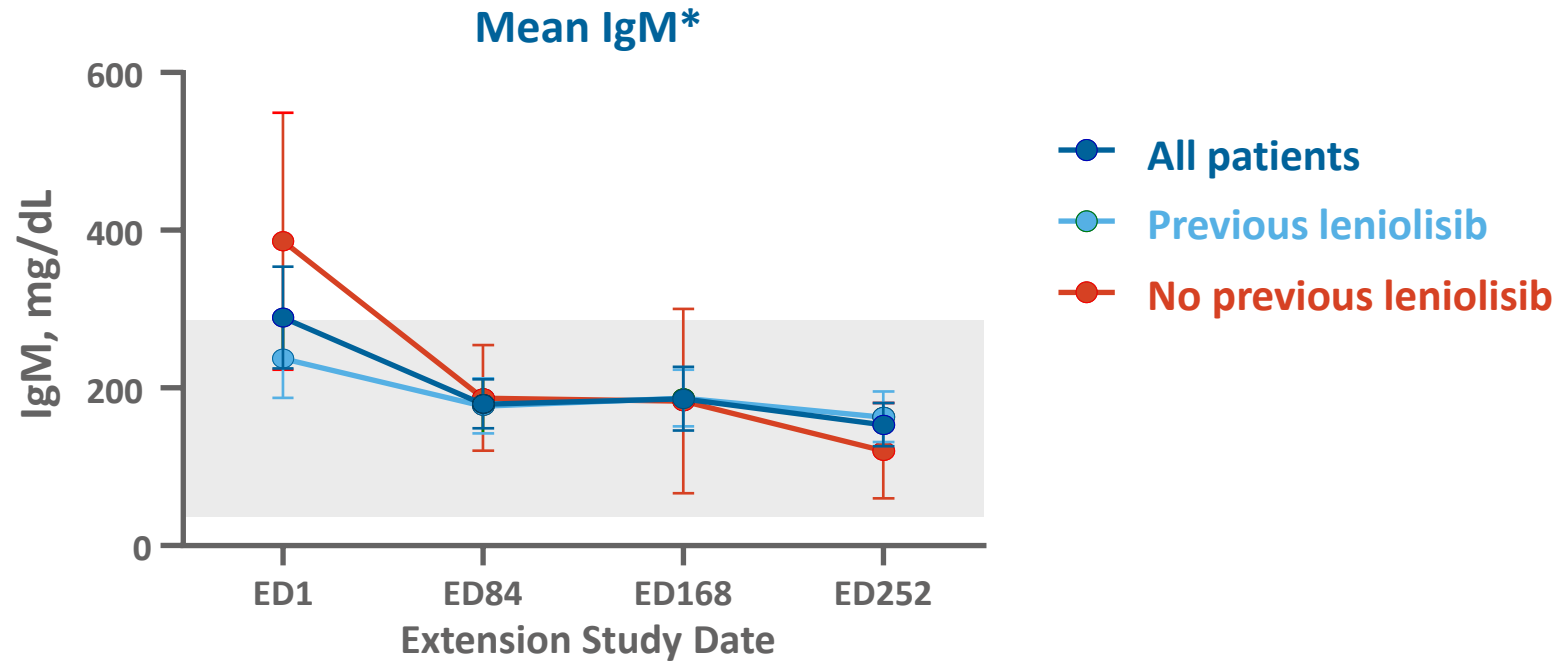
Error bars are standard error of the mean. All patients from RCT Parts 1 and 2 with measurements are included. End of Parts 1 and 2 occurred at day 85. First OLE readout occurred after an additional 168 or 252 days. D, day; OLE, open-label extension; RCT, randomized controlled trial; SCR, screen; SPD, sum of product diameters; Wk, week. Data on file. Pharming Healthcare Inc. 2022.

# Extension study: continued improvement in spleen size



Error bars are standard error of the mean. All patients from parts 1 and 2 of the phase II/III trials with leniolisib exposure and with measurements are included. End of parts 1 and 2 occurred at days 84 and 85, respectively. First OLE readout occurred after an additional 168 or 252 days. Data on file. Pharming Healthcare Inc. 2022.

# Extension study: continued reduction in IgM levels



n	23	24	21	21
	15	17	15	16
	8	7	6	5

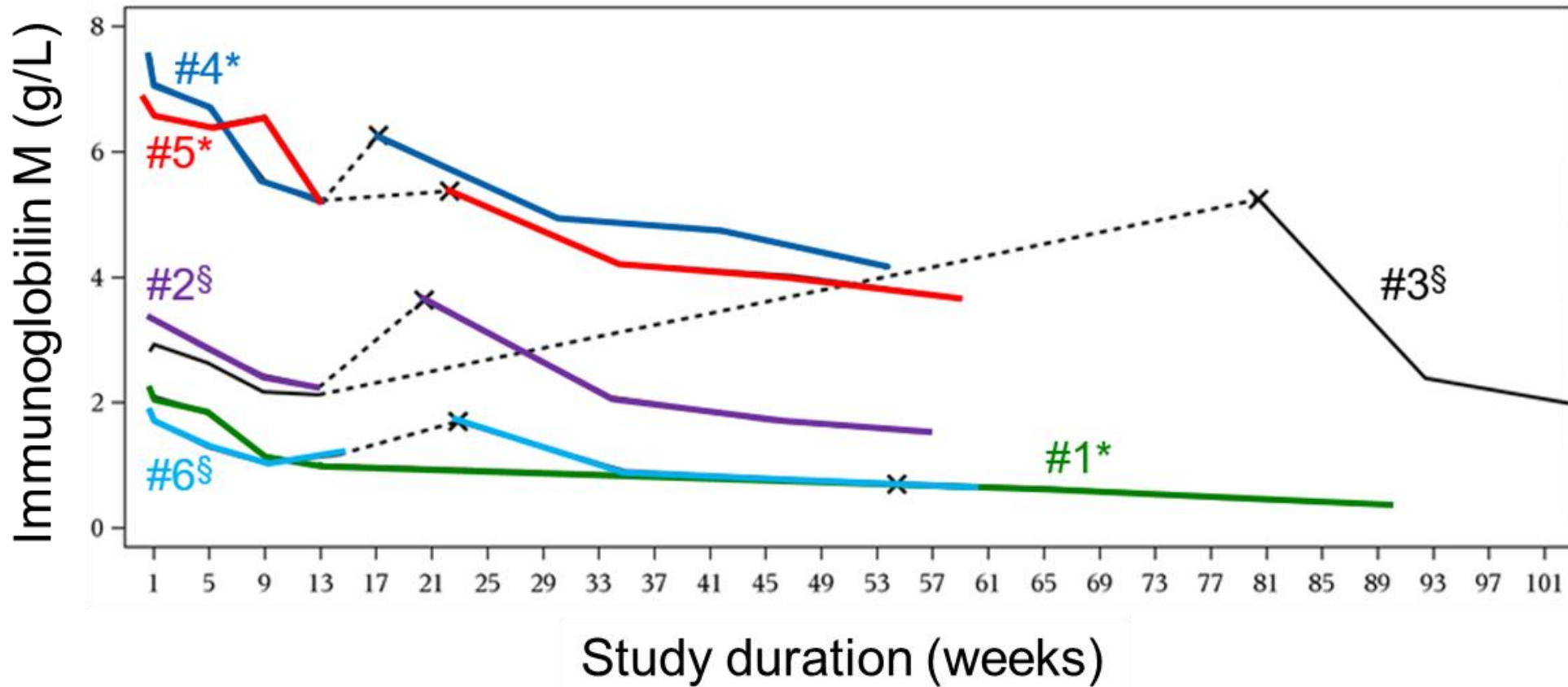
\*Excluded 1 patient due to extremely low B-cell count.

Previous Leniolisib includes patients who received leniolisib during the dose-finding trial and RCT. No Previous Leniolisib includes patients who received placebo during the RCT and patients who were enrolled in other PI3Kδ inhibitor trials. Error bars are standard error of the mean. The gray box indicates the normal range.



# Long term leniolisib results (N=6)

*Leniolisib is an investigational new drug that has not been approved for any use.*



Patients have stopped (\*) or decreased (§) immunoglobulin supplementation as a reflection of the normalization of their B cell function. Dashed lines indicate patient not on treatment