Pharming®

# Pharming Group N.V.

# Corporate Overview

**February 2023**

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 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.*

# Company Overview

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 approvals & launch of leniolisib, a PI3Kδ inhibitor in development for APDS, in 2023 (FDA approval 1Q/launch 2Q, EMA CHMP opinion 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
CEO

**Jeroen Wakkerman**
Chief Finance Officer
CFO

**Anurag Relan MD**
Chief Medical Officer
CMO

**Mireille Sanders MSc**
Chief Operations Officer
COO

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

**Stephen Toor**
Chief Commercial Officer
CCO

# Building a sustainable rare disease business

**Market RUCONEST®**
**in all major international markets**

**Positive cash flow from RUCONEST® helps fund leniolisib and pipeline development and management**

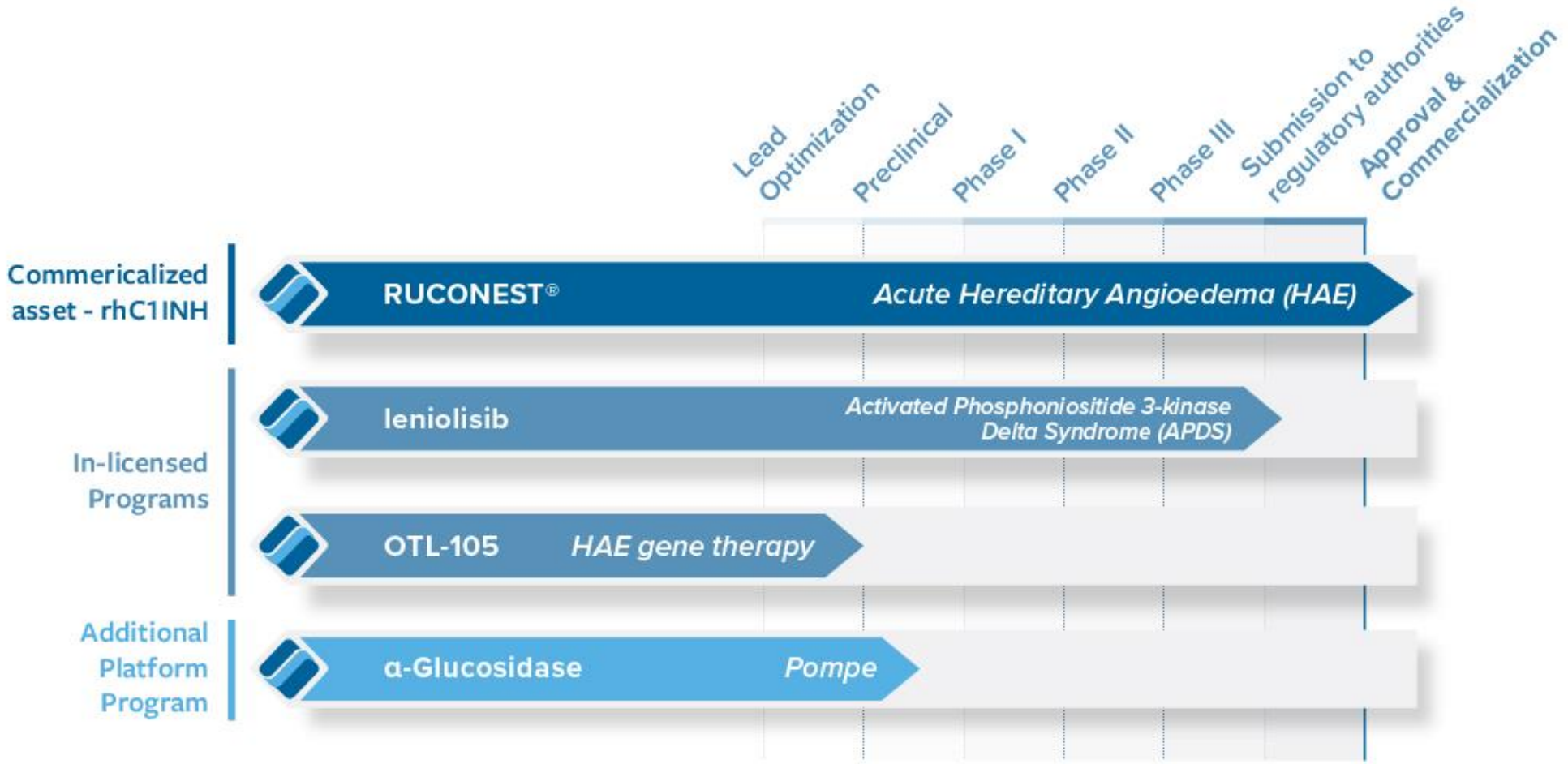
**Anticipated approval and commercialization of leniolisib**

**Successful commercialization of leniolisib for APDS and life cycle management of future indications**

**Ongoing pipeline development and management of rare disease assets**

**Advance internal projects and potential acquisitions of new, late-stage assets through in-licensing and M&A**

# Pipeline of rare disease assets



# 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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RUCONEST®

# RUCONEST® (rhC1INH): sustainable commercialized asset

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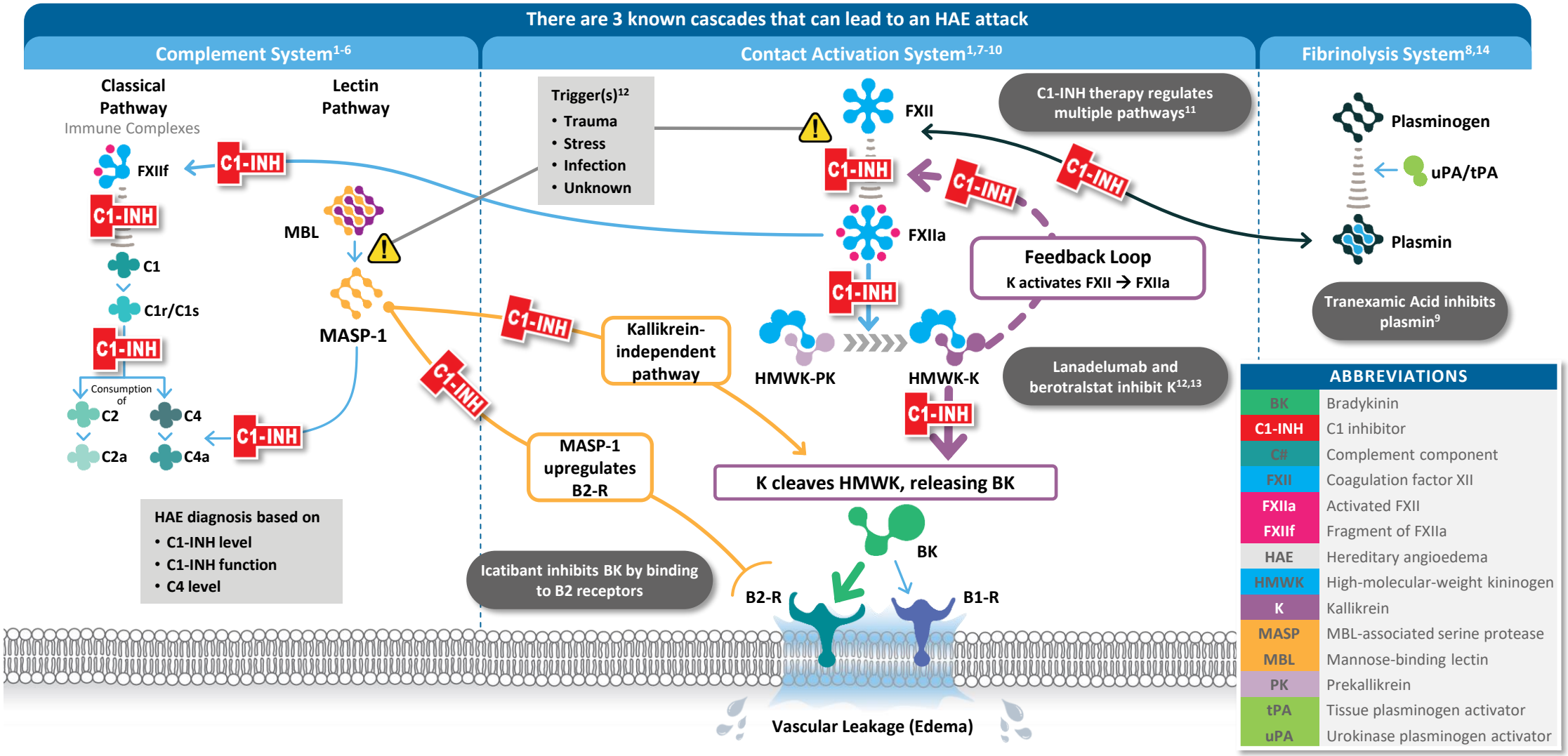
- RUCONEST® sales of US$198.9 million (FY2021), US$151.0 million (first 9M of 2022)
- Continued single digit growth of revenues expected for 2022
- The only recombinant treatment that targets the root cause of HAE by replacing missing or dysfunctional C1-INH
- Well-tolerated and effective treatment option 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®[1]
- 93% of attacks were stopped with RUCONEST® for at least three days[2]
- Patients are well managed and feel confident to administer treatment themselves[3]

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.

# Importance of C1-INH in Hereditary Angioedema




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 commitment to HAE community

- Strong patient organization support since 2000
- Over 700 physicians have prescribed RUCONEST® since 2014
- >2,000 patients with HAE have been prescribed RUCONEST®

US HEREDITARY ANGIOEDEMA ASSOCIATION

HAEi
HAE International


Pharming®
leniolisib

# Genetic defect leads to PI3Kδ hyperactivity, causing APDS symptoms

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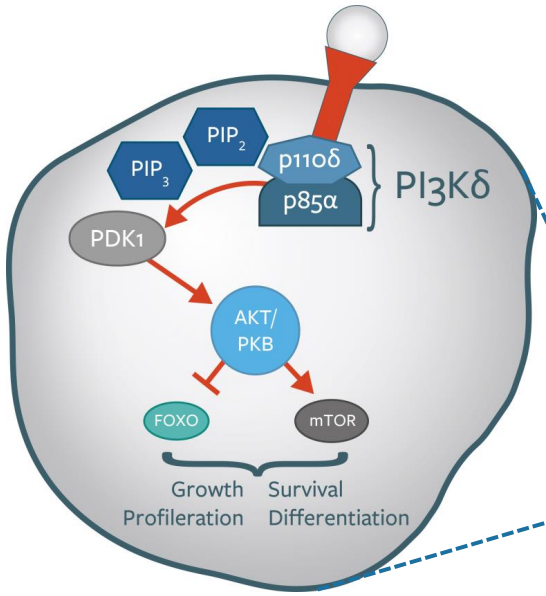
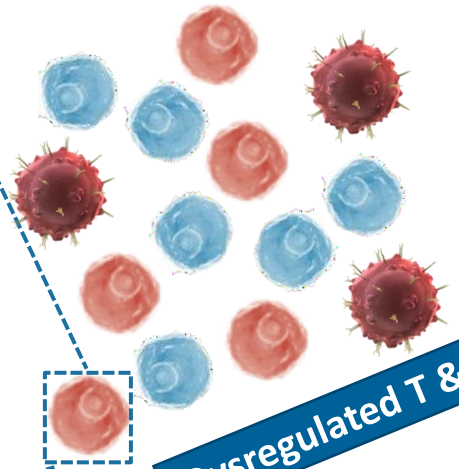
## Hyperactive PI3Kδ activity



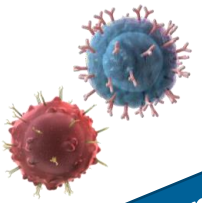

[1,2] Inside a T or B cell

## Excess of immature or senescent cells



[3-6]
- ↑ CD8+ effector/memory T cells
- ↑ CD8+ T cell senescence
- ↻ Inverted CD4+/CD8+ T cell ratio
- ↑ Transitional B cells
  - ↔ or ↑ IgM

## Deficit of functional cells



- ↓ Naïve and CD4+ T cells
  - ↓ Memory T cell function
- ↓ B cells (lymphopenia)
- ↓ Memory B cells
  - ↔ or ↓ IgG/IgA

**Dysregulated T & B cell development**

## Common Symptoms of APDS[4,5]

**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**

APDS, activated phosphoinositide 3-kinase δ syndrome; CMV, cytomegalovirus; EBV, Epstein-Barr virus; FOXO, forkhead box O; Ig, immunoglobulin; PDK1, phosphoinositide-dependent protein kinase 1; $PIP_2$, phosphatidylinositol 4,5-bisphosphate; $PIP_3$, phosphatidylinositol 3,4,5-trisphosphate; PI3Kδ, phosphoinositide 3-kinase δ; 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.

# 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.

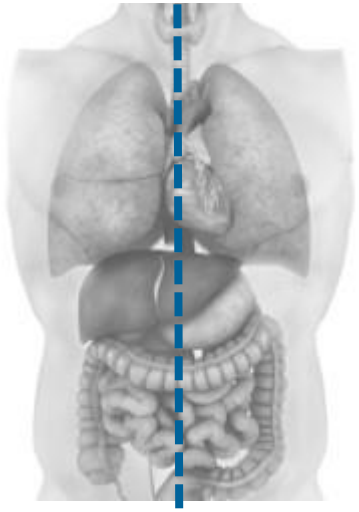
1. Coulter TI, et al. *J Allergy Clin Immunol*. 2017;139(2):597-606. 2. Elkaim E, et al. *J Allergy Clin Immunol*. 2016;138(1):210-218. 3. Rider NL, et al. *J Clin Immunol*. 2017;37(5):461-475. 4. Jiang F, et al. *Allergy Asthma Clin Immunol*. 2015;11:27. 5. Kuburovic NB, et al. *Patient Prefer Adherence*. 2014;8:323-330.

# Current Management for APDS

## Current APDS Management[1,2]

### Immune Deficiency

- Antimicrobial prophylaxis
- Immunoglobulin replacement therapy



### Immune Dysregulation

- Corticosteroids
- Other immunosuppressants
- mTOR inhibitors

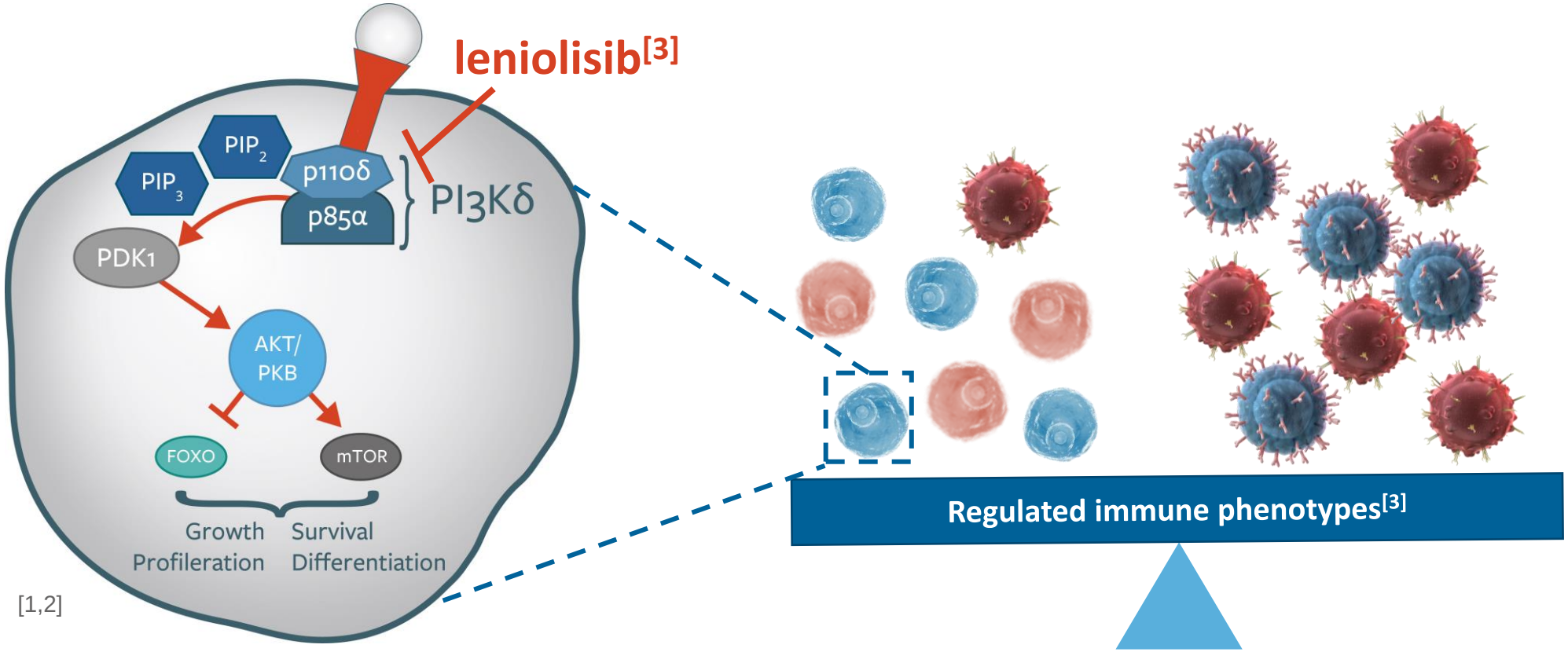
*None of these therapies are FDA-approved for APDS treatment*

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.

# Leniolisib: a targeted disease modifying treatment for APDS

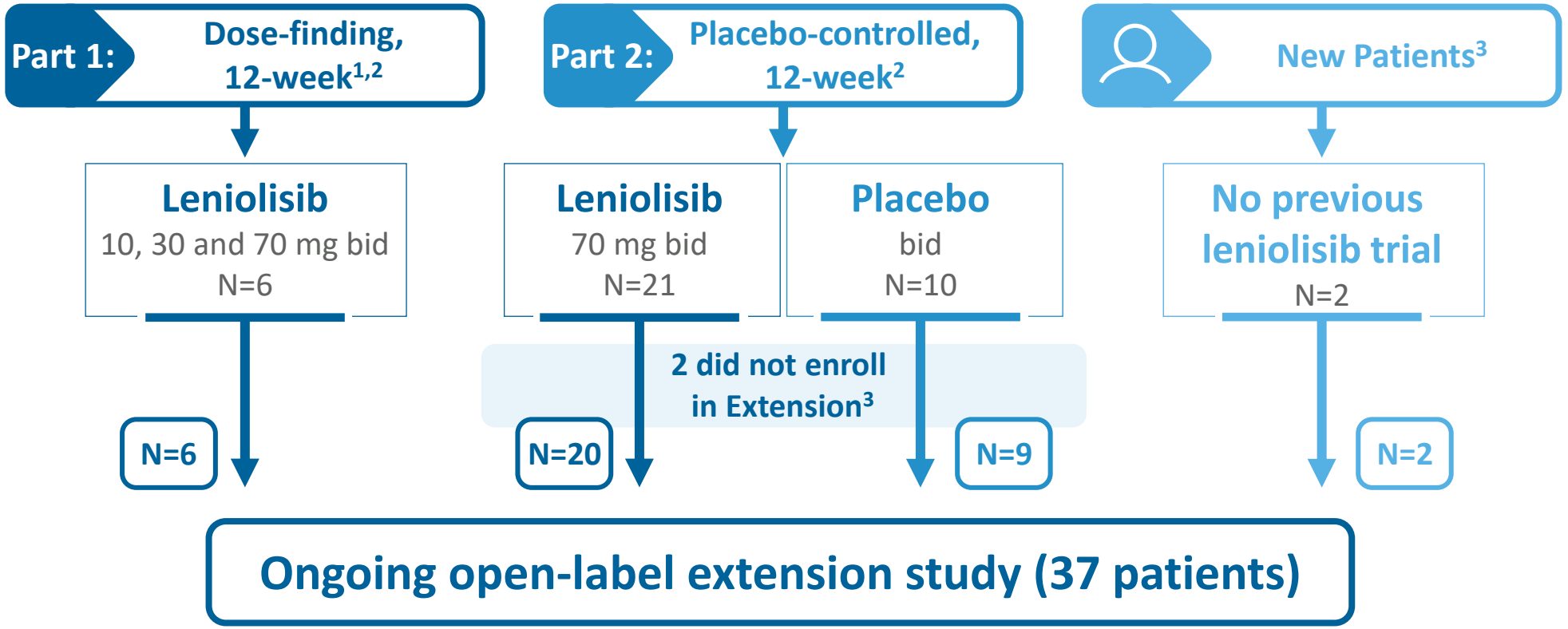



***Leniolisib balances PI3Kδ enzyme activity***
***Addressing immune deficiency and dysregulation***

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.

# Leniolisib clinical development program

## 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

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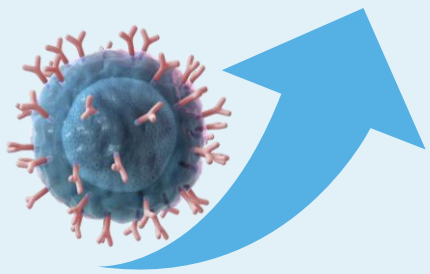
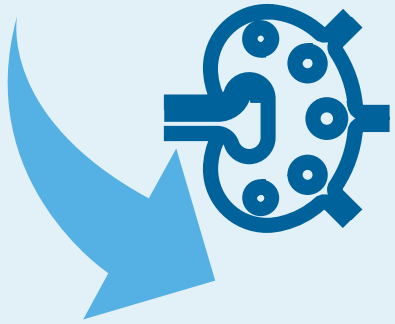
## Primary Outcomes

**Increased naïve B cells**



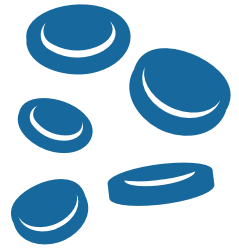
**Decreased lymphadenopathy**



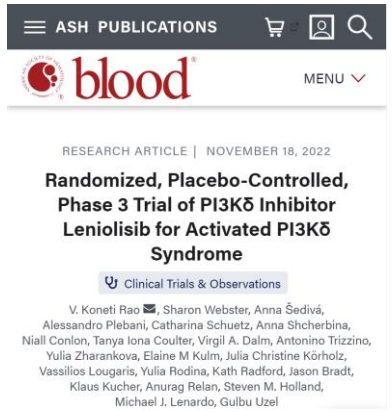
## Other Efficacy Outcomes

**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 rates (p=0.004) with each additional year of leniolisib treatment, despite concomitant reduction in immunoglobulin replacement therapy


ASH PUBLICATIONS

blood

MENU

RESEARCH ARTICLE | NOVEMBER 18, 2022

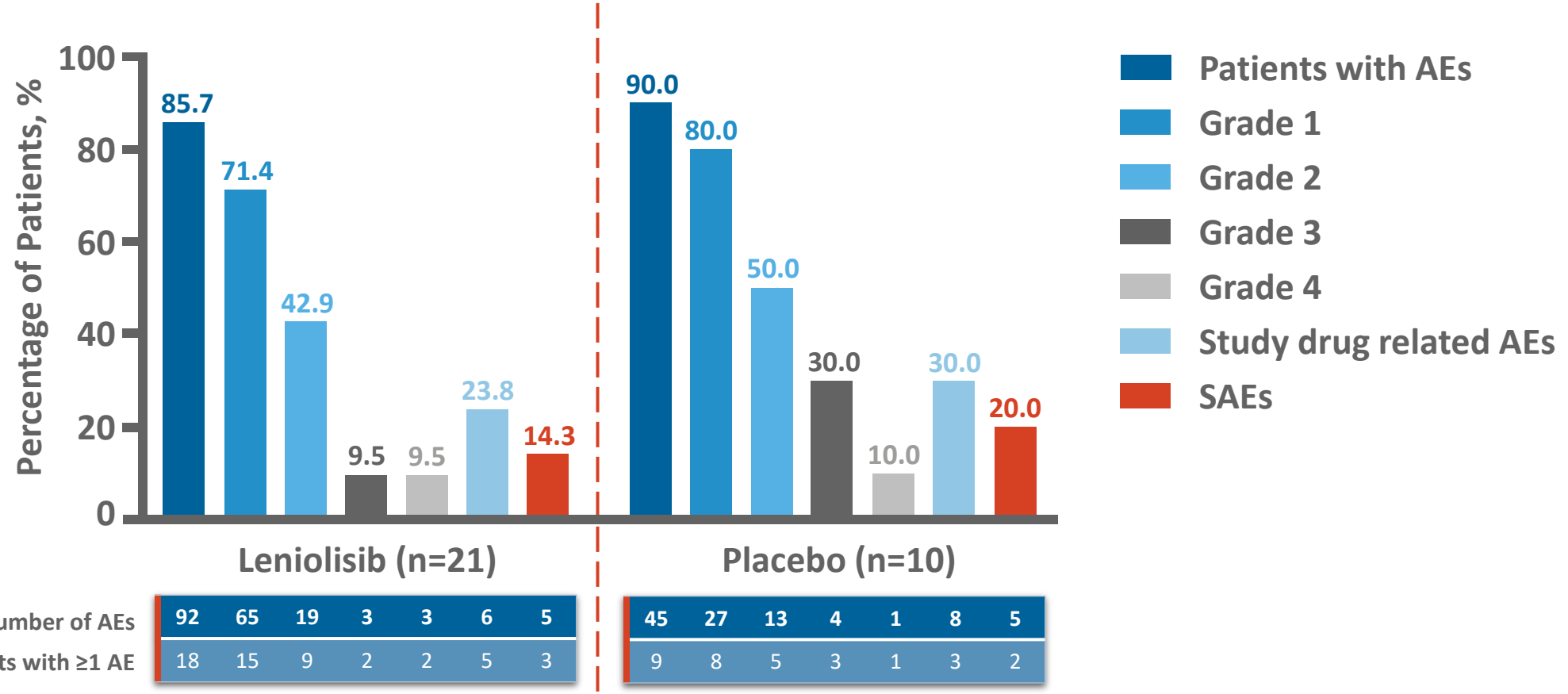
**Randomized, Placebo-Controlled, Phase 3 Trial of PI3Kδ Inhibitor Leniolisib for Activated PI3Kδ Syndrome**

Clinical Trials & Observations

V. Koneti Rao, Sharon Webster, Anna Šedivá, Alessandro Plebani, Catharina Schuetz, Anna Shcherbina, Niall Conlon, Tanya Iona Coulter, Virgil A. Dalm, Antonino Trizzino, Yulia Zharankova, Elaine M Kulm, Julia Christine Körholz, Vassilios Lougaris, Yulia Rodina, Kath Radford, Jason Bradt, Klaus Kucher, Anurag Relan, Steven M. Holland, Michael J. Lenardo, Gulbu Uzel

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

# Safety Data from RCT: Leniolisib was well-tolerated




| | Leniolisib (n=21) | | | | | | |
|---|---|---|---|---|---|---|---|
| Number of AEs | 92 | 65 | 19 | 3 | 3 | 6 | 5 |
| Number of patients with ≥1 AE | 18 | 15 | 9 | 2 | 2 | 5 | 3 |

| | Placebo (n=10) | | | | | | |
|---|---|---|---|---|---|---|---|
| Number of AEs | 45 | 27 | 13 | 4 | 1 | 8 | 5 |
| Number of patients with ≥1 AE | 9 | 8 | 5 | 3 | 1 | 3 | 2 |

- 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.

# Actively developing APDS market opportunity

Market opportunity with an estimated

**~1,500 APDS patients***

>500 patients identified by Pharming to date

(as of December 2022)

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

navigateAPDS by Pharming

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

All about APDS
Activated PI3K Delta Syndrome

Jeffrey Modell Foundation

Global Genes®
Allies in Rare Disease

Immune Deficiency Foundation

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

EHA EUROPEAN HEMATOLOGY ASSOCIATION

CIS Clinical Immunology Society

EAACI EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

AMERICAN SOCIETY OF HEMATOLOGY

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

# Regulatory status: on track for approvals in major markets

## USA

| | |
|---|---|
| SEP 28 2022 | Announced FDA accepted NDA filing with Priority Review for adults and adolescents aged 12 and older |
| OCT 1 2022 | ICD-10-CM (US CDC) reimbursement code for APDS took effect |
| MAR 29 2023 | Prescription Drug User Fee Act (PDUFA) approval date |
| 1H23 | Anticipated approval (1Q23) and commercialization (2Q23) of leniolisib |

## EEA

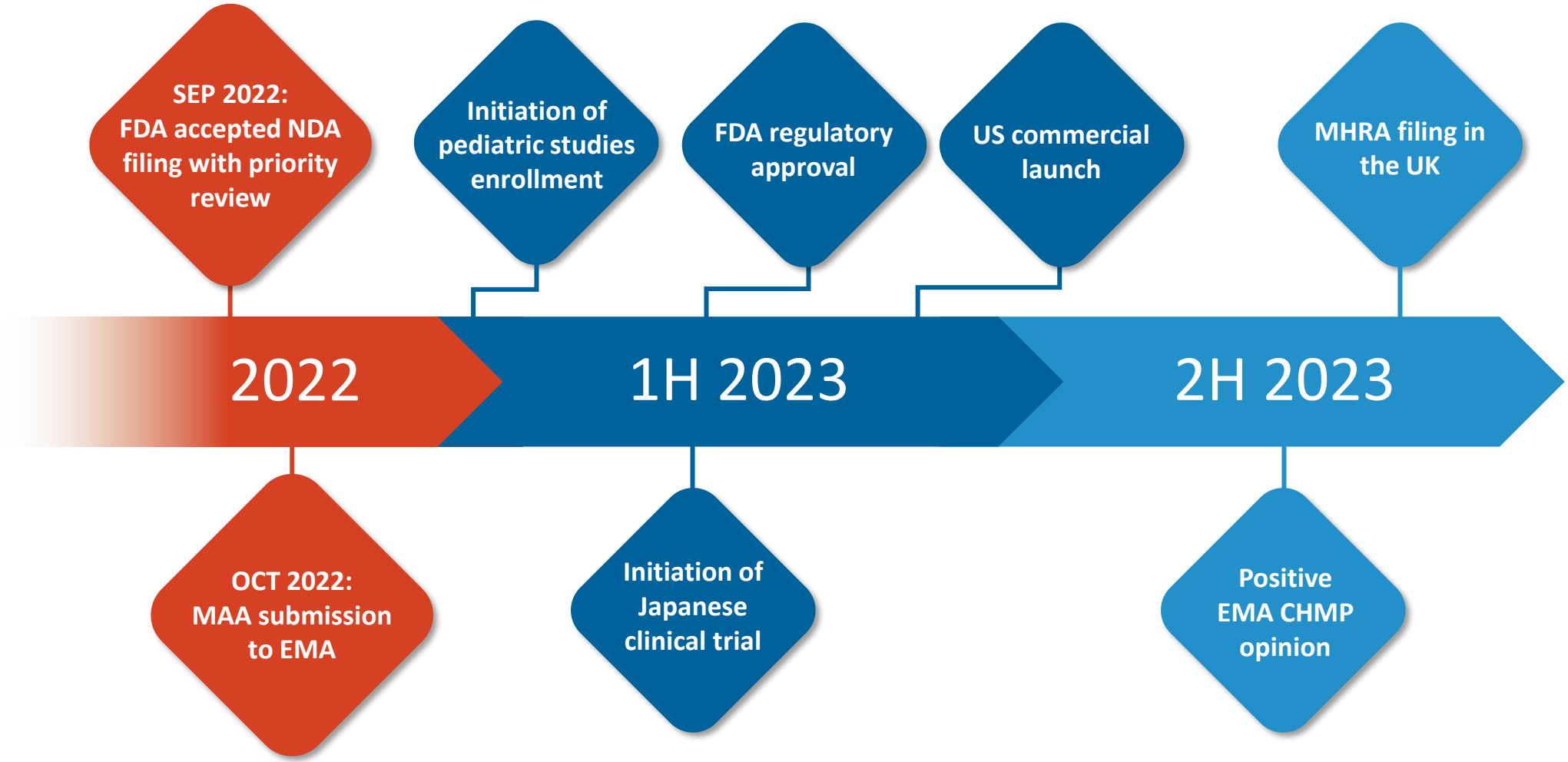
| | |
|---|---|
| JAN 6 2022 | Positive EMA decision on Pediatric Investigation Plan (PIP) for leniolisib |
| AUG 1 2022 | Announced EMA Accelerated Assessment granted for adults and adolescents ages 12+ |
| OCT 2022 | MAA submitted to EMA and validated for Accelerated Assessment* |
| 2H23 | Anticipated EMA CHMP opinion (approval to follow ~2 months later) |

## UK

| | |
|---|---|
| APR 6 2022 | MHRA grants PIM designation for patients 1 year to <18 years of age |
| 2H23 | Anticipated MHRA filing |
| 1H24 | Anticipated MHRA regulatory approval (will follow ECDRP route) |

*Subsequently changed to standard timetable

# 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.

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

# HAE gene therapy (OTL-105) & Pompe disease programs

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**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

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# Financials and Outlook

# Financial highlights (9M 2022)

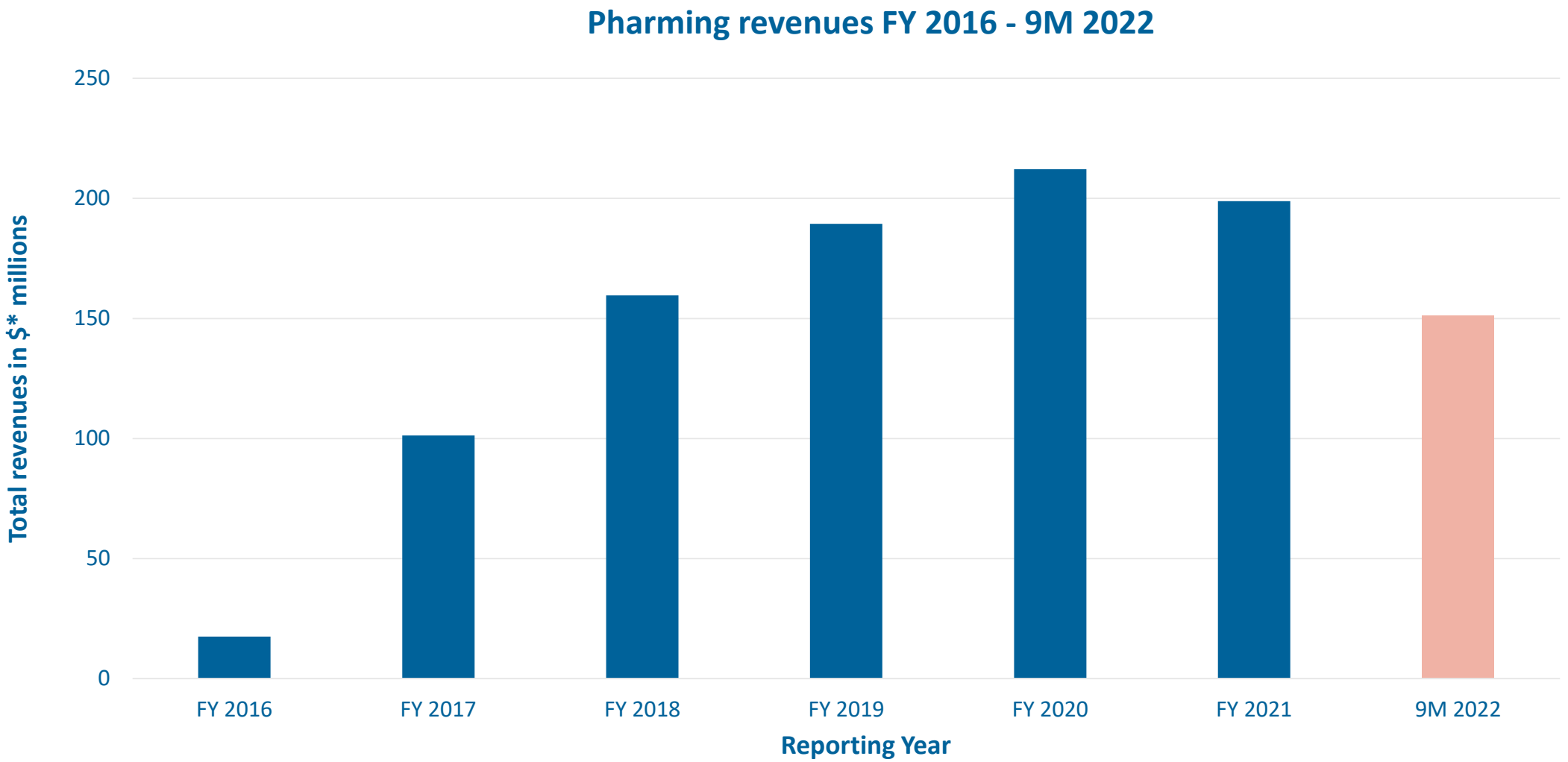
US$198.9 million total revenues for FY2021. Revenues for first 9M of 2022 increased by 3% compared to the first 9M 2021

Gross profit increased by 7% to US$139.7 million (9M 2022), 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




- 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

# Outlook

- 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 in 2H 2023, followed by approval of MAA by European Commission ~2 months later*
- Submit an ECDRP filing for leniolisib to MHRA, after anticipated positive CHMP opinion*
- 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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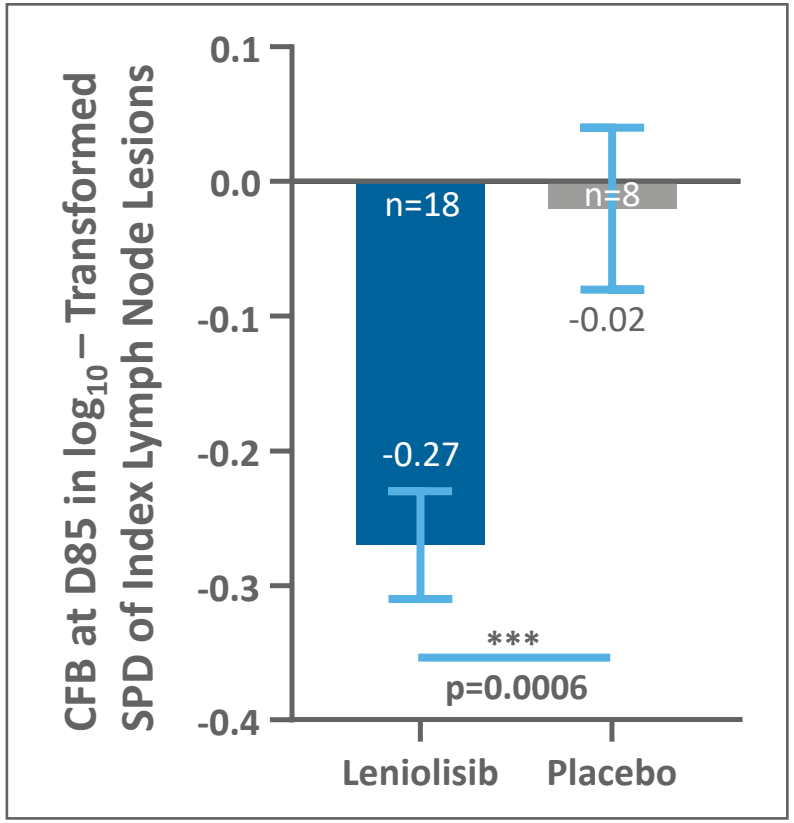
# Appendix

### leniolisib clinical trial data

# Leniolisib reduced lymphadenopathy

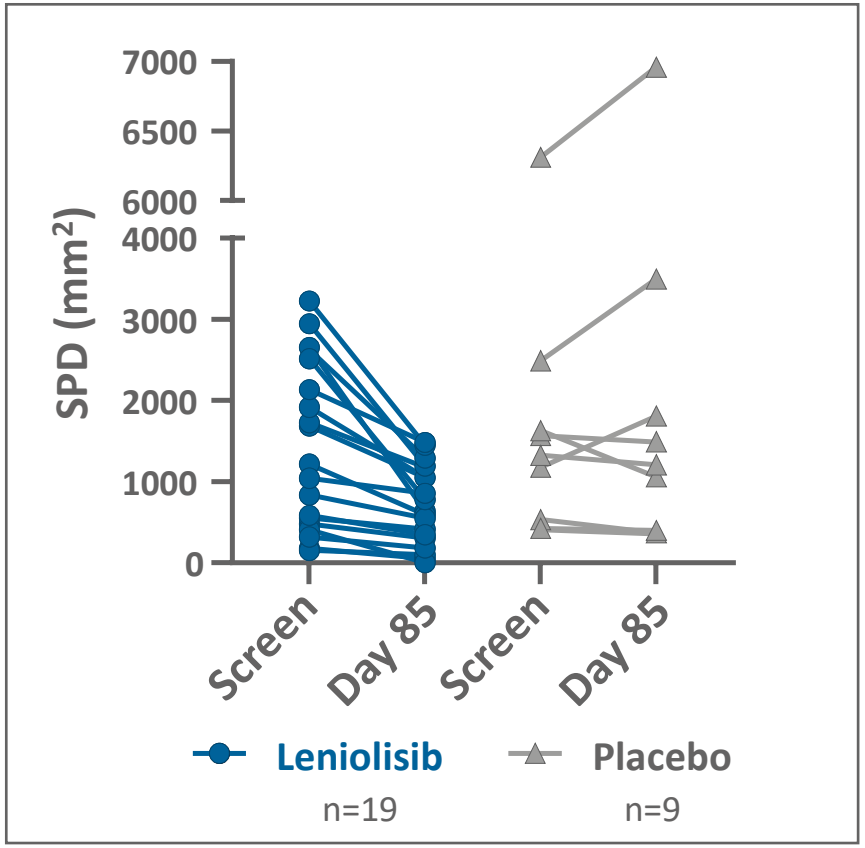
## Primary Outcome Analysis*

Change from baseline in index lesions




## Individual Index Lesion Sizes

Safety analysis set



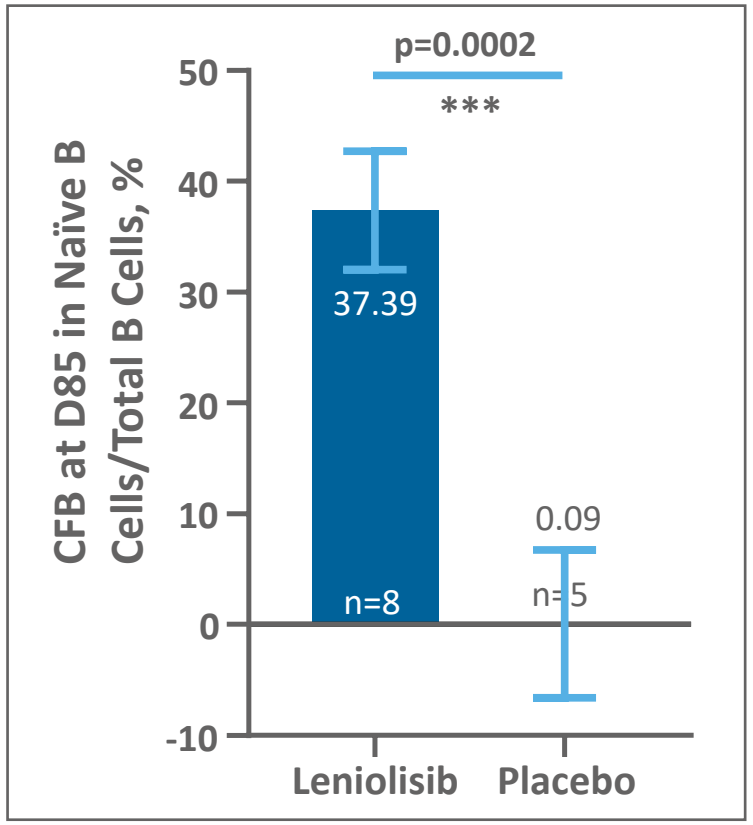

*Data were analyzed using ANCOVA model with treatment as a fixed effect and $log_{10}$-transformed baseline as a covariate. Use of glucocorticoids and IRT at baseline were both included as categorical (Yes/No) covariates. P-value is 2-sided. Least square means are graphed. Error bars are standard error 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.

CFB, change from baseline; D, day; PD, pharmacodynamics; SPD, sum of product of diameters; 3D, 3-dimensional. Data on file. Pharming Healthcare Inc. 2022.

# Leniolisib increased the percentage of naïve B cells out of total B cells

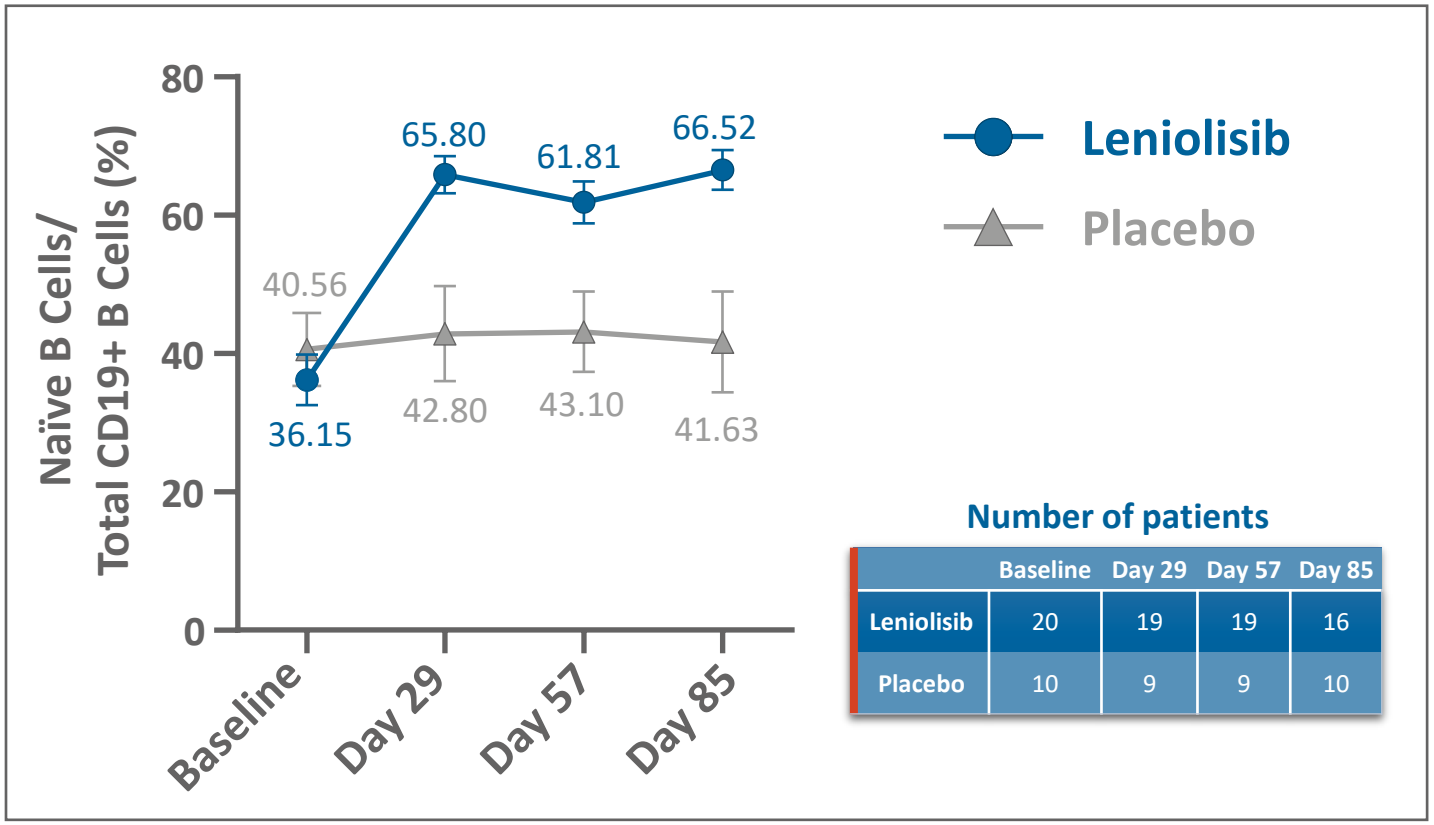
## Primary Outcome Analysis*

Change from baseline in naïve B cells




## Mean Percentage of Naïve B Cells Over Time

Safety analysis set



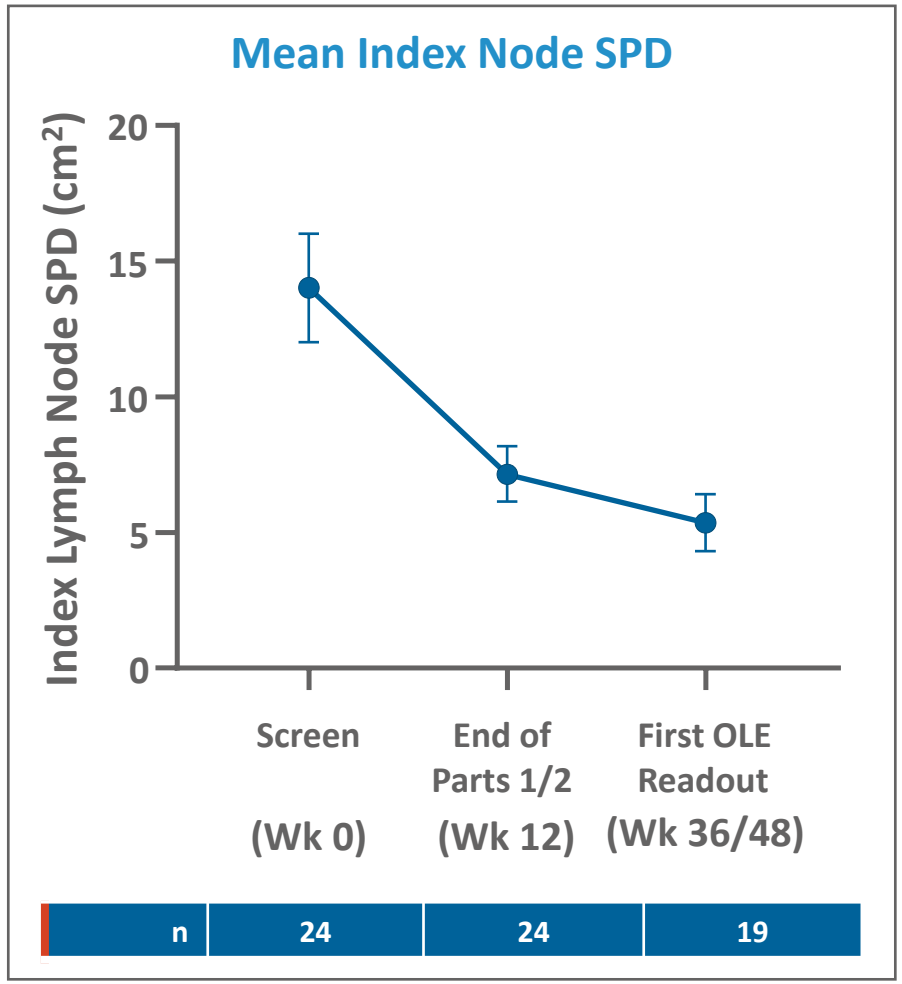

### Number of patients

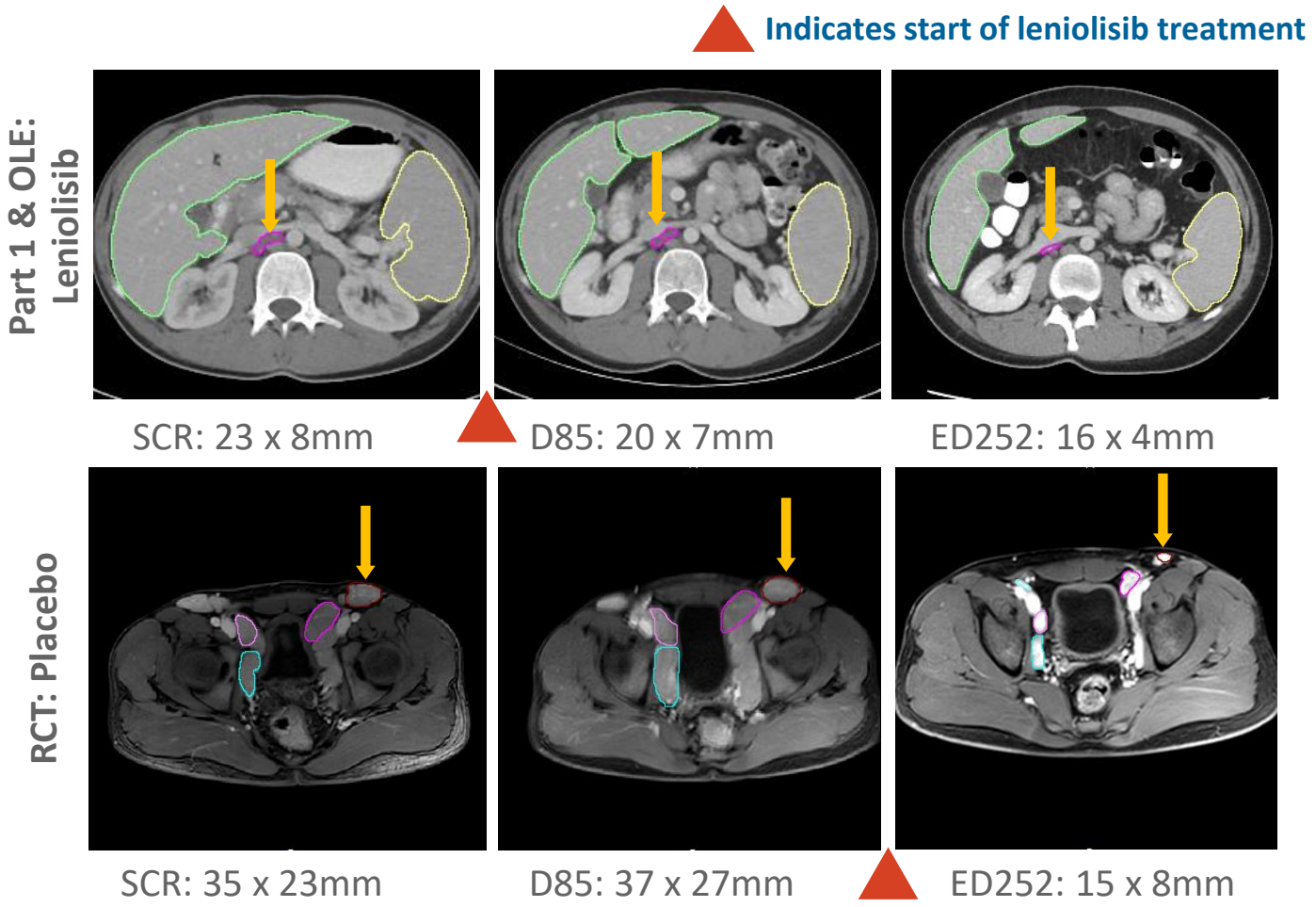
| | Baseline | Day 29 | Day 57 | Day 85 |
|---|---|---|---|---|
| Leniolisib | 20 | 19 | 19 | 16 |
| Placebo | 10 | 9 | 9 | 10 |

*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.

Data on file. Pharming Healthcare Inc. 2022.

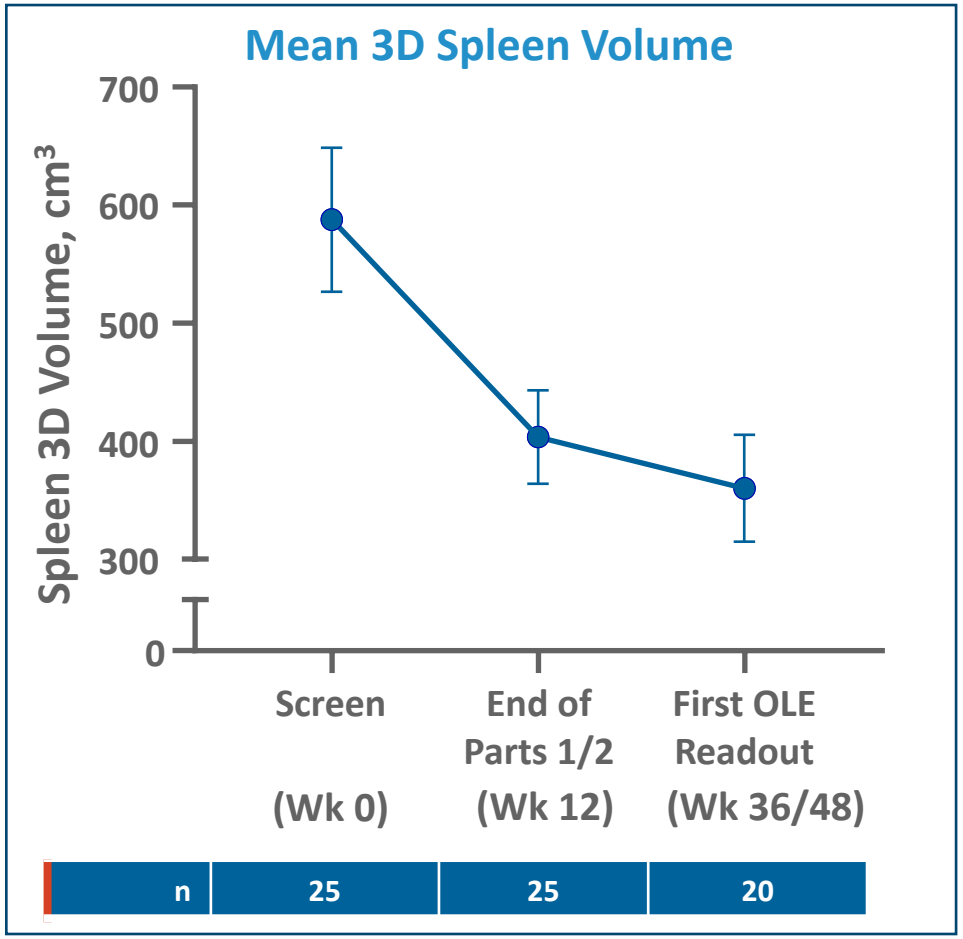
# Leniolisib continued to reduce lymphadenopathy



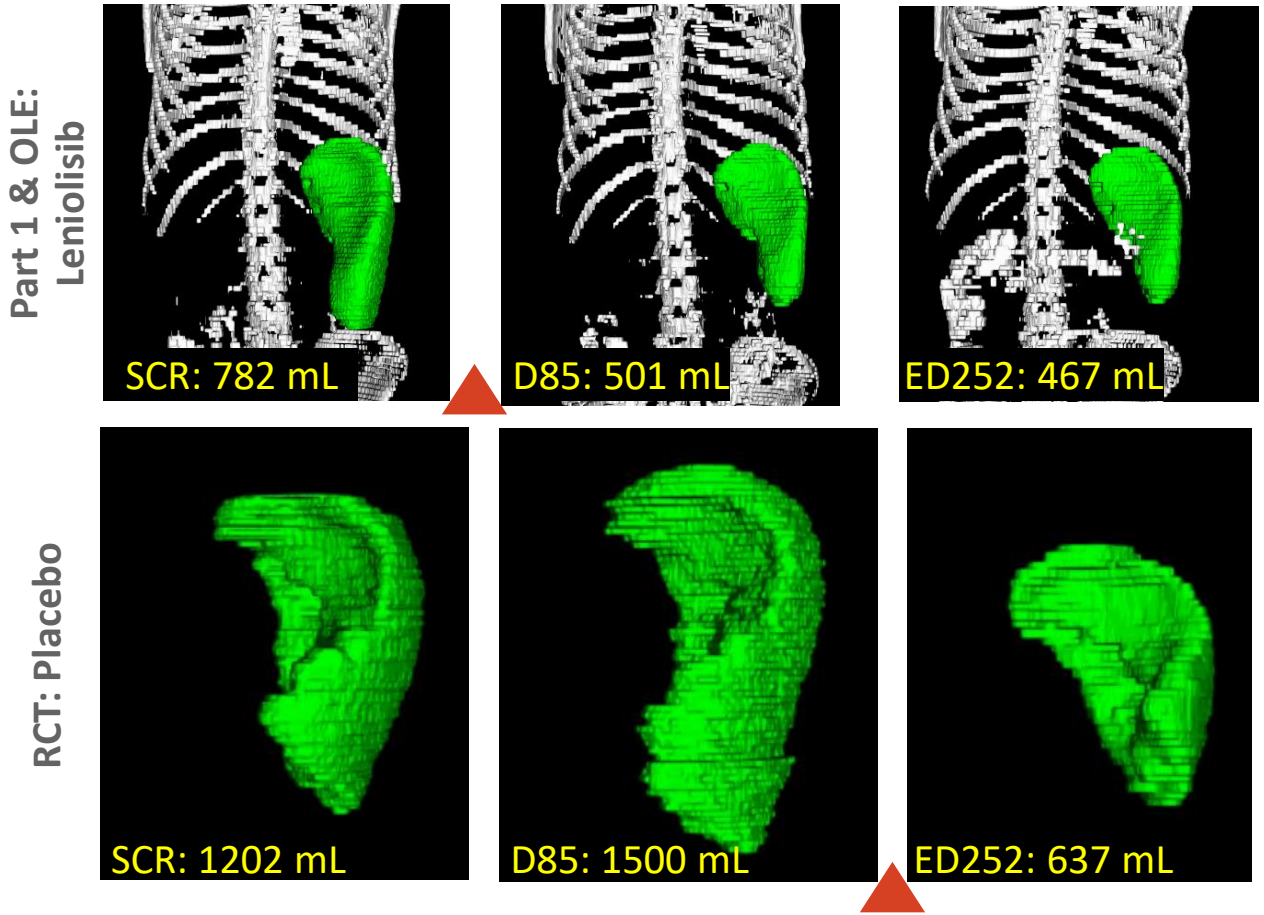




The mean index node graph has been corrected since the original ESID presentation.
Error bars are standard error of the mean. All patients from RCT Parts 1 and 2 with measurements are included. End of Parts 1 and 2 occurred at day 85. First OLE readout occurred after an additional 168 or 252 days.
D, 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



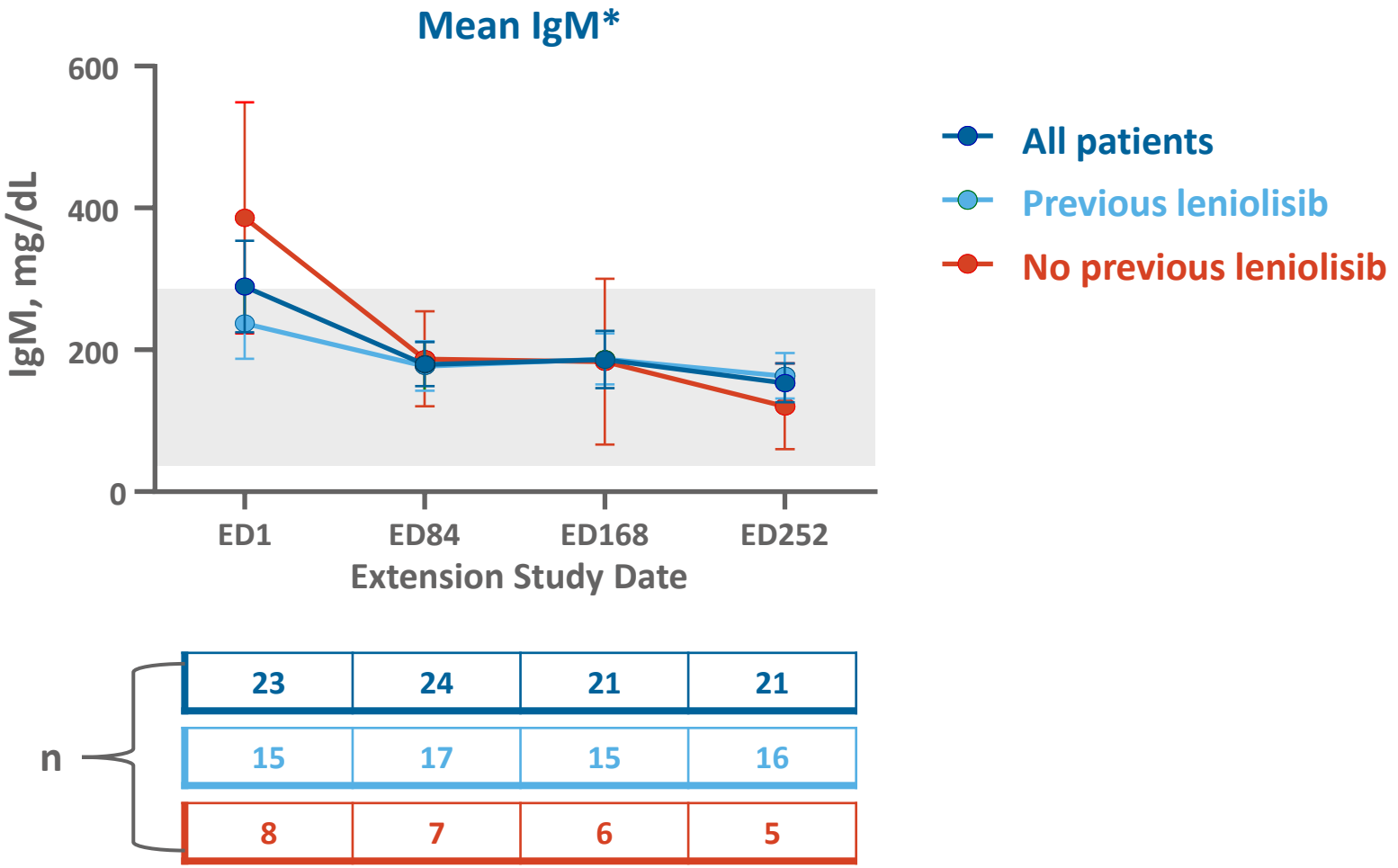

Indicates start of leniolisib treatment




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.

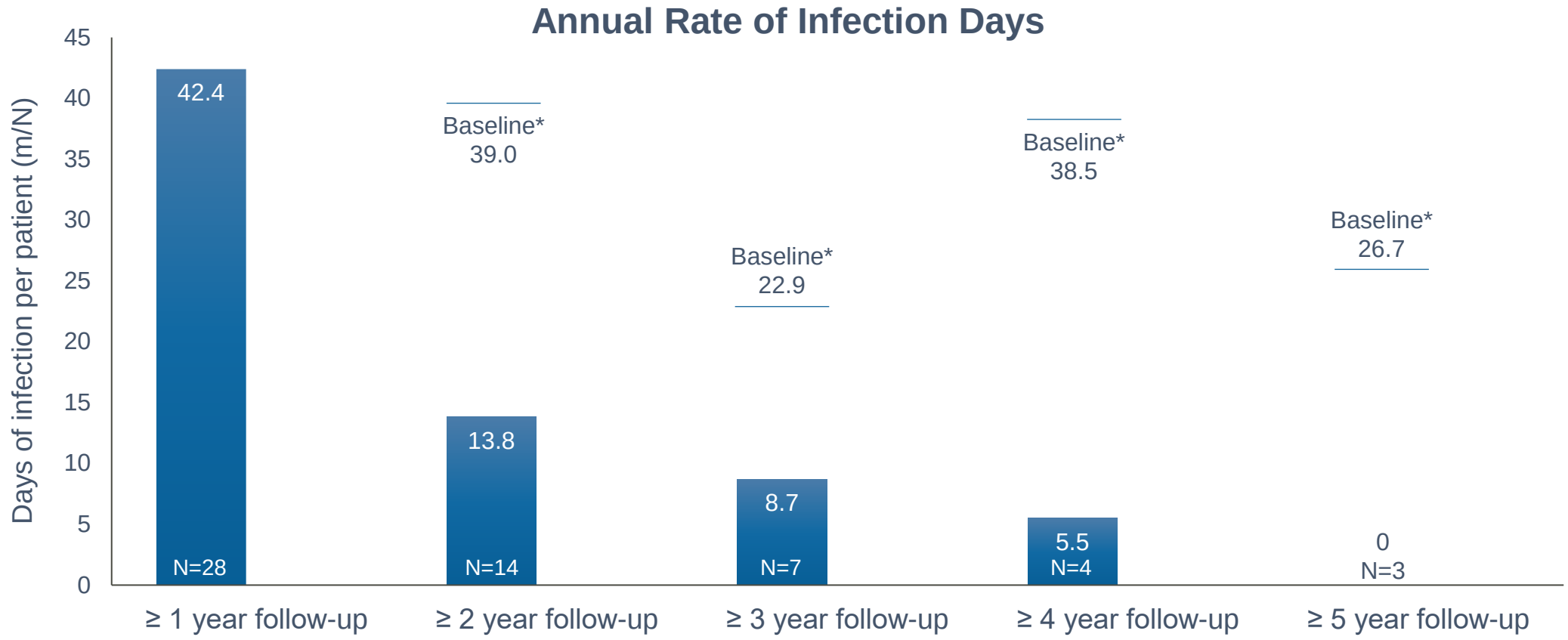
# Extension study: continued reduction in IgM levels




*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.

Data on file. Pharming Healthcare Inc. 2022.

# Extension study: continued reductions in annual infections despite decreased IRT use in 37% of patients on IRT

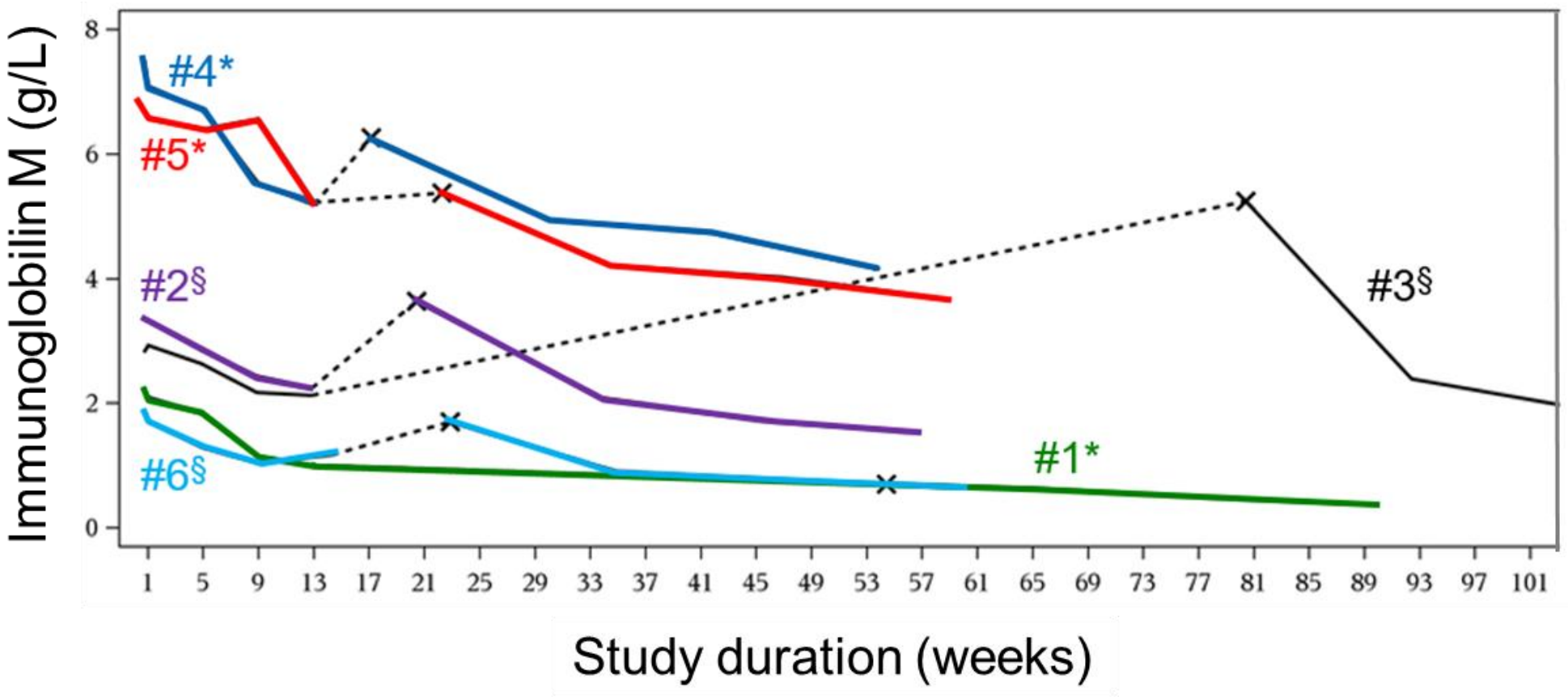



Statistically significant decrease of -0.351 (P=0.0040) in infection rates with each additional year of leniolisib treatment

Data analyzed using a log-linear negative binomial model including an offset for time spent in study, an effect for time of the start of infection (in years), and presence of baseline infection as a covariate.
*Baseline infections are each group's year 1 annualized rate of infections. N-values changed because patients were in the OLE for different lengths of time.
N, number of patients in follow-up category; m, number of infection days.
One patient was excluded from the analysis due to a wrong year recorded for an infection.
Infections that developed during the study were reported as adverse events. Investigators were requested to enquire about signs and symptoms of infections at each visit, in particular bacterial enterocolitis. Patients were not provided an infection diary to document infections occurring between visits.

# 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

Slide courtesy of Dr V. Koneti Rao. Blood (2018) 132 (Supplement 1): 3706.