

The logo consists of two overlapping, rounded diamond shapes. The front diamond is light blue and the back one is a slightly darker shade of blue. They are centered on the slide.

# Pharming Group N.V.

BioCapital Europe

Sijmen de Vries, CEO

11 March 2021

# Forward Looking Statements



*This presentation may contain forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our clinical results and other future conditions. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial or business performance, conditions, plans, prospects, trends or strategies, objectives of management and other financial and business matters; our current and prospective product candidates, planned clinical trials and preclinical studies, projected research and development costs, current and prospective collaborations; and the estimated size of the market for our product candidates, the timing and success of our development and commercialization of our product candidates and the market acceptance thereof, are forward-looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. While we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.*

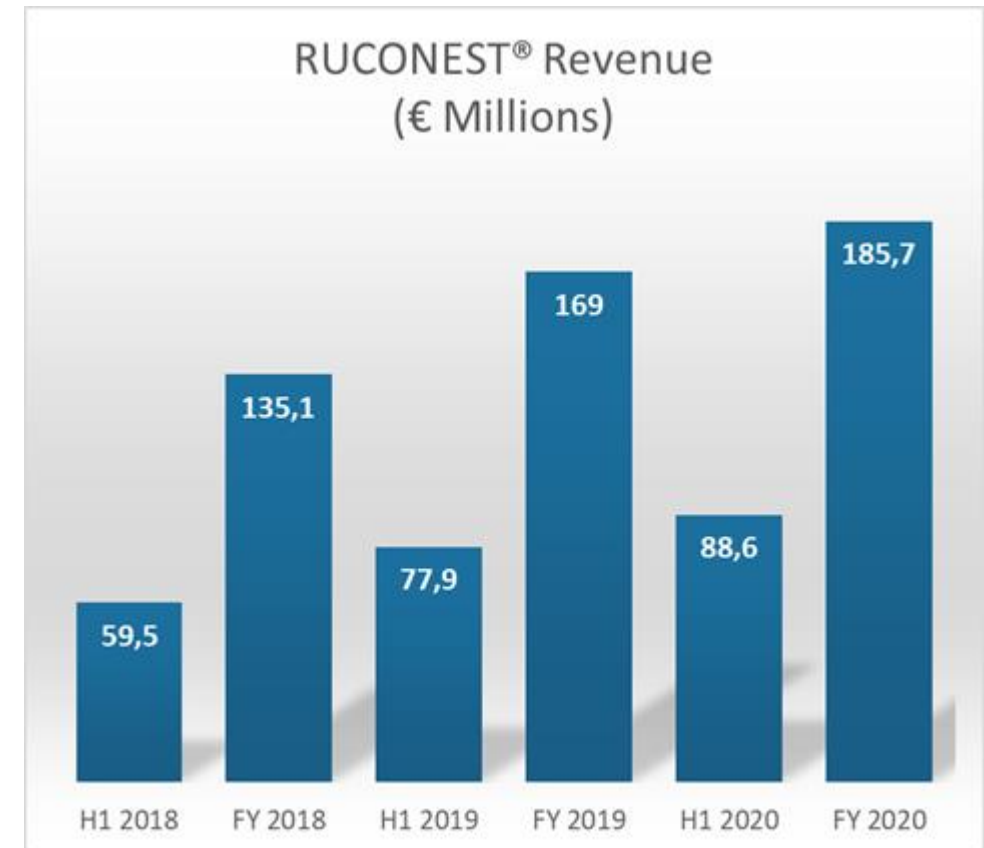
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# Company Overview

- ◆ Established in 1988, based in the Netherlands with 250+ employees
- ◆ Listed on the Nasdaq: **PHAR** & Amsterdam stock exchange: **PHARM**
- ◆ Rare and ultra-rare disease development and commercialisation:
  - Marketed lead product: **RUCONEST® (rhC1INH)**
  - Recombinant human C1-esterase inhibitor (enzyme replacement therapy) developed using our unique technology platform
  - Approved for the treatment of acute angioedema attacks in patients with hereditary angioedema (HAE)
  - Established commercial infrastructure in the USA and EU, and in partnership in Latin America, Korea and Israel
  - Clinical trials in follow-on indications
- ◆ Late-stage in-licenced product: **leniolisib**, for the treatment of Activated Phosphoinositide 3-kinase Delta Syndrome (APDS)



- Record revenue in FY 2020, 9.9% increase to €185.7m (FY 2019: €169.0m)
- Gross profits in FY 2020 increased 11.8% to €165.1m (FY 2019: €147.7m)
- Operating profit in FY 2020 increased 10.7% to €67.4m (FY 2019: €60.9m)
- Net profit in FY 2020 decrease of 9.8% to €32.7m (FY 2019:€36.2m), reflecting negative currency effects of €12.6m
- Strengthened cash position at year end to €168.3m (cash on 31 December 2019: €68.9m)
- Successfully placed €125m 3% senior unsecured convertible bonds due 2025
  - Proceeds used to redeem the remaining \$55.6m loan with Orbimed Advisors
  - Balance of proceeds to support expansion of commercialization and manufacturing infrastructure, launch of leniolisib and acquisitions/in licensing opportunities





Investing for long-term sustainable revenue growth

# Three-pillar strategy for growth

Continuing to grow RUCONEST® sales through further country launches & increasing HAE market share

- Fully commercialize RUCONEST® in all major international markets with our own sales forces
- Improve convenience of therapy for HAE patients
- Evaluate new technologies to treat HAE



Grow our HAE franchise

Expanding indications for rhC1INH & developing new recombinant proteins using our platform technology

- Developing rhC1INH for additional large unmet indications
- Leverage our transgenic manufacturing technology to develop next-generation protein replacement therapies



Extend rhC1INH franchise to larger indications and develop new Enzyme Replacement Therapies

In-licensing or acquiring late-stage clinical development candidates

- Developing leniolisib for the treatment of APDS
- Developing or acquiring new programs or companies that can be commercialized using our sales and marketing infrastructure



Leverage commercial infrastructures and accelerate expansion of portfolio

- RUCONEST® approved for the treatment of acute HAE attacks in adults and children
- Patients' treatment plans (if on prophylaxis) include break-through medication
  - New prophylactic treatments offer better attack reduction rates than previous IV plasma-derived C1INH prophylaxis treatment
  - According to published data: approximately half of the patients using new prophylaxis treatments continue to have breakthrough attacks, some frequently, and are in need of regular use of breakthrough medication
  - Although kallikrein/bradykinin inhibitors block the main pathway for symptomatology, an uncontrolled breakthrough attack can occur and become serious if no C1INH therapy is available
- Increasing recognition for prophylaxis patients to have effective and reliable C1INH treatment for breakthrough attacks at hand
  - Growth opportunity for RUCONEST® for treatment of breakthrough attacks associated with prophylaxis products

# Investment to increase capacity due to strong demand

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- Investment in de-risking and upscaling of production capacity
  - Pharming received both EMA and FDA approval for its new production facility of starting material for RUCONEST®
  - Third facility under construction to safeguard future growth in HAE supplies
  - Plans for a larger fourth facility to manufacture our other pipeline products
  - Building downstream processing facility to expand in-house processing capacity
- Patient numbers in potential new indications are much larger than in HAE
- Re-developing rhC1INH from cattle to meet future demand for large indications
- Funded from current cash generation



- Clinical trial for rhC1INH in pre-eclampsia and acute kidney injury temporarily halted due to COVID-19
- Clinical trials for rhC1INH in patients hospitalized with confirmed SARS-CoV-2 infections
  - University Hospital of Basel, Basel, Switzerland
    - Results from compassionate use study in five patients
      - Published in *Frontiers in Immunology*
    - Multinational, randomized, controlled, investigator-initiated study of up to 150 patients in Switzerland and expanded across the country and into Brazil and Mexico
      - Recruitment ongoing
  - Valley Hospital in Ridgewood, New Jersey, US
    - Randomized, open-label, parallel-group, controlled, clinical trial in up to 120 participants across centers in the US
      - Recruitment ongoing

## APDS market

- Activated PI3 kinase delta syndrome (APDS) is ultra-rare primary immunodeficiency (PID)
  - Caused by autosomal dominant mutations
  - Increased activity of phosphoinositide-3-kinase  $\delta$  (PI3K $\delta$ ) leads to malfunctioning B-(immune) cells, symptoms include; recurrent respiratory infections, organomegaly, malignancies and auto-immunity
  - Estimated prevalence 1-2/million
  - More than 240 reported in literature
  - Screening in subset of PID patients has found rates: 5/669 (1%) and 17/184 (9%)
- Current diagnosis and treatment options for APDS
  - Often misdiagnosed
  - Treatment limited to supportive therapies; antibiotics, immunoglobulin replacement therapy
  - No approved therapy for treatment
  - Genetic test only definitive diagnosis

## leniolisib program

- 'navigateAPDS' partnership in the US and Canada
  - Collaboration with Invitae for a commercially available genetic test
- leniolisib
  - Potent, selective PI3K $\delta$  inhibitor
  - Treats the root cause of APDS
  - Orally bioavailable
  - Direct PK/PD relationship observed
  - Currently in registration-enabling pivotal study
  - Expected headline data H2 2021 with potential launch H2 2022
- Orphan drug designation approved by the European Commission
  - Previously granted Orphan Drug Designation by the FDA in January 2018

# Impact of COVID-19 on Pharming's business

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Pharming continues to comply with international guidance and requirements across its operations to prioritise the health and safety of its employees during the COVID-19 pandemic.

The impact of COVID-19 on the operations of the business is summarized below:

- No impact on the upscaling or continued production of RUCONEST® to date, despite disruptions in supply chains for consumables used in production
- No impact on the availability or distribution of RUCONEST® to HAE patients
- The recruitment of new patients in ongoing clinical trials halted as result of COVID-19 priorities and disruptions in supply chains of test materials; patients already incorporated into ongoing clinical trials are continuing to receive treatment

- Continued growth in revenues from sales of RUCONEST<sup>®</sup>, mainly driven by the US and expanded EU operations, subject to the progression of the COVID-19 pandemic, with quarterly fluctuations in revenues expected, as a result of the ongoing effects of the pandemic on access to customers and phasing of ordering patterns.
- Maintenance of positive net earnings during the year, we therefore do not expect to require additional financing to maintain the current business.
- Investments in acquisitions and in-licensing of new development opportunities and assets, as these occur
- Continued investment in the expansion of production of RUCONEST<sup>®</sup> and production of leniolisib
- Investment in:
  - Ongoing registration-enabling study for leniolisib and pre-marketing activities
  - Ongoing clinical trials for rhC1INH
  - Additional development activities
- Continued close monitoring of the ongoing COVID-19 pandemic and the potential impact on the business

No further specific financial guidance for 2021 is provided.

As previously announced, as of 1 January 2021, the Company changed its reporting currency from Euro to US dollar.

[www.pharming.com](http://www.pharming.com)

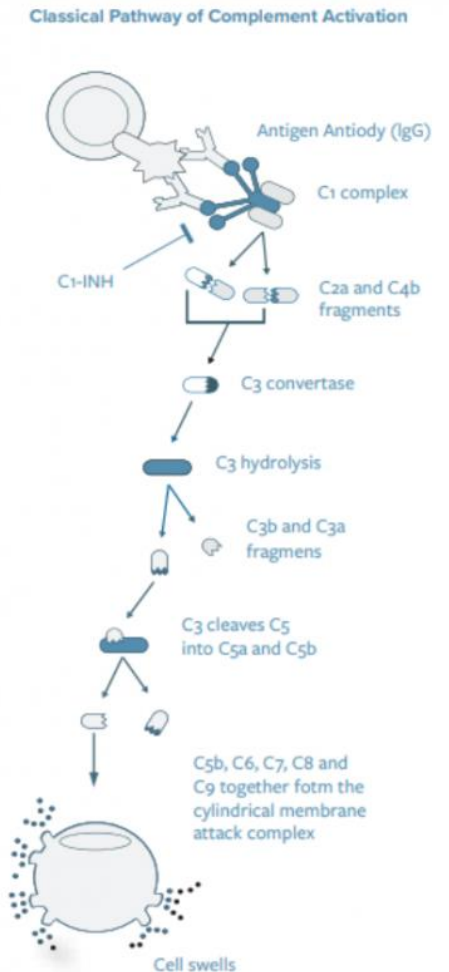
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Nasdaq: PHAR

Bloomberg: PHAR.AS

# rhC1INH and severe complications of COVID-19 infections

- ◆ C1INH is a protein that naturally occurs in the human body. It regulates several inflammatory pathways in the body by inhibiting certain proteins that are part of the human immune system.
  - In diseases like HAE, deficiency of functional C1 inhibitor leads to excessive activation of the complement system and other immunological and haemostatic pathways, giving cause to angioedema attacks.
- ◆ Systemic hyperinflammation is a hallmark of more severe stages of COVID-19 leading to acute respiratory distress syndrome, mechanical ventilation and ultimately death.
- ◆ C1 inhibitor production naturally increases during inflammatory conditions, such as infections. Despite this, a relative deficiency may occur and complement activation continues unchecked, often leading to a cytokine storm.
- ◆ Treatment with rhC1INH may;
  - dampen uncontrolled complement activation and collateral lung damage,
  - reduce capillary leakage and subsequent pulmonary edema by direct inhibition of the kallikrein-bradykinin system, and
  - reduce the generation of microthrombi by inhibiting MASP-1 induced clot formation and factor XII amplified thrombo-inflammation.



# Average Clinical Trial Trajectory



## Preclinical

Basic research  
Drug discovery  
Preclinical research

**Average duration:**  
1-6 years

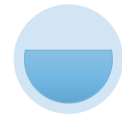


## Phase 1

Typically enrolling 20-100 volunteers or mildly affected patients

Measures safety and investigates possible side effects of treatment

**Average duration:**  
Typically up to 1 year



## Phase 2

Approximately 70% of all new drug research reaches Phase 2

Typically involves several hundred patients with varying levels of disease severity.

Measures the effectiveness of the drug and checks for side effects

**Average Duration: Several Months to 2 years**



## Phase 3

Approximately 33% of new drug research reaches Phase 3

Tests the largest number of patients possible (in relation to the disease size)

**Average Duration: 1 – 4 years**



## Approval & commercialisation

Only 25 to 30% of treatments are approved.

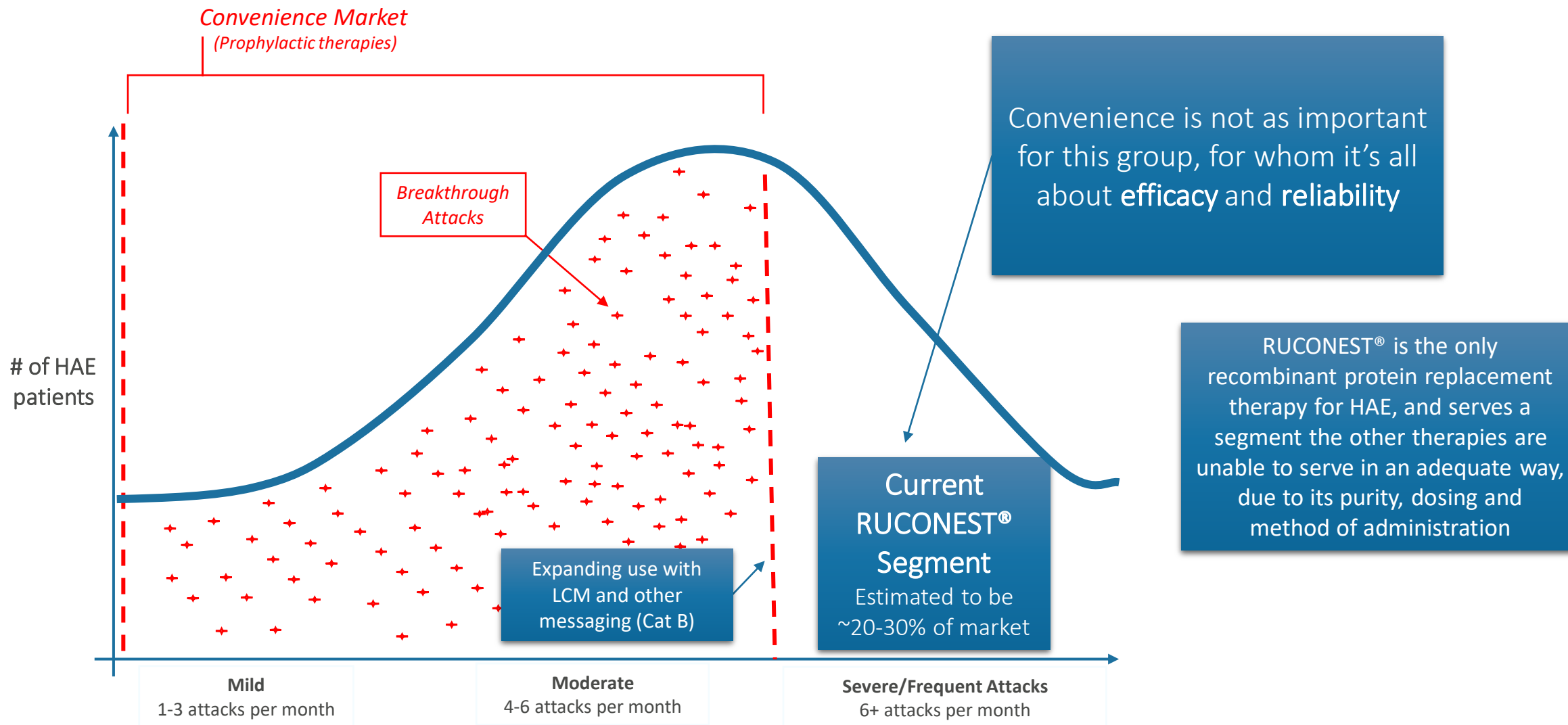
After completing Phase 3 a pharmaceutical company can move forward with a New Drug Application (NDA) or a BLA in the US and a marketing authorisation approval (MAA) in the EU

**Total Average Duration:**  
6 – 7 years

Variation in this trajectory:

- Orphan/rare disease
- Product availability
- New drug or a new indication for an existing drug

# RUCONEST®: Patient Segmentation in HAE





## Conestat Alfa in the Prevention of Severe SARS-CoV-2 Infection in Hospitalized Patients With COVID-19

- **Investigator initiated study:** University Hospital Basel, Basel, Switzerland
- **Led by:** Prof. Michael Osthoff
- **Start date:** August 6, 2020 in Basel, Switzerland. Study to expand to centers in Mexico and Brazil shortly.
- **Recruiting status:** Recruiting
- Phase 2 trial
- Up to 150 participants
- Randomised, open-label, parallel-group, controlled, multi-center trial
- **Treatment:** Initial double dose followed by 8 single doses: 20 vials over 72 hours
- **Outcome measured over 14 days by:** Disease severity, time to clinical improvement, number of patients not requiring invasive or non-invasive ventilation and Acute Lung Injury.

## Prevention of Severe SARS-CoV-2 Infection in Hospitalized Patients With COVID-19

- Pharming Technologies B.V. study
- **Estimated start date:** September 15, 2020 in multiple centers in the US
- **Recruiting status:** Recruitment open
- Phase 2 trial
- 120 participants
- Randomised, open-label, parallel-group, controlled, multi-center trial, pilot in the United States
- **Treatment:** Patients receive 8 single doses (2 vials) with a maximum of 16 vials over 96 hours.
- **Outcome measured over 14 days by:** Disease severity, time to clinical improvement, number of patients not requiring invasive or non-invasive ventilation and Acute Lung Injury.

## Study of Efficacy of Leniolisib in Patients With APDS/PASLI + Extension study

- Novartis Pharmaceuticals in partnership with Pharming Technologies B.V. study
- **Start date:** August 24, 2015
- **Recruiting status:** Recruiting
- **Estimated end date:** June 8, 2021
- **Launch:** H2 2022

### Phase 2/3: 2-part trial with 36 participants:

- i. Open-label, non-randomized to establish safety and pharmacokinetics.
- ii. Randomized, subject, investigator blinded, placebo-controlled study to determine optimal dose in target population

### Treatment:

- **Part 1** was with-in patient dose escalation with leniolisib 10, 30, 70mg bid.
- **Part 2** is randomized placebo-controlled with leniolisib 70mg bid and matching placebo.

### Outcome: over 12-week timeframe

- **Part 1** safety, tolerability, dose PD and PK/PD relationship of leniolisib in patients with APDS
- **Part 2** Assess clinical efficacy
  - Change from baseline assessment of organ volumes determined by MRI/CT imaging
  - Change from baseline in percentage of naïve B cells out of total B cells

### Extension study to investigate long-term safety, tolerability, efficacy and pharmacokinetics:

- **Start date:** September 9, 2016
- **Recruiting status:** Recruiting
- **Estimated end date:** September 1, 2026
  - Follow-up extension
  - Open-label, non-randomised
  - Treated daily with 140mg leniolisib

Study of Efficacy in the treatment of patients with Pre-Eclampsia with rhC1 INH (conestat alfa).

- Pharming Technologies B.V. study
- **Start date:** on hold due to COVID-19
- **Recruiting status:** Recruiting
- **Trial locations:**
  - University hospital Groningen in the Netherlands
  - University hospital Adelaide in Australia
  - Private Hospitals in Mauritius
- Phase 1/2 trial
- 30 participants with mild/late stage pre-eclampsia
- Multi-center, open-label, parallel-group, controlled study
- **Treatment:** 50 U/kg twice weekly until delivery + Standard of Care.
- **Outcome measured by:** Time from start of treatment to delivery, proportion of patients reaching gestation of week 37 and change from baseline of urine protein levels.

Study to evaluate the efficacy of conestat alfa compared to placebo after PCI in NSTEMI patients.

- Following positive results from a Phase 2 investigator-initiated study of RUCONEST® in a double-blind, placebo-controlled clinical trial in patients at risk of nephropathy resulting from contrast-enhanced examinations.
- **Pharming Technologies B.V. study**
- **Start date:** H2 2020
- **Recruiting status:** Not yet recruiting
- Phase 2 trial
- 220 participants
- Double-blind, randomized, controlled study
- **Treatment:** 50 U/kg Conestat or 100 U/kg conestat alfa or Placebo.
- **Outcome measured by:** The peak increase of urinary NGAL within 24 hours after PCI. With a 6 month follow up.