Cinclus PHARMA

Company Presentation
December 2021

AGENDA

1. Introduction
2. GERD overview
3. *Linaprazan glurate* (former X842)
4. Strategy

Cinclus PHARMA

Cinclus Pharma in brief

- Cinclus Pharma is a clinical stage pharma company developing small molecules for the treatment of gastric acid related diseases. Its lead candidate, linaprazan glurate, has successfully completed phase I clinical trials
- Founded in 2014
- Headquartered in Stockholm, Sweden
- Pre-IPO placement was recently settled in order to fund phase II clinical trials

Cinclus PHARMA

Highlights ***linaprazan glurate*** (former X842)

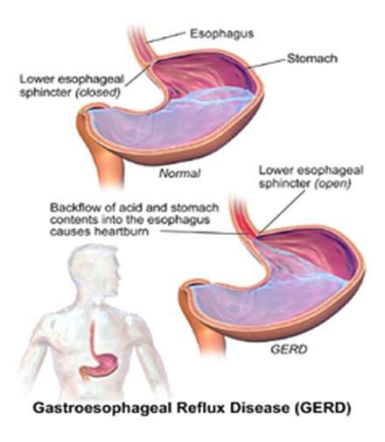
1. Lead candidate *linaprazan glurate* addressing a large unmet medical need – 18.5 million patients in Europe and NA with severe eGERD[1)] not adequately treated with available therapy with a market potential of **USD ~5-10bn**
2. Product candidate *linaprazan glurate* is a next generation improved NCE[2)] with superior safety and pharmacokinetic profile, built on linaprazan from AstraZeneca
3. Phase II was initiated in H2 2021 within a de-risked clinical development programme based on experience from precedent trials on its active metabolite linaprazan. Linear response and excellent biomarker results from phase I predicting clinical outcome
4. Patent protection for prodrug molecule *linaprazan glurate* valid until 2029/30 plus a potential extension of approximately five years plus additional patent possibility
5. CSO and CMO key members from Nexium, Losec and linaprazan development projects
6. Cinclus Pharma owns the worldwide commercial rights (licensee in South East Asia)

Note: 1) eGERD = erosive gastroesophageal reflux disease. 2) NCE = New chemical entity.

Addressing an unmet medical need in eGERD

What is reflux disease?

- Gastroesophageal reflux disease (GERD) is a digestive disorder that affects the lower esophageal sphincter (LES), the ring of muscle between the esophagus and stomach
- Though GERD symptoms vary from person to person, chronic heartburn and acid regurgitation are the most common symptoms



Why does the disease occur?

- GERD occurs when the esophageal defence mechanisms are overwhelmed by gastric contents that reflux into the esophagus
- Relocation of the upper part of the stomach above the diaphragm, i.e. hiatal hernia, is a common cause of GERD
- Prevalence increases with age

How do you manage the disease?

- Symptoms from GERD include heartburn, chest pain, difficulty in swallowing, regurgitation of food or sour liquid
- Acid exposure, i.e. pH <4 causes erosions
- Erosions and symptoms require effective treatment
- Current standard of care include primarily PPIs, e.g. Nexium, Takepron, Losec etc.
- Surgery for those with ”volume reflux” which leads to higher costs and severe implications on quality of life

What are the challenges?

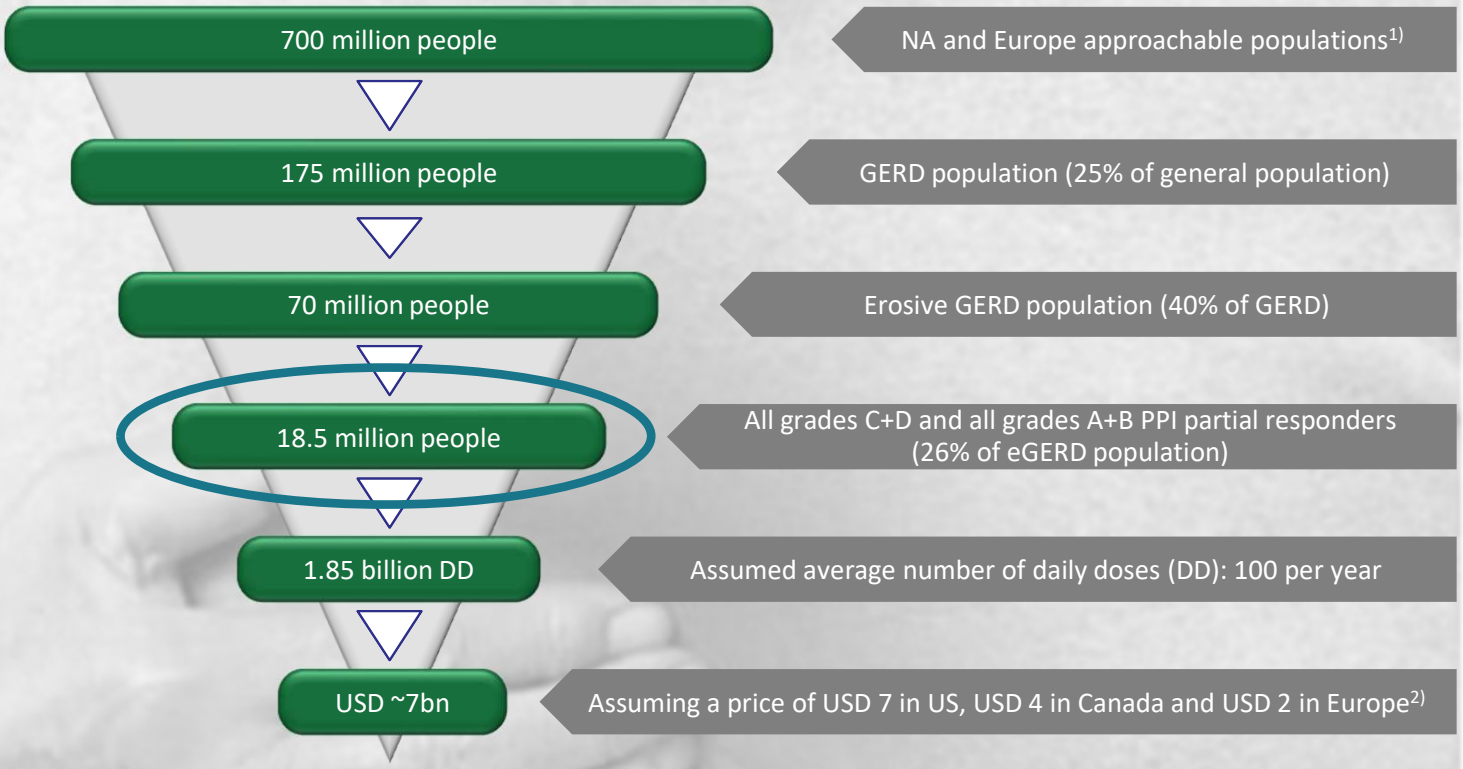
- 1/3 of patients with eGERD grade C remain unhealed after four weeks with standard PPI therapy
- 56% of patients with eGERD grade D remain unhealed after four weeks with standard PPI therapy
- 10% of patients with eGERD grades A and B are unhealed after four weeks with standard PPI therapy

A NEW SOLUTION REQUIRED FOR PATIENTS THAT ARE NOT PROPERLY HEALED BY CURRENT MEDICATION

Sources: Lagergren J, et al (1999). National Institute for Health and Care Excellence (2014)

Linaprazan glurate target population estimated at 18.5 million

- Approximately **25%** of the population suffers from GERD. **40%** of these suffer from tissue damage (eGERD)
- 4.5 million of the **18.5 million target group** are grades A+B PPI partial responders
- **Increase in awareness** about GERD as well as population growth will increase target population
- Assumed number of daily doses of linaprazan glurate is **100** per year (four cycles)

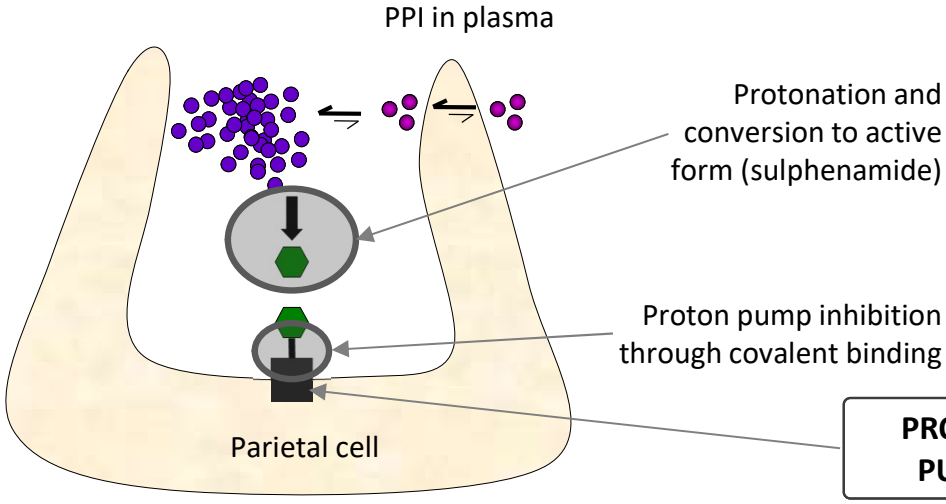


Lead candidate *linaprazan glurate* addressing a large unmet medical need – 18.5 million patients in Europe and NA with severe eGERD not adequately treated with available therapy, representing a billion dollar market

Note: 1) People above 18 years of age. Canada represents 30 million, US represents 260 million and Europe represents 410 million. 2) Please see page 30 for further information. Sources: Worldometers. Statista Kahrilas P, et al (2007). Dickman R, et al (2015). Lauritsen K, et al (2003). Donnellan M.B ,et al (2004)

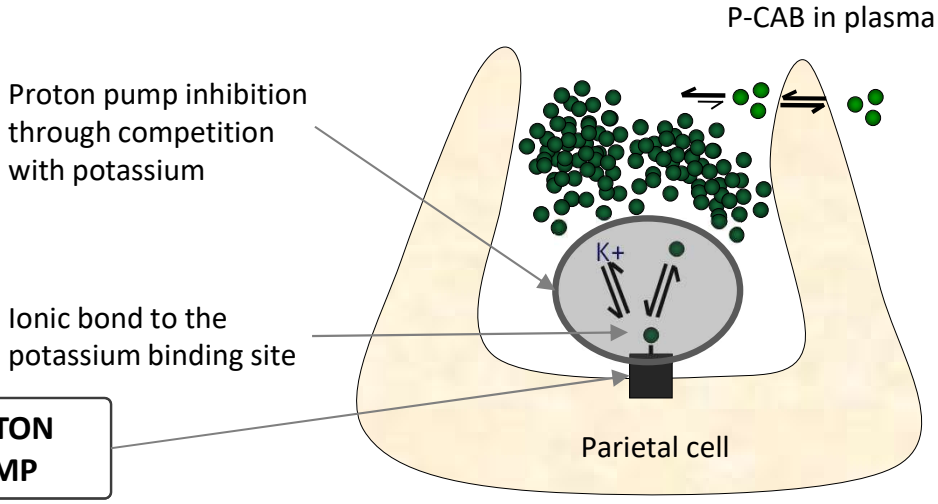
Mode of action – PPIs versus P-CABs

Proton Pump Inhibitor (PPI)



- Plasma half-life is 1-1.5 hours
- Up to three times daily – duration still less than 18 hours
- Slow onset to maximum effect (3-5 days)
- Prodrugs that require acid for activation yet are unstable in acidic conditions

Potassium-Competitive Acid Blocker (P-CAB)



- ✓ Plasma half-life is 5-10 hours
- ✓ Once or twice daily provides 24h acid control
- ✓ Fast onset (~1-2 hour)
- ✓ No activation required and stable in acidic conditions

PROTON PUMP

The access to a more efficient drug on the market will change the responsible prescriber's risk evaluation and potentially avoid off-label prescription of high-dose PPIs with uncertain safety profiles

Sources: Andersson K, et al (2005). Andersson K, et al (2006)

Next generation improved NCE – built on linaprazan from AstraZeneca

Issues highlighted during the linaprazan project…

- As not all patients are properly healed by existing medication, AstraZeneca identified an unmet medical need which led to the launch of a P-CAB development project
- Intended to develop the successor to Losec and Nexium
- Comprehensive data from 23 phase I studies including more than 600 subjects and two phase II studies including approximately 2000 patients shows that linaprazan was well tolerated, with a fast onset of action and full effect at first dose

ISSUES

→ Linaprazan was quickly eliminated from the body and had too short duration of acid inhibition. To achieve long acid control linaprazan had to be overdosed. As a result, it was not possible to show superiority

→ The resulting Cmax levels were on average 20 times higher than the level required for full inhibition of acid secretion, resulting in liver problems

…are now solved with *linaprazan glurate*

- The prodrug development aims to:
  - Design a new chemical entity with strong IP properties
  - Prolong the plasma half-life to obtain long duration effect
    - Accomplished with *linaprazan glurate* in animal experiments and in two phase I studies
    - Solid oral formulation in place
    - Next generation oral formulation in development, expected to be finished by phase III

SOLUTIONS

→ Accomplished with *linaprazan glurate* in animal experiments and in three phase I studies

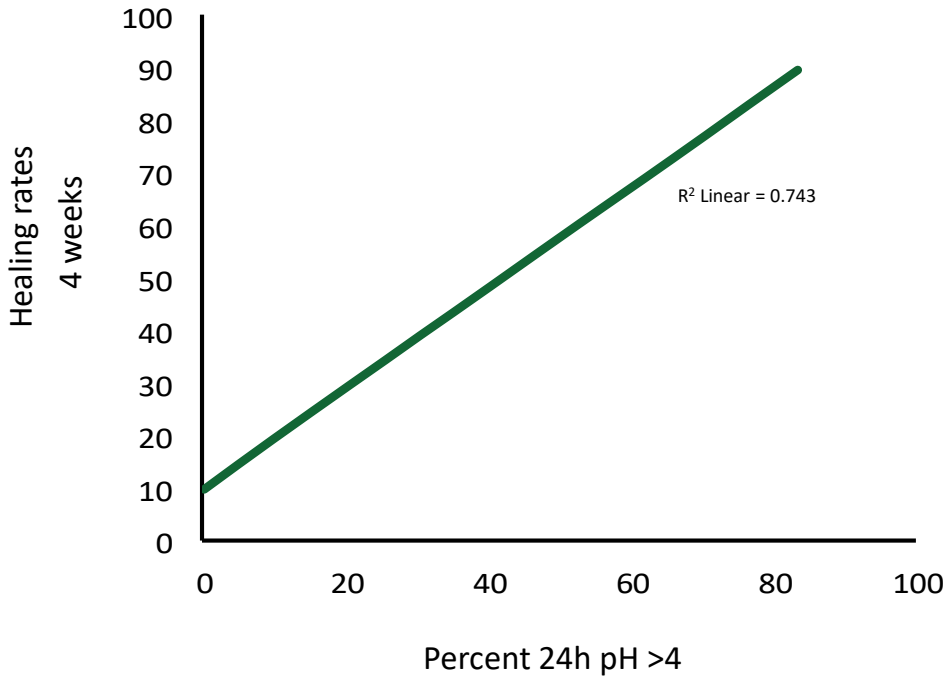
→ Lower the Cmax value in order to avoid overdosing and minimise the load to the liver

pH control – an excellent biomarker for efficacy

Efficacy predictable from phase I

- Excellent biomarker in phase I to predict clinical outcome in phase II and III (healing of esophagitis)

Mean percentage of time the intragastric pH >4 determines healing rate[4)]

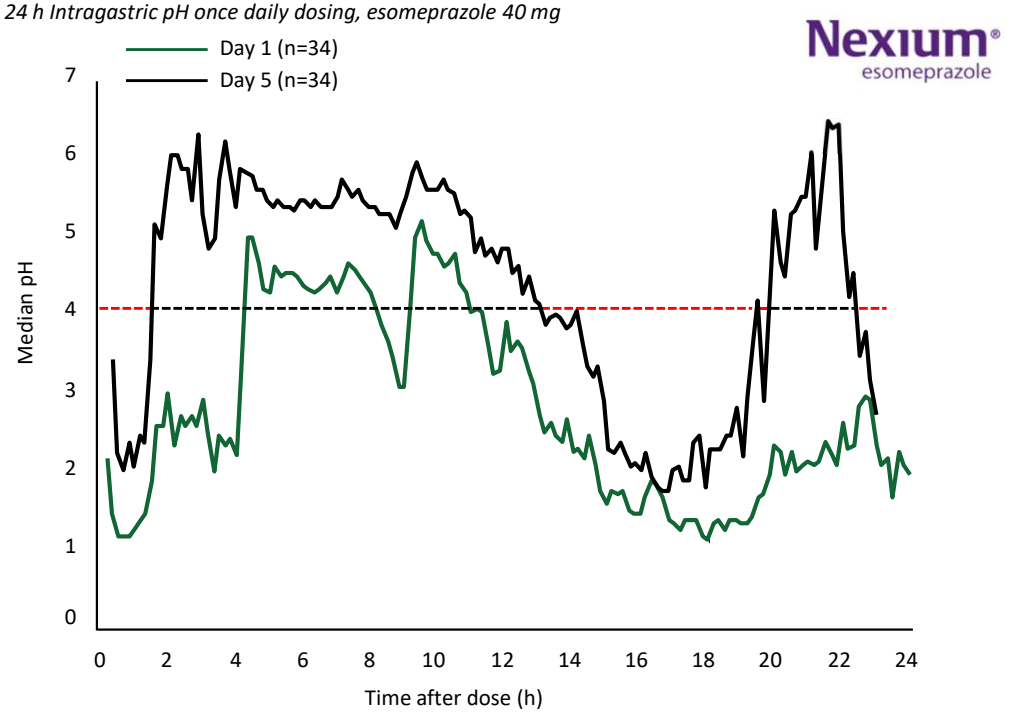


Source: Yuan Y et al 2007

PPI versus first generation P-CAB – room for improvement

PPI

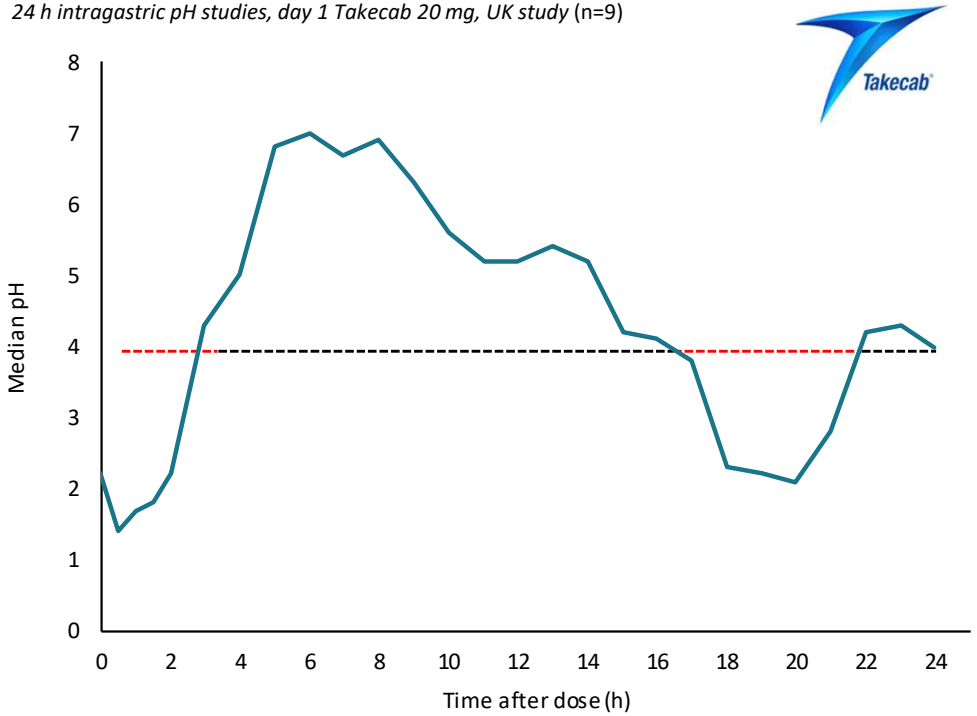
24 h Intragastric pH once daily dosing, esomeprazole 40 mg



- 40 mg Nexium day one after first daily dose: modest inhibition of intragastric pH, due to buffer effect by meals
- 40 mg Nexium day five after fifth daily dose: pH control, pH > 4, until 12-14 hours

P-CAB

24 h intragastric pH studies, day 1 Takecab 20 mg, UK study (n=9)



- 20 mg Takecab day one after first dose: fast onset of 15-16 hours of pH control, i.e. six hours acidic content

Sources: Wilder-Smith C et al, (2001). Jenkins et al, APT (2015)

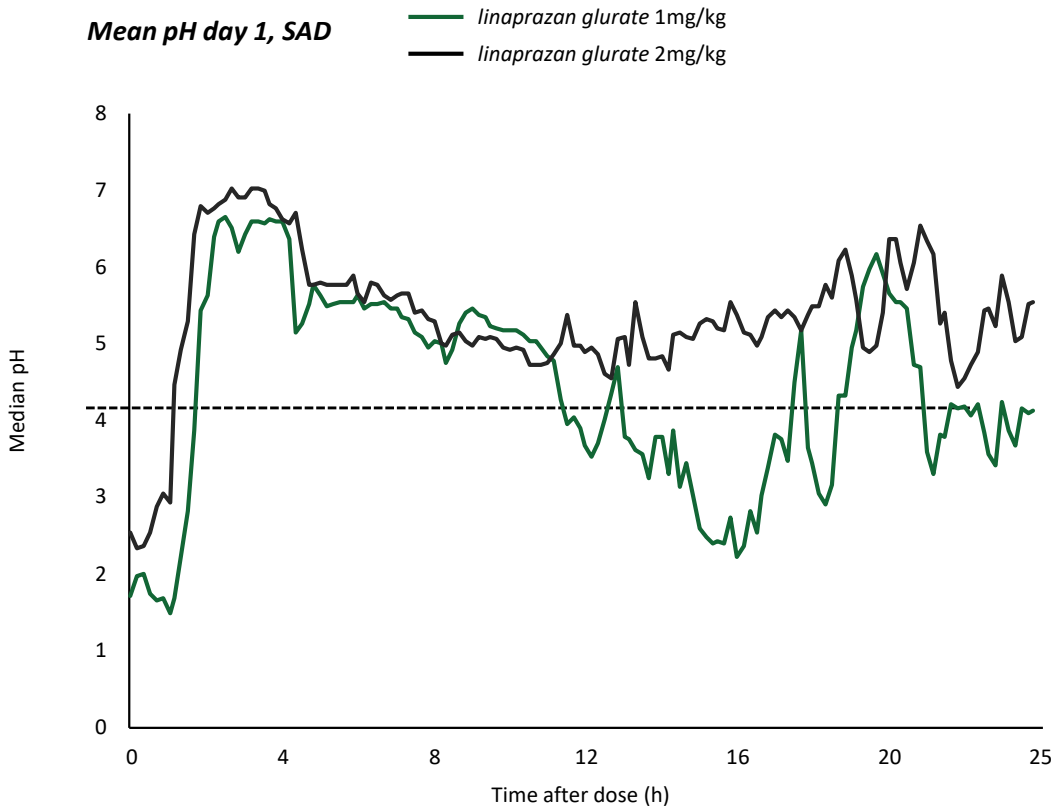
Phase I – overview of SAD/MAD study[1)]

Primary objective and results	• *Linaprazan glurate* was safe and well tolerated. No SAE[2)] occurred after dosing
Secondary objective and results	• Dose linear pharmacokinetics • Dose linear acid inhibition and clear PK/PD relationship • No effect of food was detected • Study Maximum Dose was reached • Gastric acid inhibition was maintained over 24 hours at certain dose levels
Description	• Single and multiple ascending dose • Liquid formulation • First-in-human design • ClinicalTrials.gov identifier: NCT03105375
Endpoints	• Frequency of adverse events, lab results and vital signs • Standard PK parameters • Dose limiting toxicity • PK/PD where PD is intragastric pH over 24h
# of patients	• In total, 28 subjects were treated of which 9 subjects were treated more than once • Performed at CTC Uppsala Sweden
Timetable	• Initiated in February 2017 • Final study report in February 2018

Note: 1) SAD = Single ascending dose, MAD = Multiple ascending dose. 2) Serious adverse event

Phase I results show acid control over 24 hrs

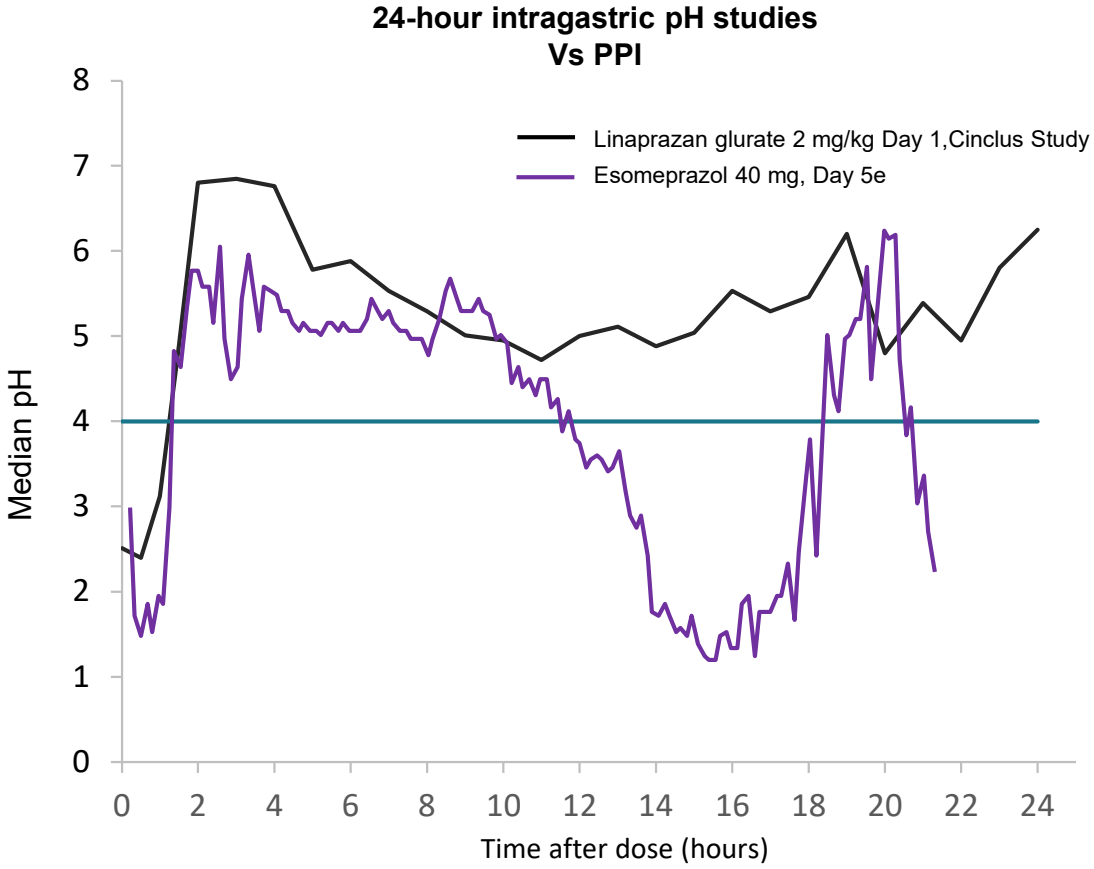
linaprazan glurate – liquid formulation



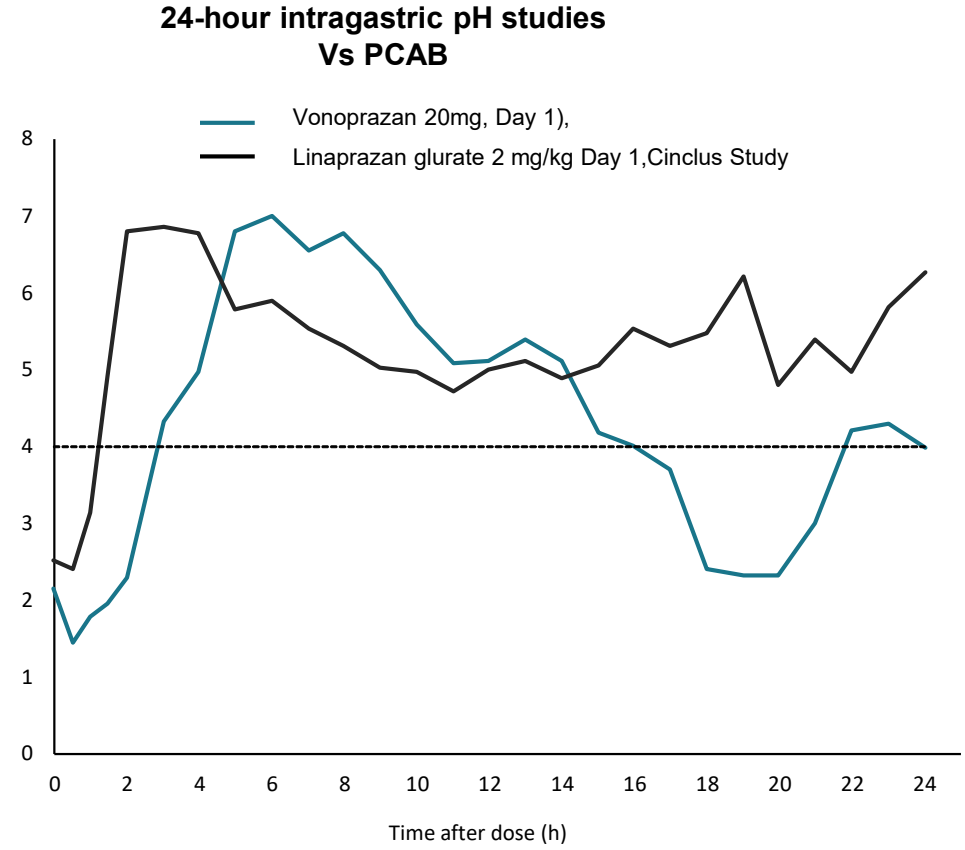
- 1 mg/kg *linaprazan glurate* day one after first dose: fast onset and pH control 11-13 hours similar to PPI
- 2 mg/kg *linaprazan glurate* day one after first dose: fast onset and pH control 24 hours (mean of 10 median values)

Sources: linaprazan glurate study.

Linaprazan glurate provides superior acid control over both PPI and Takecab, indicating superior healing rates



- Day 1 Linaprazan Glurate : no acid breakthrough
- Day 5 Esomeprazole: 9 hours with pH less than 4.

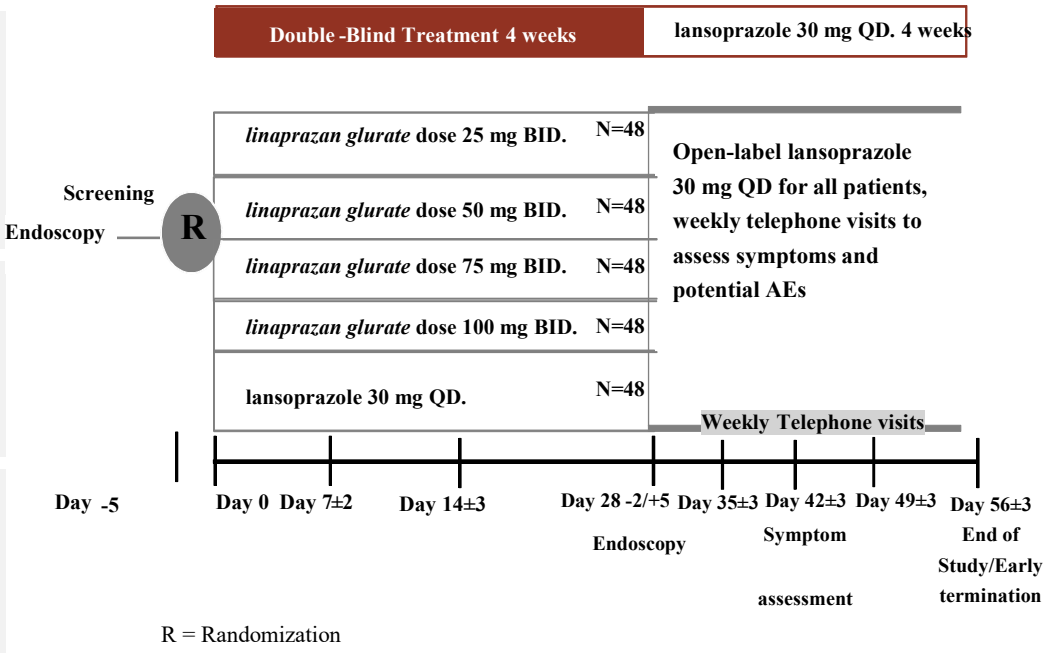


- The dose of 2 mg/kg Linaprazan glurate gave no acid breakthrough
- while the pH control after PCAB left about six hours without control

- Sources: linaprazan glurate study. Takecab study: Jenkins et al, APT (2015). Takecab 20 mg and linaprazan glurate 2 mg/kg od. Wilder-Smith C et al, (2001)

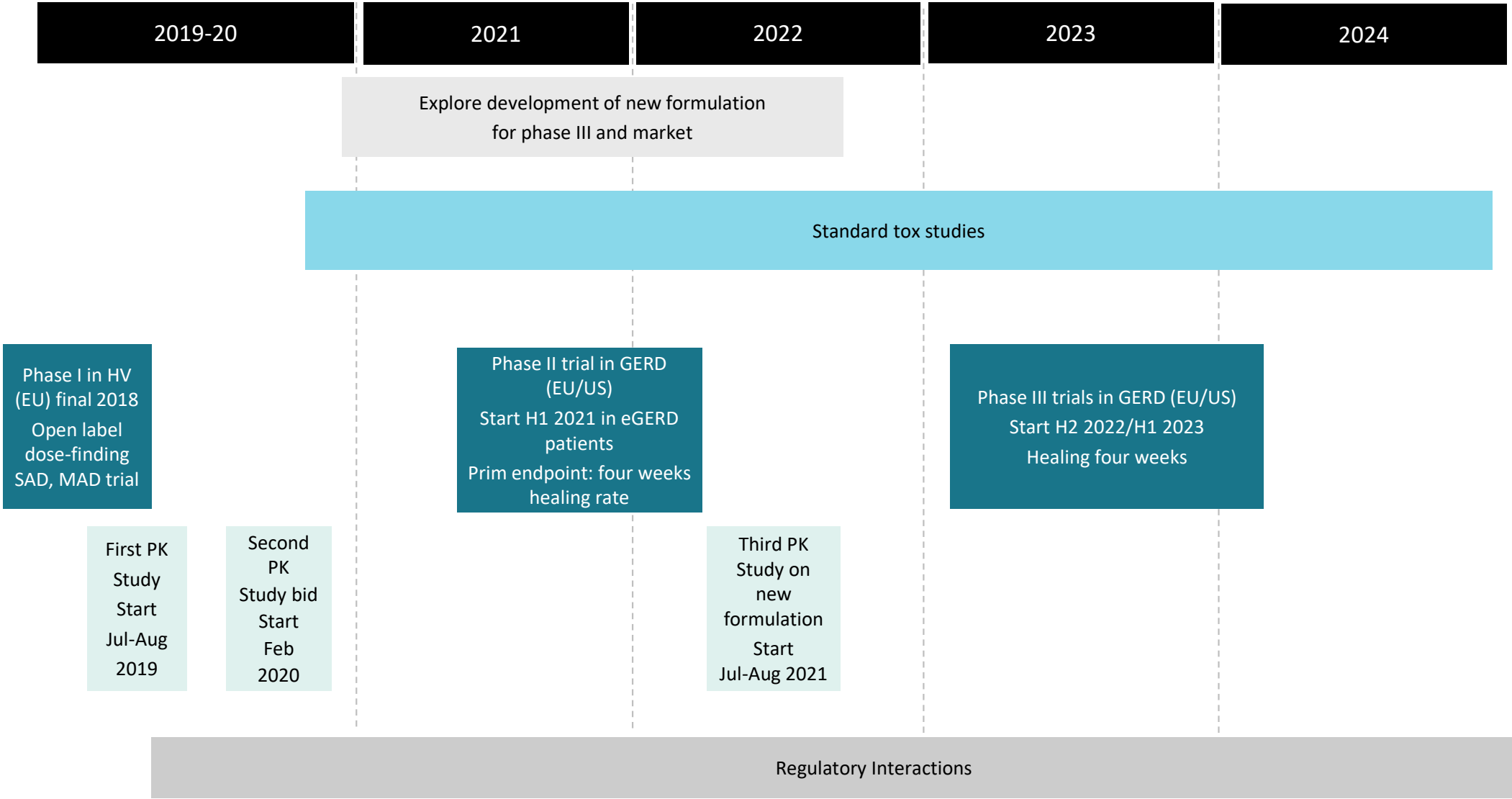
Phase II design

Primary objective	• The primary objective of the study is to support dose selection of *linaprazan glurate* for Phase 3 studies based on four weeks healing of esophagitis.
Secondary objective	• Evaluate the safety and tolerability of *linaprazan glurate* compared to standard PPI • Compare the symptom response after four weeks with three dose levels of *linaprazan glurate* compared to standard PPI • Model the optimal dose of *linaprazan glurate* using healing rates and PK data in patients treated with *linaprazan glurate*
Description	• A multi-center, randomised, double-blind, active comparator-controlled, parallel group design study with four arms conducted in patients with reflux esophagitis grade C and D and patients still unhealed after four weeks standard treatment healing course with PPI
Endpoints	• The primary endpoint is the healing rates of eGERD after four weeks treatment • Evaluate the safety and tolerability of *linaprazan glurate* • Symptom response during and after four weeks • Model the optimal dose of *linaprazan glurate* for phase 3
# of patients	• At least 200 evaluable patients • Approximately 60 sites • Approximately 10 countries in Europe and US
Timetable	• FPFV[1)] in H2 2021 and LPLV[2)] H1 2022



Note: 1) FPFV = First patient first visit. 2) LPLV = Last patient last visit

Clinical development plan



Linaprazan glurate – a novel approach to eGERD

1 Product candidate

- **linaprazan glurate is a Potassium-Competitive Acid Blocker (P-CAB) and a prodrug of linaprazan**
- **Best in class with favourable safety and pharmacokinetic profile**
- **linaprazan glurate's gastric acid control has so far shown to be superior to current medication**

2 Target segment

- **Niche indication severe erosive GERD (Grades C+D) and patients with incomplete PPI response who are still unhealed**
- **Estimated 18.5 million people in target population based on epidemiological data**
- **Market potential: 5-10 BUSD**

3 Clinical development

- **Phase I initiated in February 2017 and final study report in February 2018**
- **Phase II was initiated in H2 2021 within a de-risked clinical development programme (proven mode of action of linaprazan, linear response and excellent biomarker results from phase I predicting clinical outcome)**
- **Phase III to be initiated in 2022/23 within a de-risked clinical development programme**

4 Commercial rights and potential add-ons

- **Cinclus Pharma owns the worldwide commercial rights**
- **Attractive potential additional indications: on-demand treatment of GERD, *H.pylori* eradication, nocturnal GERD symptoms and bleeding ulcer**

Cinclus
PHARMA