GESTHERA

Pregnancy Therapeutics

Drug Development, With Multiple Lives in Mind

Because every mother and baby deserves better options

www.gesthera.com

Table Of Content

Company & Drug Product

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Executive Summary

Gesthera & GST001

- **Gesthera** secured rights on **GST001** in 2025
- GST001 is a PGF2α receptor antagonist developed in **Preterm Labor**

CLINICAL OPPORTUNITY

- High unmet medical needs in obstetrics
- Positive, clinically meaningful Phase 2a POC results in Preterm Labor
- Favorable maternal, fetal and neonatal safety

PRODUCT OPPORTUNITY

- First-in-class, oral PGF2α antagonist with validated MoA
- Superior benefit-risk profile vs standards of care
- Patent protection through 2037-2041, with extension potential

EXECUTION OPPORTUNITY

- Experienced Women's Health Team (> 80 years combined)
- Prior successful Phase 2a execution in preterm labor
- Proven ability to recruit in acute obstetrics settings

INVESTMENT OPPORTUNITY

- Capital-efficient in-licensing structure
- Large, underserved market opportunity (US/EU > $2bn)
- Clear path to value inflection and potential exit within < 3 years

Agile & highly experienced team

With 80+ years of experience in women's health

Fabien de Ladonchamps

President & Co-Founder

25+ years in corporate functions
$450m raised, from Series A to Nasdaq IPO
BSc Finance & Administration

Obseva · addex Therapeutics

Michel Brethous

Head of Clinical Development & Co-Founder

25+ years in clinical development
Former lead of GST001 clinical trials
MSc Molecular Biology & Pharmacology

Obseva · Roche · MERCK

Advisors

Medical Advisor
Ernest Loumaye, MD, PhD

Regulatory Advisor
P.M., BSc

CMC Advisor
J.A., PhD

Scientific Advisor
Jean-Pierre Gotteland, PhD

Intellectual Property
Clark & Elbing, U.S.A.

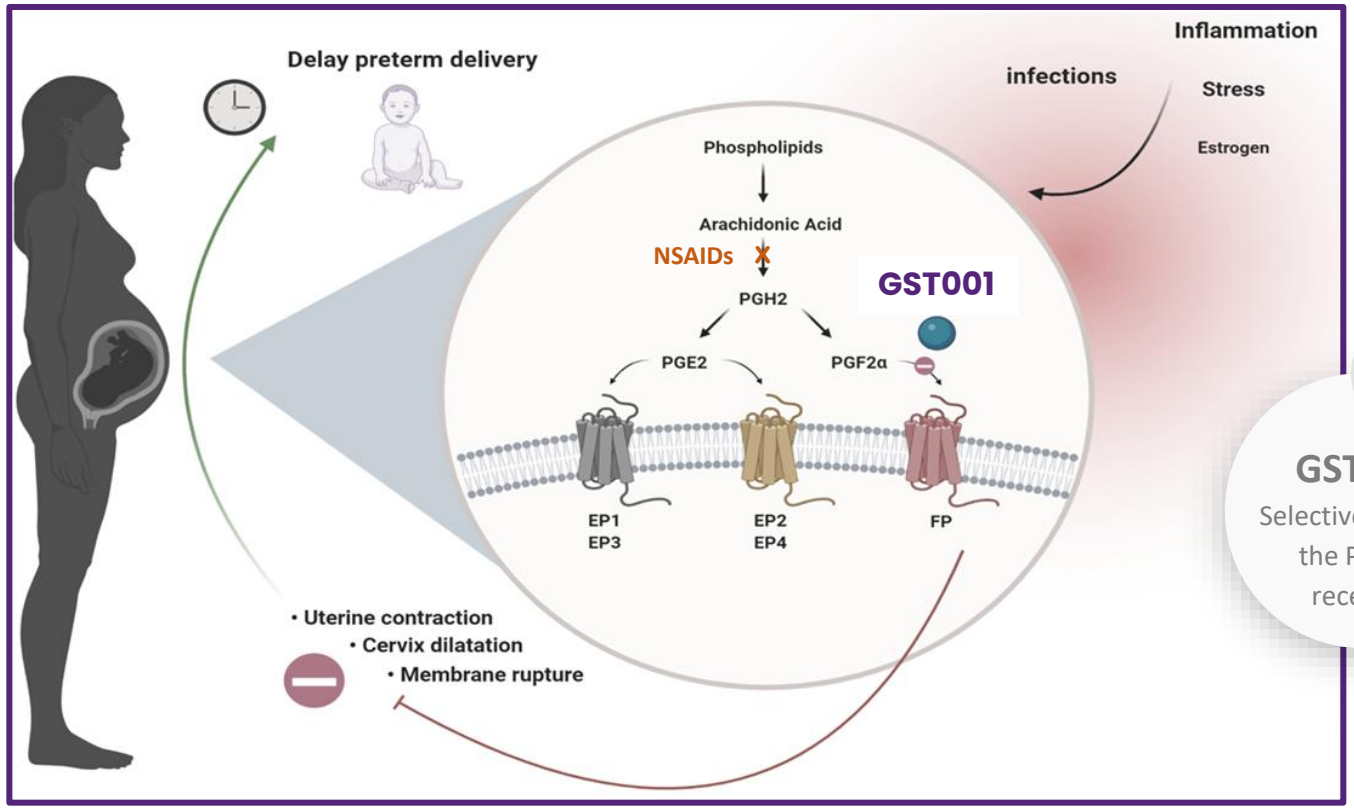
& **KOL engagement** with input received from experienced maternal-fetal medicine specialists

all previously involved in GST001 development

GST001

Mechanism of Action

GST001 is a novel, **orally available**, small molecule, **selective** prostaglandin F2α receptor antagonist which is being developed for the treatment of spontaneous preterm labor.



Prostaglandin inhibitors (NSAIDs) had the best combination of tolerance and delayed delivery in a meta-analysis* but are associated with fœtal side effects.

GST001
Selectively blocks the $PGF2_{2\alpha}$ receptor

GST001 selectivity offers a **targeted approach to reduce inflammation and uterine contractions while minimizing the fetal risks** associated with non-specific NSAIDs, like premature ductus arteriosus closure, oligohydramnios, neonatal renal dysfunction, necrotizing enterocolitis, intraventricular hemorrhage.

** Tocolytic Therapy. Haas et al, Obstet Gynecol 2009; 113:585–94.*

GST001

Potential & target indications

GST001 capacity to reduce inflammation and uterine contractions makes it a valid candidate for the treatment of several indications in women's health.

Target Indications (Highest Unmet Medical Needs)

- **Threatened spontaneous preterm labor (treatment)**
  Threatened preterm labor is a clinical diagnosis indicating a risk of preterm delivery before 37 weeks of gestation, based on symptoms and signs, but without active labor progression.
- **Recurrence of preterm labor (prevention)**
  Risk factors: 1. previous PTB (strongest predictor), 2. multiple gestation, 3. cervical or uterine factors (short cervix, cervical insufficiency, uterine abnormalities, previous cervical surgery), 4. Infections, 5. placental problems, 6. certain maternal conditions (hypertension, diabetes, preeclampsia…), 7. Demographic and socioeconomic factors (extremes of maternal ages, race/ethnicity, low socioeconomic status, stress, depression), 8. Lifestyle (smoking, substance abuse, inadequate weight, short interpregnancy interval).
- **Increase of success rate of embryo implantation procedures in ART(*)**
  Through reduction of pre-implantation peristalsis and contractions without impacting uterine perfusion.
  (*) ART = Assisted Reproductive Technologies.

- **Endometriosis**
  Chronic, estrogen-dependent inflammatory disease characterized by the presence of endometrial-like tissue growing outside the uterine cavity.
- **Adenomyosis**
  Presence of endometrial tissue growing aberrantly within the muscular wall of the uterus resulting in a diffusely enlarged, tender uterus, often accompanied by heavy menstrual bleeding and painful periods.
- **Dysmenorrhea**
  Painful menstruations.

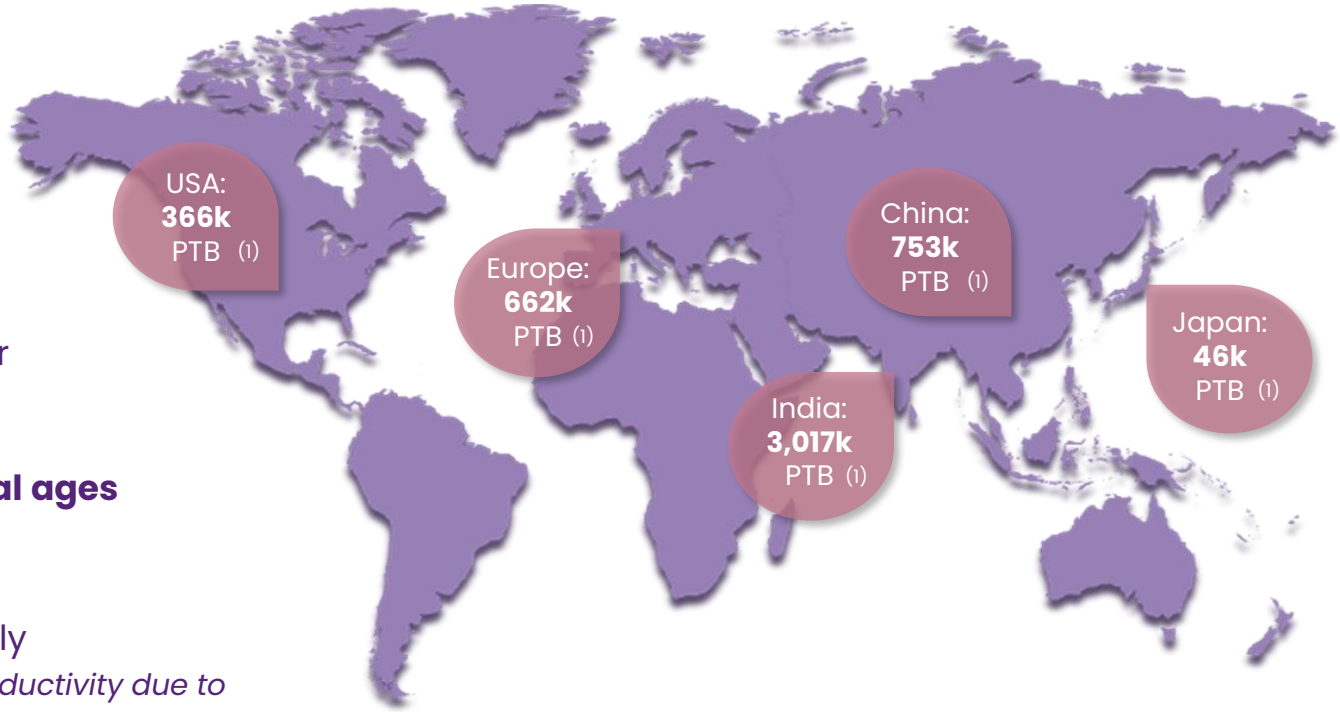
Lead Indication

Preterm Labor

Preterm birth: a major medical and economical burden

- **13.4m PTB in 2020[1], about 10% of all births**
- 50% of PTL patients deliver at term[2,3]

  → **1 PTB patient = 2 PTL patients**
- **Increased morbidity and mortality**:
  PTB complications are the leading cause of death among children under 5 years of age, responsible for approximately **1,000,000 deaths in 2021**[4]
- **Major economic burden, higher at earlier gestational ages**
  - $76k average cost for a preterm infant in the US
  - $604k per survivor born 24wk in the US[5]
  - **Over $25bn** of US prematurity-related costs annually
    (incl. medical care $17.1bn ; delivery care $2.0bn ; loss of productivity due to associated disabilities in adults $4.8bn)[6]



(1) Ohuma E O et al - National, regional, and global estimates of preterm birth in 2020, with trends from 2010: a systematic analysis – The lancet 2023
(2) Slattery M et al. – Preterm delivery – The Lancet 2002
(3) Hyagriv N et al. – Prevention of Preterm Delivery – The New England Journal of Medicine 2007
(4) Born too soon: decade of action on preterm birth. Geneva: World Health Organization 2023
(5) Beam A L et al, Estimates of healthcare spending for preterm and low-birthweight infants in a commercially insured population: 2008-2016, Journal of Perinatology 2020
(6) Waitzman N J et al. - Preterm birth lifetime costs in the United States in 2016: An update. – Seminars in Perinatology 2021
(7) Changes in preterm and extremely preterm birth rates in Japan after the introduction of obstetrical practice guidelines in 2008, Shimano S et al., J Obstet Gynaecol Res. 2023

Preterm Labor

The critical 48-hour window in acute preterm labor

Preterm birth causes[1,2]

- Idiopathic: 45–50%
- PPROM: 30%
- Medically indic.: 15–20%

48-hour[3] prolongation of pregnancy provides a critical window for impact on neonatal outcomes

Allows full effect of corticosteroids on neonatal lung maturity

→ Prematurity associated with respiratory complications due to insufficient lung maturation

→ Corticosteroids used to speed up maturation process

→ Maximum effect occurs ~48+ hours after administration

Allows patient transfer to centers with NICU

Potential to

improve newborn health

& reduce medical costs

	Second Trimester								Third Trimester												
Months of pregnancy	4		5			6			7				8				9				
Gestational age in weeks	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
Preterm birth category	Extremely preterm								Very preterm				Moder. to late pret.								
Proportion of preterm births per category [2]	~5%								~15%				~80%								
Window for tocolysis					~40%[2]																

[1] Zeitlin J et al. - Preterm birth time trends in Europe: a study of 19 countries – BJOG, 2013
[2] Goldenberg RL et al. - Epidemiology and causes of preterm birth. Lancet, 2008
[3] WHO recommendation on tocolytic therapy for improving preterm births outcomes, 2022

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Preterm Labor

Unmet need for an effective and safe tocolytic

Class	Most common maternal side effects	Foetal or newborn side effects	Medication	Route	Status & Use
Oxytocin antagonists	Nausea, headache, dizziness, hot flushes, vomiting, **tachycardia**, **hypotension**, reaction at site of injection, **hyperglycaemia**	**No known adverse effects**	**Atosiban**	**iv.** **Continous/48h**	**Approved (ex-US & Japan)**
Calcium channel blockers	Dizziness, flushing, and **hypotension. Elevation of hepatic transaminases.** **Suppression of heart rate when used with $MgSo_4$**	**No known adverse effects**	**Nifedipine** Nicardipine	**Oral** **Every 6 hours**	**Off-label use**
Nonsteroidal anti-inflammatory drugs (NSAID)	Nausea, esophageal reflux, gastritis, and emesis.	**In utero constriction of ductus arteriosus, olygohydramnios. Necrotizing enterocolitis, and patent ductus arteriosus in newborn.**	**Indomethacin** Sulindac Celecoxib	**Oral** **Every 6 to 8 hours**	**Off-label use** **Not recommended or restricted to early gestational ages**
Beta-adrenergic receptor agonists	**Tachycardia, hypotension**, tremor, palpitations, shortness of breath, chest discomfort, **pulmonary oedema, hypokalemia, hyperglycemia.**	**Tachycardia, hypoglycemia, hyperinsulinism.**	Ritodrine Terbutaline Fenoterol Salbutamol Hexoprenaline	**iv.** **iv.** **sc.** **sc.** **oral**	**Off-label use** **WHO guidance 2022 recommends to stop using this class**
→ Clear need for a new effective and safe tocolytic: GST001					
PGF2a antagonist	Constipation, diarrhoea, flatulence	**No known adverse effects**	GST001	**Oral** **Twice a day**	**- in development -**

Based upon ACOG - Practice Bulletin No171 Management of preterm labor_2016

Current tocolytics used to suppress contractions (e.g. atosiban, nifedipine, indomethacin, ritodrine,)

- Recommended for short-term use (48 h) to allow for corticosteroid administration or in utero transfer
- **All have maternal or neonatal side-effects and limited efficacy**

Atosiban = only drug approved for the treatment of PTL

- Indicated to delay imminent preterm birth
- Authorized in 67 countries (amongst which EU, India, Korea, China, Mexico …), **excluding US and Japan**

Existing Data Package

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Preclinical & Ph 1 Studies

Summary

EFFICACY

01 GST001 **inhibits contractions** induced by PGF2a or oxytocin **in a dose-dependent manner**

02 **Additive effect** of GST001 when administered with atosiban or nifedipine ✓

SAFETY

03 **No safety concerns**, including **no** NSAID-related adverse events (targeted selectivity) **No QTc prolongation**

04 **SAD, MAD** **Food effect** **DDI** with betamethasone, $MgSO_4$, nifedipine, atosiban ✓

Phase 2a: Unlocking recruitment in PTL

Overcoming recruitment barriers through operational & clinical innovation

Industry Challenge

- **The recruitment wall**
  Historically low enrollment in PTL (e.g. Retosiban Ph3: 97/330 in 2.5y & 25/900 in 1.5y)
- **Efficacy and safety barriers**
  First in pregnant-women study with GST001
- **Regulatory landscape**
  Atosiban is the only EU-approved standard of care for PTL

Smart Design

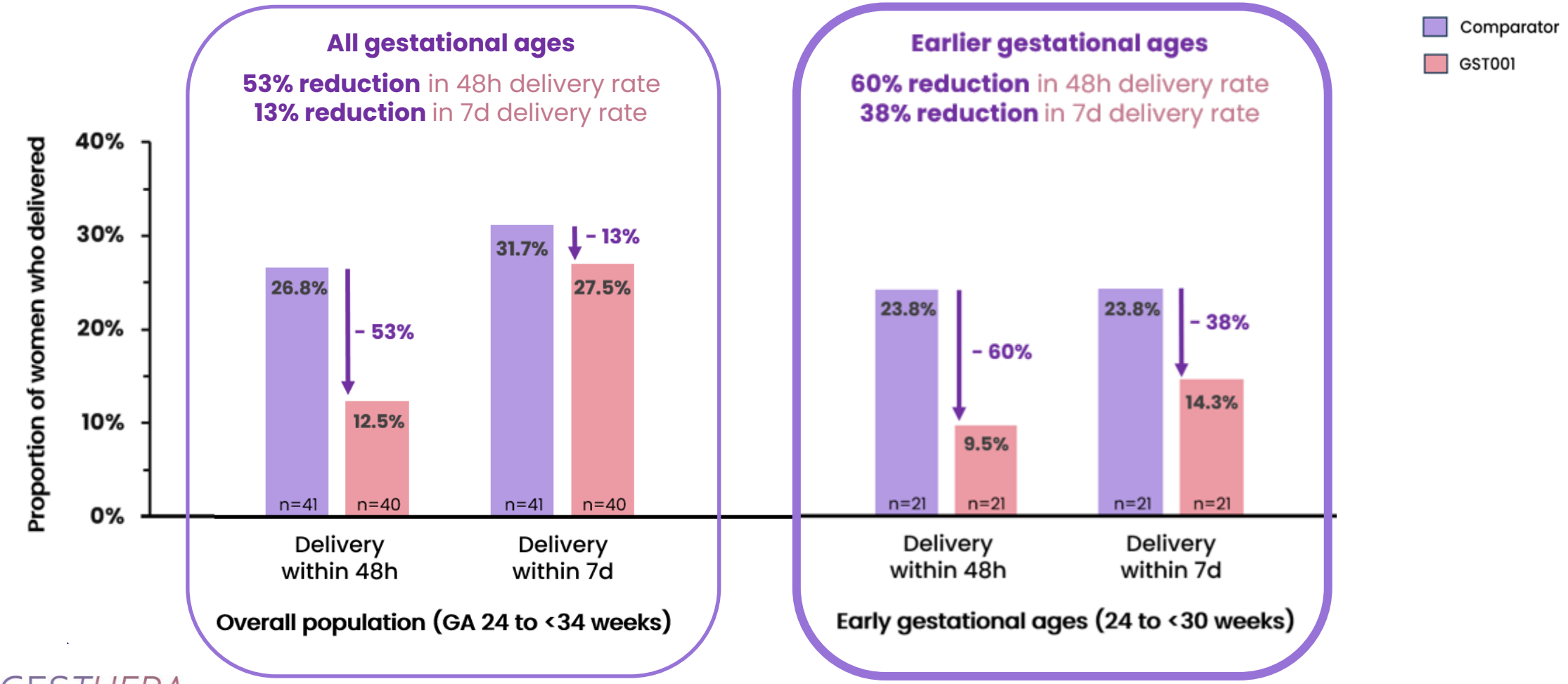
- **Ethically optimized design**
  Add-on therapy design to ensure every subject receives active background therapy, increasing investigator and patient willingness to enroll
- **Adaptive two-part approach**
  Open-label Part A (n=9) to secure safety signals and preliminary efficacy before initiating the double-blind Part B
- **Scientific-led site advocacy**
  On-site scientific briefings to build clinical trust.

Execution Outcomes

- **Achieved swift recruitment**
  115 subjects in 14 months: 1 pat/site/M
- **High site engagement:**
  14/16 initiated sites recruited patients
- **Very low screen failure rate:** 7/122
- **Excellent treatment compliance**
  >98% in both arms.

Phase 2a – Efficacy

Delivery within 48 hours and 7 days in singletons



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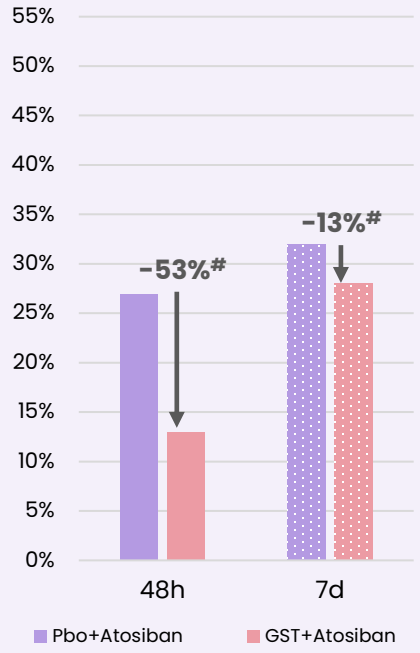
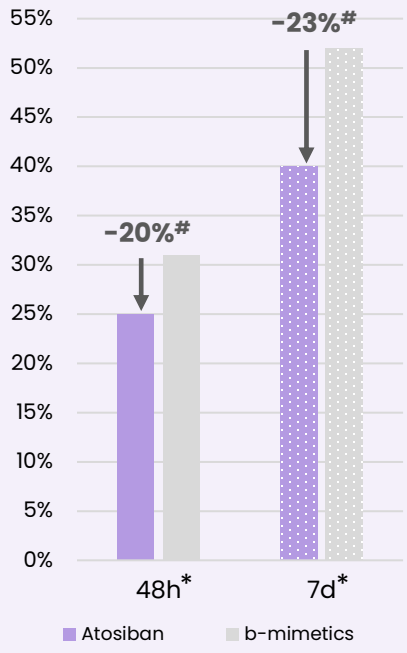
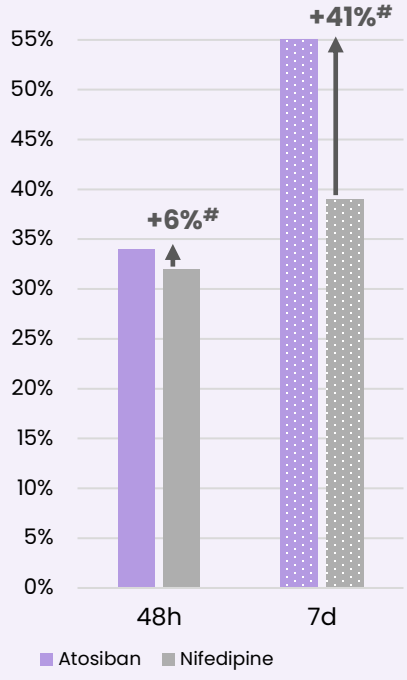
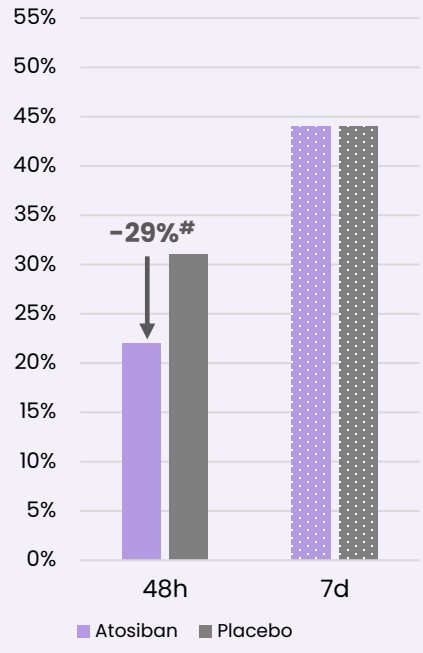
Comparative Efficacy (Relative difference)

Delivery within 48 hours and within 7 days

	GST001 Ph2a PoC GST001+ato vs Pbo+ato	CAP-001 studies Atosiban vs β-mimetics	APOSTEL 3 Atosiban vs Nifedip	APOSTEL 8 Atosiban vs placebo
Main inclusion criteria	• GA 24 to <34 wks • ≥4 contractions / 30 min • Cerv dil 1-4 cm • Cerv L ≤25mm or cerv ch or +fFN	• GA 24 to <34 wks • ≥ 4 contractions / 30 min • Cerv dil 1-3 cm • Cerv eff ≥50%	• GA 25 to <34 wks • ≥ 3 contractions / 30 min • Cerv L 11–30 mm • +fFN or RM	• GA 30 to <34 wks • Uterine contractions • Cerv length <15mm or • Cerv length 15-30 mm & +fFN or RM
Sample size	113 patients	681 patients (3 Ph3)	510 Patients	755 Patients
Key endpoints: Delivery within 48h Delivery within 7d				

* Time to failure within 48h or 7d (defined as the time from the start of study therapy to delivery or first rescue tocolytic)
+fFN: positive fetal fibronectin test / RM: Ruptured membranes / # Relative difference

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Intellectual Property

Patent Portfolio Global Overview

Patent coverage (pending & granted):

. To 2037: Brazil, Eurasia, Indonesia, Israel, India, Mexico, South Korea, Singapore, Ukraine, South Africa

. To 2041: USA, Europe, Australia, Hong-Kong, Japan, Canada, China

Patent Family		Scope	Expiry date (*)
Family I	CoM, Use	Chemical genus of compounds encompassing GST001, as well as methods of using same	Exp. : 11Dec2024
Family II	CoM, Use	Composition-of-matter claims protecting GST001 as an NCE, including any salt thereof, as well as methods of using same	Exp. : 04Jan2037
Family III	Use	Claims directed to […] GST001 active moiety	Exp.: 04Jan2037
Family IV	Use	Claims directed to dosing regimens for administration of GST001 […]	Exp.: 14May2039
Family V	Use	Claims directed to dosing regimens for administration of GST001 […]	Exp.: 16Nov2041
New patent	Use	2026-2028: New formulation (new formulation work)	Exp.: 2046-2048
New patent	Use	2028: New dosing regimen (after phase 2 conf.)	Exp.: 2048
New patent	Use	2031: New indications (ART & Prevention of PTL)	Exp.: 2051

(*) Expiry dates do not take into account any PTE/SPC (Patent Term Extension / Supplementary Protection Certificate), and regional market exclusivity are to be considered on top of existing and future patent protection (10 years in Europe, 5 to 7 years in the U.S.)

Development Strategy & Financials

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Development Plan

Optimized Strategy in Preterm Labor

#1 GST001 as Monotherapy

instead of add-on

Operationally

→ Streamlines clinical development
→ One program fits all
→ Shortens time to market

Commercially

→ Enables broader use of GST001
→ Grants access to U.S. and Japanese markets
→ Better commercial positioning

#2 Target Earlier GA (< 32 weeks)

instead of all GA (< 34 weeks)

Medically

→ Highest unmet medical need
→ Greater impact for a prolonged treatment
→ Greater inflammatory involvement

Operationally

→ Enriches the patient population
→ Enables Orphan Drug Designation requests

Commercially

→ Better positioning for access to premium pricing

Development Plan

Overview

Concept Phase

GST001 potential

NSAIDs efficacy with a better safety

Possibility to treat over 48 hours

Proof of Concept Phase

Valid feasibility & Proof of Concept

Demonstrate initial efficacy and safety

and ability to overcome recruitment barrier

NOW

2026-2028 Value Inflection Phase

SERIES A, €5-10m

Phase 2a monotherapy Read-Out mid-2028

vs nifedipine, in earlier GA (<32wk)

FDA written feedback 1Q27

Decision point / U.S. development

2028-2032 Pivotal Phase

Phase 2b/3 program

Earlier gestational ages (<32wkGA)

Extended treatment duration

2032+ Value Optimization Phase

Commercial readiness

MAA & NDA filings in acute PTL

Label expansion

Later gestational ages 32wk+GA

CONTACT US

The Gesthera team looks forward to connecting with you to discuss any business opportunity!

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