GB-0895, a high-affinity anti-TSLP mAb, demonstrates prolonged half-life and sustained pharmacological activity supporting every 6-month dosing in asthma

Generate:Biomedicines℠

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Aims of Study

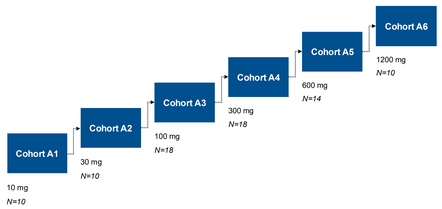
- Thymic stromal lymphopoietin (TSLP) is a validated target in asthma that drives lung inflammation
- Generate:Biomedicines developed GB-0895, a next generation, anti-TSLP mAb with
  - ~20-fold higher affinity for TSLP compared to tezepelumab
  - YTE Fc modifications for extended half-life
- Here we present interim data from an ongoing phase 1 randomized, placebo-controlled trial in participants with mild to moderate asthma
  - The study aimed to characterize safety, pharmacokinetics, and pharmacodynamics of GB-0895
  - All safety data are summarized by blinded cohorts
  - PK/PD data are presented in aggregate across active doses versus placebo to maintain trial integrity
  - Only data from the Part A (single ascending dose) are presented

Study Design

GB-0895 Phase 1, Double Blind, Placebo-Controlled Clinical Trial in Mild-to-Moderate Asthma Patients

- Mild-to-moderate asthma patients
- Subcutaneous administration
- Sentinels 1:1 randomization; Remainder 3:1 randomization
- Blood eosinophils ≥ 150 cells/µL
- Asthma controlled on as-needed SABA and stable low-to-moderate dose of ICS or stable low-to-moderate dose of ICS/LABA combination
- FEV1 ≥ 60% of predicted normal value
- ACT > 19

Part A: Single-ascending dose (SAD) | N=80



Conducted in the United Kingdom, Germany, and USA at 8 sites

MAD portion of study enrolled an additional 16 participants

Results

Baseline characteristics are consistent across cohorts of our Ph 1 study

	Cohort A1 10mg (N=10)	Cohort A2 30mg (N=10)	Cohort A3 100mg (N=18)	Cohort A4 300mg (N=18)	Cohort A5 600mg (N=14)	Cohort A6 1200mg (N=10)	Total (N=80)
Age, *years* Mean (SD)	40 (12)	42 (12)	40 (13)	41 (13)	36 (13)	41 (11)	**40 (13)**
Sex, M/F %	70/30	50/50	72/28	56/44	50/50	70/30	**61/39**
Baseline Eos, *cells/uL* Mean (SD)	255 (123)	231 (59)	276 (166)	269 (110)	338 (136)	244 (100)	**273 (126)**
FEV1, *Predicted %* Mean (SD)	87.5 (9.9)	88.0 (19.8)	85.8 (9.2)	90.3 (11.9)	85.9 (11.1)	92.6 (10.7)	**88.2 (12.0)**
FeNO, *PPB* Mean (SD)	37.7 (12.4)	25.8 (19.8)	34.8 (33.1)	32.7 (24.6)	33.6 (13.6)	28.8 (27.8)	**32.6 (23.8)**
ACT Score Mean (SD)	21.7 (1.7)	23.7 (1.3)	23.2 (1.7)	22.6 (1.7)	23.0 (1.6)	22.5 (1.5)	**22.8 (1.7)**

Each cohort includes randomized active and placebo participants; presented blinded to preserve trial integrity

GB-0895 has been well-tolerated

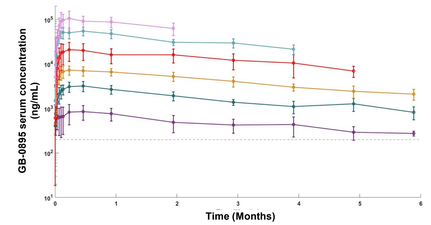
Safety data are summarized by blinded cohorts including active and placebo subjects

- 80 subjects received a single dose of GB-0895 or placebo; followed ≥ 26 weeks
- Most common TEAEs by PT (≥10% incidence in all treatment groups): nasopharyngitis, rhinitis, headache
- 3 SAEs reported: Occurred in cohort A3: 100mg (n=2) and cohort A4: 300mg (n=1)
  - All Grade 3, Not Related to study drug
- All other TEAEs mild-moderate in severity (Grade 1-2); ISR all Grade 1
- No trend in increasing incidence or severity of TEAEs vs dose

Subject Incidence of:	Cohort A1 (10mg) N=10	Cohort A2 (30mg) N=10	Cohort A3 (100mg) N=18	Cohort A4 (300mg) N=18	Cohort A5 (600mg) N=14	Cohort A6 (1200mg) N=10	Total N=80
Any TEAE	9 (90.0%)	8 (80.0%)	18 (100%)	17 (94.4%)	12 (85.7%)	9 (90.0%)	**73 (91.3%)**
Any ISR*	1 (10.0%)	0 (0.0%)	1 (5.6%)	3 (16.7%)	4 (28.6%)	1 (10.0%)	**10 (12.5%)**

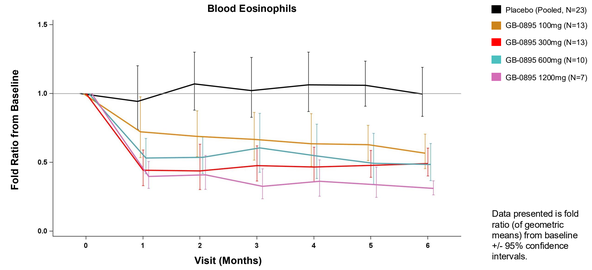
*ISRs include AEs reported under the MedDRA High Level Term 'Injection Site Reactions'
TEAE = Treatment emergent adverse event; ISR = Injection Site Reaction; SAE = Serious adverse event, PT = Preferred Term

Clinical PK data for GB-0895 show half-life of ~89 days



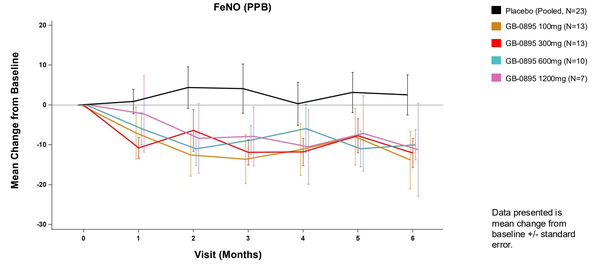
- **Dose proportional PK**
- **No evidence of target mediated drug disposition**
- **No evidence of ADA impacting GB-0895 half-life**

A single subcutaneous administration of GB-0895 leads to sustained reductions in blood eosinophils for 6 months at 100-1200 mg doses



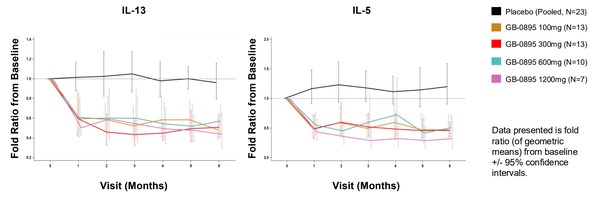
Data presented is fold ratio (of geometric means) from baseline +/- 95% confidence intervals.

A single subcutaneous administration of GB-0895 leads to sustained reductions in FeNO for 6 months at 100-1200 mg doses



Data presented is mean change from baseline +/- standard error.

A single subcutaneous administration of GB-0895 leads to sustained reductions in IL-13 and IL-5 for 6 months at 100-1200 mg doses



Data presented is fold ratio (of geometric means) from baseline +/- 95% confidence intervals.

Conclusions

- GB-0895 has been well tolerated
- GB-0895 demonstrates dose-proportional pharmacokinetics with a half-life of ~89 days
- A single subcutaneous dose provides 6 months of pharmacologic activity, as evidenced by reductions in EOS, FeNO, IL-5, and IL-13
- Broad anti-inflammatory activity of GB-0895 is consistent with the mechanism of action as previously reported with tezepelumab
- These data support dosing of GB-0895 subcutaneously every 6-months for severe asthma

PHASE 3 TRIALS OF GB-0895 EXPECTED TO INITIATE IN Q4 2025

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