Inhaled Molgramostim Improves Pulmonary Gas Exchange, Quality of Life, and Exercise Capacity in Patients with Autoimmune Pulmonary Alveolar Proteinosis (aPAP)

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Disclosures

- FB received speaker and advisor honoraria from Savara Inc.

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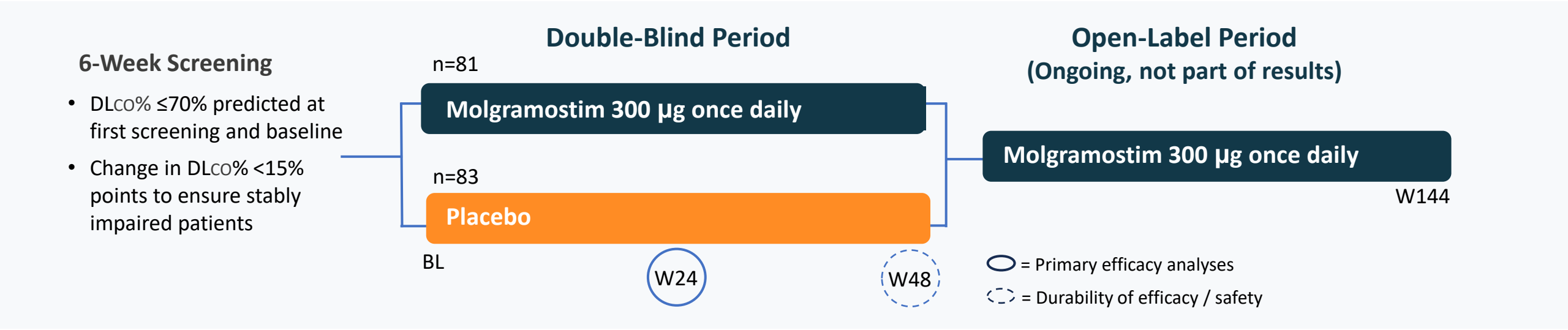
Background and IMPALA-2 Study Design

- Autoimmune pulmonary alveolar proteinosis (aPAP) is a rare lung disease caused by autoantibodies to GM-CSF
- Molgramostim inhalation solution (molgramostim) is a non-glycosylated form of recombinant human GM-CSF
- Molgramostim is being studied for the treatment of autoimmune PAP in a randomized, double-blind, placebo-controlled Phase 3 clinical trial conducted at 43 clinical trial sites across 16 countries



Primary Endpoint

- Change from baseline in DLCO% at W24

Secondary Endpoints

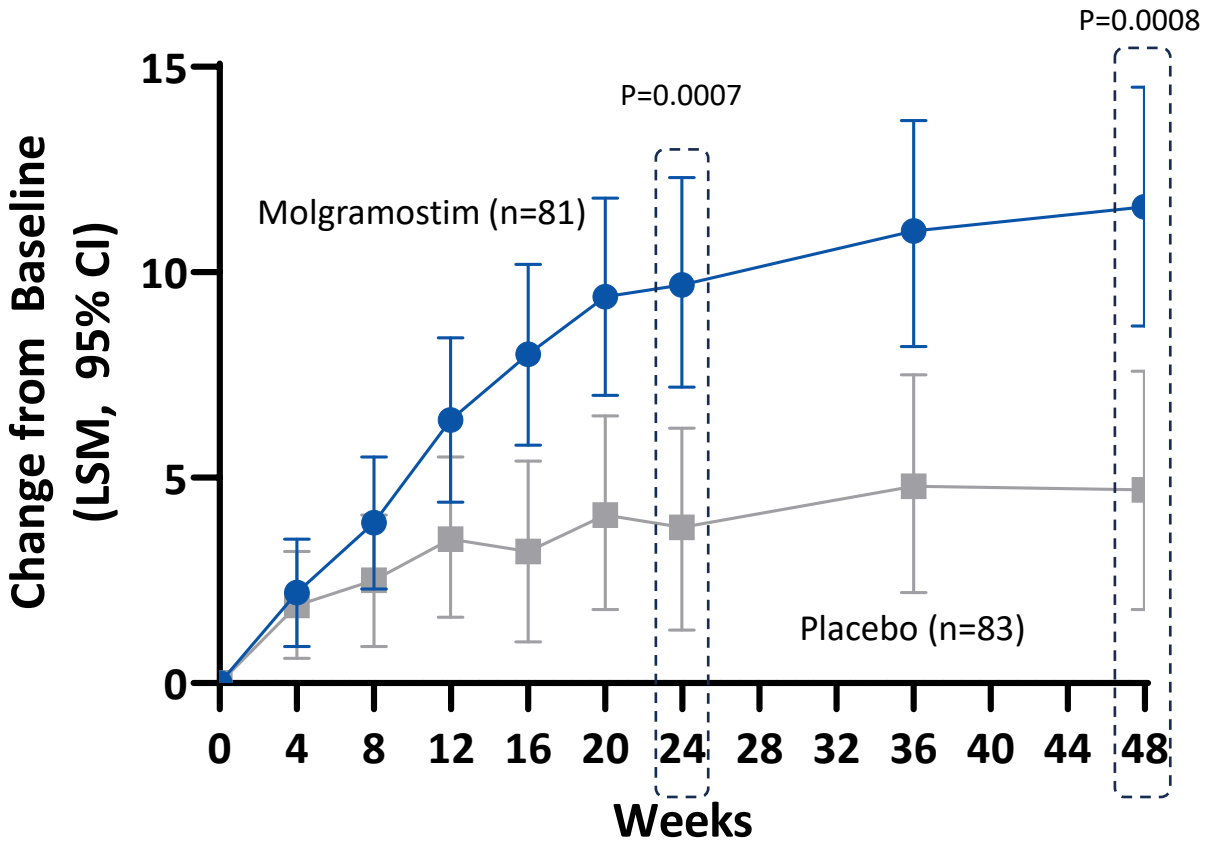
Change from baseline in:

- DLCO% at W48
- SGRQ Total Score at W24 and W48
- SGRQ Activity Score at W24 and W48
- Exercise capacity at W24 and W48

BL, baseline; DLCO%, hemoglobin-adjusted percent predicted diffusing capacity of the lungs for carbon monoxide; SGRQ, St. George's Respiratory Questionnaire; W, week.

IMPALA-2 Results: Molgramostim Improved Pulmonary Gas Transfer

DLco%



	LSM Change from Baseline	Between-group LSM difference*	P-value
Week 24	Mol: 9.8 Pbo: 3.8	6.0	0.0007
Week 48	Mol: 11.6 Pbo: 4.7	6.9	0.0008

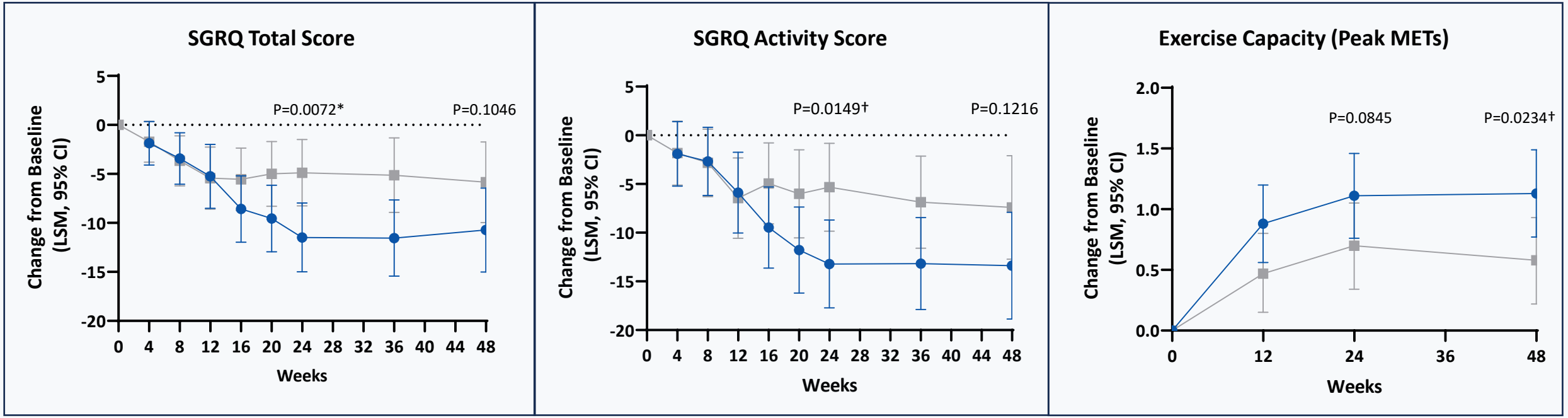
Absolute mean DLco% increased from 52.6 at Baseline to 64.8 at 48 weeks in the molgramostim group and from 52.6 to 56.5 in the placebo group

*Mean change from baseline compared with placebo. P-values are for difference in LSM compared with placebo and met the threshold required in the pre-specified hierarchical testing procedure to control the overall Type 1 error rate at 0.05.

CI, confidence interval; DLco%, hemoglobin-adjusted percent predicted diffusing capacity of the lungs for carbon monoxide; LSM, least squares mean; Mol, molgramostim; Pbo, placebo.

IMPALA-2 Results: Molgramostim Improved Health-Related Quality of Life and Exercise Capacity

Secondary Endpoints



*Mean change from baseline compared with placebo. P-values are for difference in LSM compared with placebo and met the threshold required in the pre-specified hierarchical testing procedure to control the overall Type 1 error rate at 0.05. †P-value nominally significant: P-value ≤0.05 but did not meet the p-value threshold required in the pre-specified hierarchical testing procedure.
CI, confidence interval; LSM, least squares mean; METs, metabolic equivalents; SGRQ, St. George's Respiratory Questionnaire.

IMPALA-2 Results: Molgramostim Was Well Tolerated

Adverse events during the double-blind treatment period

Treatment-Emergent Adverse Event	Molgramostim N=81 n (%)	Placebo N=83 n (%)
Any adverse event	69 (85)	71 (86)
Severe adverse events	13 (16)	16 (19)
Treatment related	20 (25)	16 (19)
Serious adverse events	14 (17)	20 (24)
Treatment related*	1 (1)	0
Leading to death	0	0
Leading to drug discontinuation	2 (2)	1 (1)
Special interest	9 (11)	6 (7)
Serious special interest	0	1 (1)

Adverse events in >10% of patients in any treatment arm during the double-blind treatment period

Treatment-Emergent Adverse Event	Molgramostim N=81 n (%)	Placebo N=83 n (%)
Most common		
COVID-19	18 (22)	8 (10)
Cough	17 (21)	18 (22)
Pyrexia	11 (14)	9 (11)
Nasopharyngitis	11 (14)	7 (8)
Arthralgia	9 (11)	7 (8)
Headache	9 (11)	7 (8)
Diarrhea	9 (11)	2 (2)
Alveolar proteinosis	4 (5)	12 (14)

98% of Patients Completed the Double-Blind Treatment Period

*Serious adverse event of delusions resulting in psychiatric hospitalization in patient with a past medical history of seizure disorder treated with levetiracetam, which is labeled for psychiatric side effects, including delusions; the event was assessed as possibly related to study drug by the investigator.

IMPALA-2: Conclusions

- Largest and longest controlled trial of inhaled GM-CSF therapy for autoimmune PAP ever conducted
- Met its primary endpoint; statistically significant improvement in DL_{CO}% at 24 weeks, which was maintained at 48 weeks
- Improvements in multiple secondary endpoints
  - Pulmonary gas transfer
  - Quality of life
  - Exercise capacity
- Molgramostim was well-tolerated with a favorable risk-benefit profile
  - 98% of patients completed the entire blinded treatment period
  - 100% of patients who completed the double-blind period elected to continue treatment in the open-label period