DT120 (Lysergide) Safety Profile From Phase 1 and Phase 2 Clinical Studies

Poster 198

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Background

- Lysergic acid diethylamide (LSD) is a semisynthetic psychedelic drug derived from the ergoline family[1]
- Preclinical and clinical evidence shows that LSD has low physiological toxicity and an acceptable safety profile when used in a clinical setting[2-4]
- DT120 (lysergide tartrate; MM120) is a novel drug compound under development by Definium Therapeutics for treatment of generalized anxiety disorder (GAD) and major depressive disorder (MDD)
- DT120 at a single 100-µg dose demonstrated rapid symptom relief, better efficacy than standard of care for GAD, durability of up to 12 weeks, and a favorable tolerability profile[5]
- The safety analysis presented here was performed according to current United States Food and Drug Administration guidelines regarding psychedelics[6]

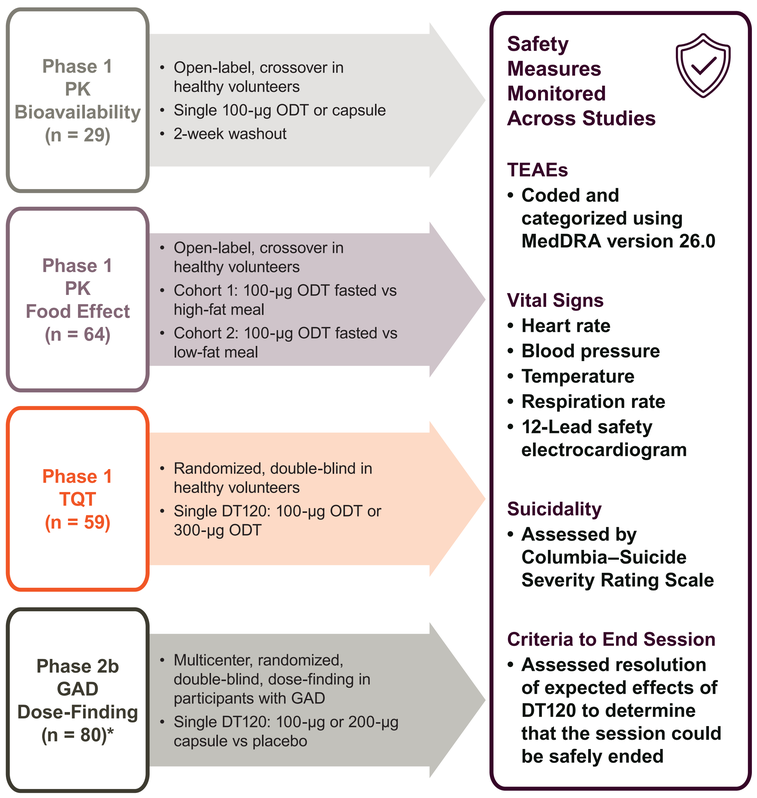
Objective

- To characterize the safety of a single 100-µg, 200-µg, or 300-µg DT120 dose across 4 studies

Methods

- Safety data were derived from 4 clinical studies: the phase 1 pharmacokinetic (PK) bioavailability study, the phase 1 PK food effect study, the phase 1 thorough QT (TQT) study, and the phase 2b GAD dose-finding study (**Figure 1**)

Figure 1. Overview of Studies Used for Safety Analysis



*n values represent participants who received the shown doses of DT120.
GAD, generalized anxiety disorder; MedDRA, Medical Dictionary for Regulatory Activities; ODT, orally disintegrating tablet; PK, pharmacokinetic; TEAE, treatment-emergent adverse event; TQT, thorough QT.

- Treatment-emergent adverse events (TEAEs) were categorized by timing: dosing day and non-dosing days
- Predetermined safety criteria were used to assess readiness to end the dosing session, such as orientation to person, place, and time; resolution of cognitive, perceptual, and emotional effects; and no evidence of suicidal ideation

Results

- Across all 4 studies, there were no treatment-related serious adverse events (AEs), hallucinogen persisting perception disorder, or deaths after treatment with DT120
- Similarly, there was no worsening of preexisting passive suicidal ideation, no active suicidal ideation or behaviors, and no evidence of session-induced suicidal ideation
- Changes in vital signs were not clinically significant
- Overall, the majority of TEAEs were mild to moderate in severity and were consistent with the pharmacodynamic profile of DT120 (**Tables 1** and **2**)
- At all dose levels, the majority of TEAEs occurred on dosing day: 100 µg (1610/1734, 92.8%), 200 µg (227/290, 78.3%), and 300 µg (314/325, 96.6%; **Figure 2**)
  - More participants had post-dose AEs with the 200-µg dose, which had a 12-week follow-up period, than with the 300-µg dose, which had an 8-day follow-up period
- DT120 was not shown to prolong the QT interval

Table 1. Overview of TEAEs in the Phase 1 and 2b Studies

	Phase 1 PK bioavailability study D120 ODT (n = 29)	Phase 1 food effect study		Phase 1 TQT study DT120 ODT (n = 58)	Phase 2b GAD study overall (n = 80)
		DT120 ODT + high-fat meal (n = 31)	DT120 ODT + low-fat meal (n = 28)		
Any TEAE	25 (86.2)	31 (100.0)	28 (100.0)	57 (98.3)	79 (98.8)
TEAE leading to treatment withdrawal	0	1 (3.2)	2 (7.1)	0	1 (1.3)
Severity					
Mild	15 (51.7)	24 (77.4)	22 (78.6)	27 (46.6)	27 (33.8)
Moderate	9 (31.0)	7 (22.6)	5 (17.9)	27 (46.6)	51 (63.8)
Severe	1 (3.4)	0	1 (3.6)	3 (5.2)	1 (1.3)
Any related TEAE	25 (86.2)	31 (100.0)	28 (100.0)	57 (98.3)	78 (97.5)

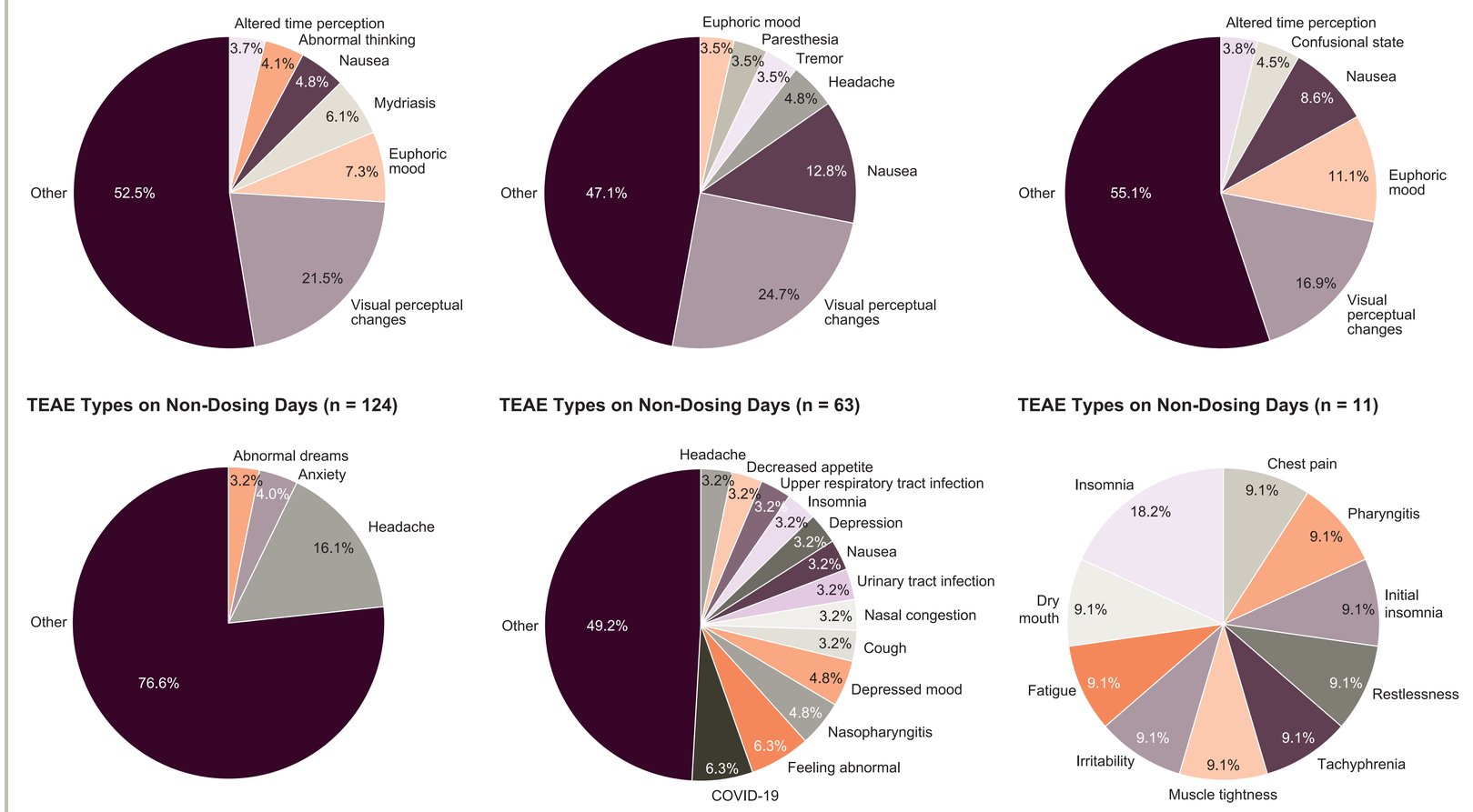
Data presented as n (%).
GAD, generalized anxiety disorder; ODT, orally disintegrating tablet; PK, pharmacokinetic; TEAE, treatment-emergent adverse event; TQT, thorough QT.

Table 2. Overview of TEAEs in the Phase 2b Study

	Placebo (n = 39)	DT120 100 µg (n = 40)	DT120 200 µg (n = 40)
Any TEAE	22 (56.4)	39 (97.5)	40 (100.0)
TEAE leading to study withdrawal	0	1 (2.5)	0
Relationship to study drug			
Related	16 (41.0)	38 (95.0)	40 (100.0)
Not related	6 (15.4)	1 (2.5)	0
Severity			
Mild	12 (30.8)	15 (37.5)	12 (30.0)
Moderate	10 (25.6)	23 (57.5)	28 (70.0)
Severe	0	1 (2.5)	0

Data presented as n (%).
TEAE, treatment-emergent adverse event.

Figure 2. TEAE Occurrence on Dosing Day and Non-Dosing Day Across All 4 Studies



N represents the total number of participants who received the specified DT120 dose; n represents the number of TEAEs. Data are presented as percentages of n.
COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event.

Conclusions

Across 4 studies (226 participants), a single administration of DT120 100 µg, 200 µg, or 300 µg was characterized by the following:

- Transient clinically significant perceptual, affective, and emotional effects that primarily occurred on dosing day
- Clinically insignificant physiological effects

Dose increases beyond 100 µg showed similar AE profiles with no observed increased physiological or psychological safety risks

These findings demonstrate a consistent safety profile across studies, supporting further clinical evaluation of DT120

References

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