

# Safety of INM-755

**Conclusion:** Excellent safety profile in preclinical studies supports human clinical testing for up to 28 days

Safety Studies	Good Outcome
<b>Outcome: Data support starting human studies</b>	
Cardiac safety	✓
CNS function	✓
Respiratory function	✓
Topical 28-day safety	✓
Systemic 28-day safety	✓
Genotoxicity	✓
Phototoxicity	✓
Ocular irritation	✓
Skin sensitization	✓

Pharmacology Study for Central Nervous System Effects
<b>Outcome: No adverse effects observed</b>
Subcutaneous injection of drug in rats with high dose giving <b>more than 10,000 times the plasma concentration</b> expected after topical dosing in humans
Observations at 1, 2, 4, 5, and 8 hr in home cage, in hand, or in arena
<b>108 aspects</b> of behaviour, posture, gait, and movement evaluated
<ul style="list-style-type: none"> <li>• Body temperature and respiration (9 qualities)</li> <li>• Behaviour (29 qualities) <ul style="list-style-type: none"> <li>○ Stereotypic behaviour (8 qualities)</li> <li>○ Aggressiveness, Vocalization, Alertness, Reactivity to handling</li> <li>○ Other behaviour (17 qualities)</li> </ul> </li> <li>• Body tone, posture, and tail position (11 qualities)</li> <li>• Gait (12 qualities)</li> <li>• Activity and uncontrollable movements (8 qualities)</li> <li>• Eye movement, skin, fur and general appearance (13 qualities)</li> <li>• Secretions &amp; excretions (8 qualities)</li> <li>• Elicited responses (14 qualities)</li> <li>• Quantified activities in arena (4 qualities)</li> </ul>

## Margins of Safety from 28-day Preclinical Studies for Planned Human Dosing

The *no adverse effect levels* were determined in preclinical studies where the drug was applied either as a cream (local) or injected under the skin (systemic) daily for 28 days. **No adverse effects were observed even at the highest doses.**

Highest preclinical dose tested for:

- local safety was **383 times** the planned clinical dose
- systemic safety was **more than 10,000 times** the planned clinical dose

## Safety of Cream Base (no drug) on Human Skin

### Summary of Local Reactions on Intact Skin Treated with Cream Base (10 mg cream/cm<sup>2</sup> skin)

Local Reaction	Number of Subjects by Severity of Local Reactions			
	Cream Base		Untreated	
	Bandage n=10	No Bandage n=10	Bandage n=10	No Bandage n=10
Stinging/burning	1 mild	0	1 mild 1 moderate	0
Erythema (redness)	2 mild	0	1 mild 1 moderate	0
Edema (swelling)	0	0	0	0
Scaling	1 mild	0	2 mild	0

### Summary of Local Reactions on Blister Wounds Treated with Cream Base (100 mg cream/cm<sup>2</sup> skin)

Local Reaction	Number of Subjects by Severity of Local Reactions	
	Cream Base + Bandage n=10	Untreated + Bandage n=11
Contact dermatitis to Tegaderm	1 mild	3 mild
Erythema (redness)	0	1 mild
Pruritis (itch)	1 mild	0