

GT-002, A GABA_A PAM: PRECLINICAL AND CLINICAL CHARACTERISATION

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INTRODUCTION GT-002 is a novel, $\alpha 3$ -preferring GABA_A positive allosteric modulator designed to provide antipsychotic and procognitive benefits without benzodiazepine-like sedation. Preclinical electrophysiology demonstrates subunit-selective activity, and clinical multimodal imaging data (simultaneous EEG–fMRI) reveals that GT-002 produces a distinct, non-sedative neural signature in humans. GT-002 has been shown to be safe and well tolerated in single ascending (SAD) and multiple ascending (MAD) Phase I clinical studies.

1. PRECLINICAL ELECTROPHYSIOLOGY

Performed using automated patch-clamp recordings to assess GT-002 activity across recombinant GABA_A receptor subunits.

	GT-002				GT-005	GT-204
GABA _A $\alpha 3\beta 2\gamma 2$	175 % (3uM)	153% (1uM)	-	-	-35%	
GABA _A $\alpha 5\beta 1\gamma 2$	44%	-	-	-	-64%	
GABA _A $\alpha 5\beta 2\gamma 2$	19%	28%	20%	16%	-62%	-59%
GABA _A $\alpha 5\beta 3\gamma 2$	44%				-62%	

Summary Table: % Activity relative to GABA EC10-20 of compounds tested against GABA_A receptors in PAM mode on SyncroPatch platform.

CONCLUSIONS The GABA_A receptor PAM, GT-002, is safe and well-tolerated, and shows $\alpha 3$ -preferring, non-sedative GABA_A modulation with a unique EEG/fMRI neural fingerprint distinct from benzodiazepines. GT-002 is currently being tested in Phase IIa clinical trials.

2. GT-002 $\alpha 3\beta 2\gamma 2$ L

GT-002 EC₅₀ against GABA_A $\alpha 3\beta 2\gamma 2$ L

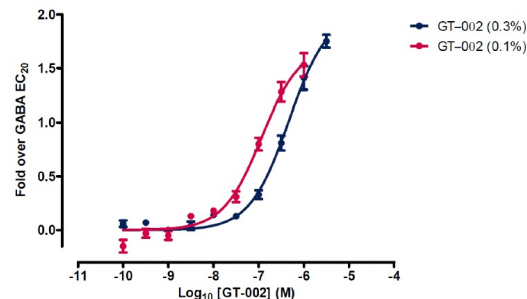


Fig 1 GT-002: $\alpha 3$ PAM compound. A limited PAM effect was recorded against the GABA_A $\alpha 5\beta 2\gamma 2$ L subtype. Max response was 28% at the top concentration tested. A dose dependent activation against the GABA_A $\alpha 3\beta 2\gamma 2$ L subtype

GT-005 IC₅₀

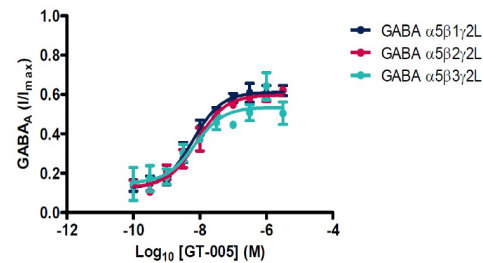


Fig 2 GT-005: $\alpha 5$ NAM compound A concentration-dependent negative modulation against the GABA_A $\alpha 5\beta 1-3\gamma 2$ L a similar modulatory activity observed at all three subtypes.

3. CLINICAL – HEALTHY VOLUNTEERS

Multimodal imaging with simultaneous EEG and resting-state fMRI reveals GT-002's non-sedative, subtype-selective GABA_A modulation distinct from GABA_A benzodiazepines. GT-002 shows precise subunit engagement, acting as an $\alpha 3$ -preferring PAM with minimal $\alpha 5$ activity and has been shown to be safe and well tolerated in SAD and MAD dose studies.

4. CLINICAL – SCHIZOPHRENIA

GT-002 is currently in a Clinical Phase II trial for cognitive impairment associated with schizophrenia, CIAS, comparing the effects of GT-002 to oxazepam.

<https://innovationsfonden.dk/en/news/danish-researchers-test-new-drug>

5. MORE INFORMATION

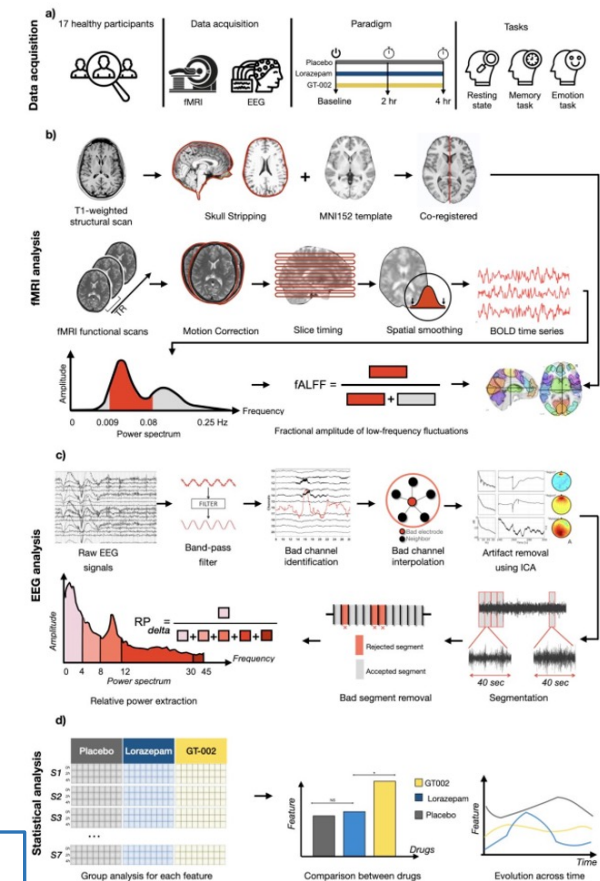
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