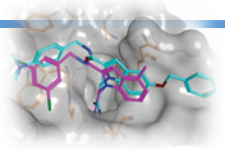
SOM3355 (Bevantolol)

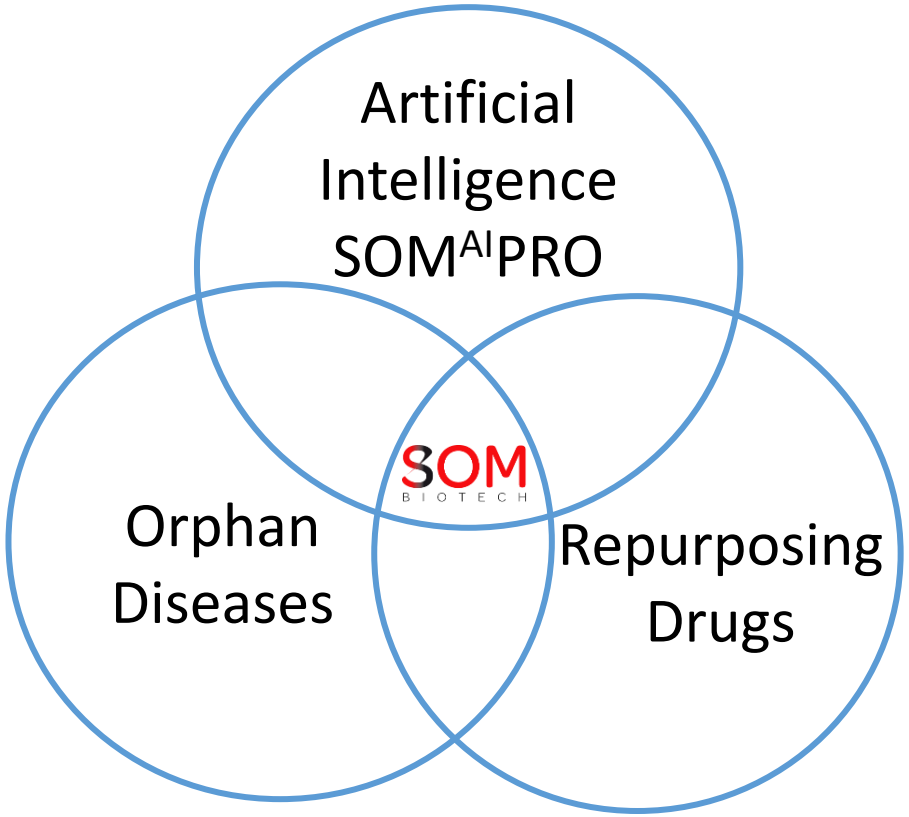
Candidate selected with **SOM^{AI} PRO** as potent VMAT2 inhibitor to treat chorea in Huntington's Disease

Dr Catherine Scart
(SOM Biotech - Chief Medical Officer)

SOM uses AI to efficiently repurpose drugs for orphan diseases



Orphan Indications	SOM Biotech **proprietary** SOM^{AI} PRO **technology**	**Experimental Validation** In vitro Ex vivo In vivo	**IP Protection ODD**	**Clinical PoC Phase 2a**	**Phase 2/3 Program & Commercialization** Or **Licensing**



Faster and derisked development

Accelerating drug discovery by repositioning drugs in new MoA and indications in rare diseases

Selection of bevantolol (SOM3355) as potent VMAT2 inhibitor to treat chorea in Huntington's Disease

SOM BIOTECH

SOM^{AI}PRO

- **SOM ^{AI} PRO Artificial intelligence screening**
  - to repurpose known drugs in the target indication Huntington's Disease
  - identification of bevantolol as a potential Vesicular Monoamine Transporter type 2 (VMAT2) inhibitor
  - bevantolol is an antihypertensive drug used for years with no psychiatric problems

Preclinical

- ***in vitro* functional studies**
  - SOM3355 inhibitory activity at VMAT2
- ***in vivo* studies**
  - brain penetration
  - no induction of catalepsy in rats, like tetrabenazine (TBZ), even at very high doses

Clinical

- **Phase 2a Proof-of-concept study completed**
  - SOM3355 reduces chorea in patients with Huntington's Disease (HD)
- **Phase 2b SOMCT03**
  - test 2 doses of SOM3355
  - 12-week double-blind, randomized, placebo-controlled trial

SOM3355 was first tested in a Phase 2a Proof of Concept study

Double-blind, randomized, cross-over study testing SOM3355 compared to placebo

32 male and female patients with **mild to moderate symptoms of chorea** were recruited in 4 sites

24-week treatment period in which all patients received Placebo, 100 mg BID SOM3355 and 200 mg BID SOM3355

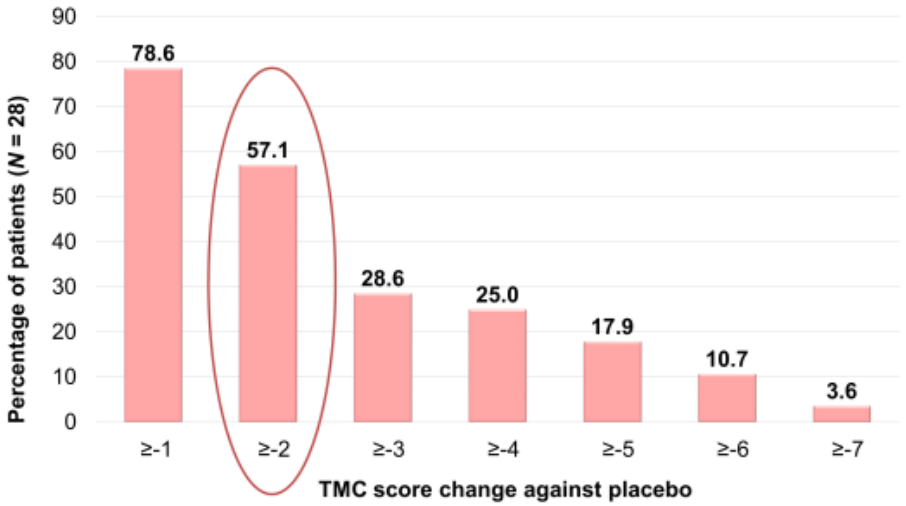
Primary endpoint :
improvement of at least 2 points in the Total Maximal Chorea (TMC) score in any active drug period compared with the placebo period

Secondary endpoints: Clinical Global Impression of Change (CGI-c),
Patient Global Impression of Change (PGI-c),
UHDRS functional and motor subscales,
Columbia-Suicide Severity Rating Scale (C-SSRS), and Safety

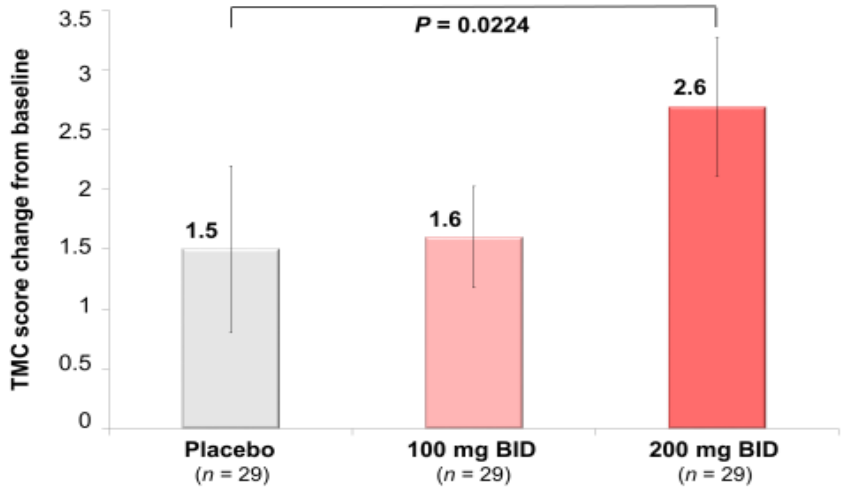
Exploratory endpoints: Prolactin levels in plasma, and SOM3355 plasma concentration

SOM3355 has shown effect on chorea in a first PoC study

Distribution of the reduction of TMC chorea score with SOM3355 versus placebo



Mean change from baseline of TMC score



- ✓ **57.1%** of the patients had an **improvement in the TMC ≥2 points compared to placebo** in any active drug period
- ✓ SOM3355 **200 mg BID induced a significant improvement of TMC score compared to placebo** (*p*=0.0224, Mixed Model)
- ✓ **CGI-c and PGI-c** scales both showed **improvement in >70% of patients** in at least one period under SOM3355 versus 31% under Placebo

⇨ **Confirmation of the expected effect on chorea symptoms - related to VMAT2 inhibition - measured by TMC score**

⇨ **And confirmation of the good tolerability of SOM3355 in patients with Huntington's Disease**

SOMCT03 – Phase 2B Study

Phase IIb, randomized, double-blind, placebo-controlled study in parallel groups
assessing the efficacy and safety of two doses of SOM3355
in patients suffering from Huntington's Disease with choreic movements

EudraCT number: 2021-003453-28

Phase 2b – SOMCT03 – Study design

Phase IIb, randomised, double-blind, placebo-controlled, study in parallel groups assessing 2 doses of SOM3355 (200 mg BID and 300 mg BID) in patients suffering from HD with choreic movements

In 129 patients recruited by 22 sites in 7 European countries

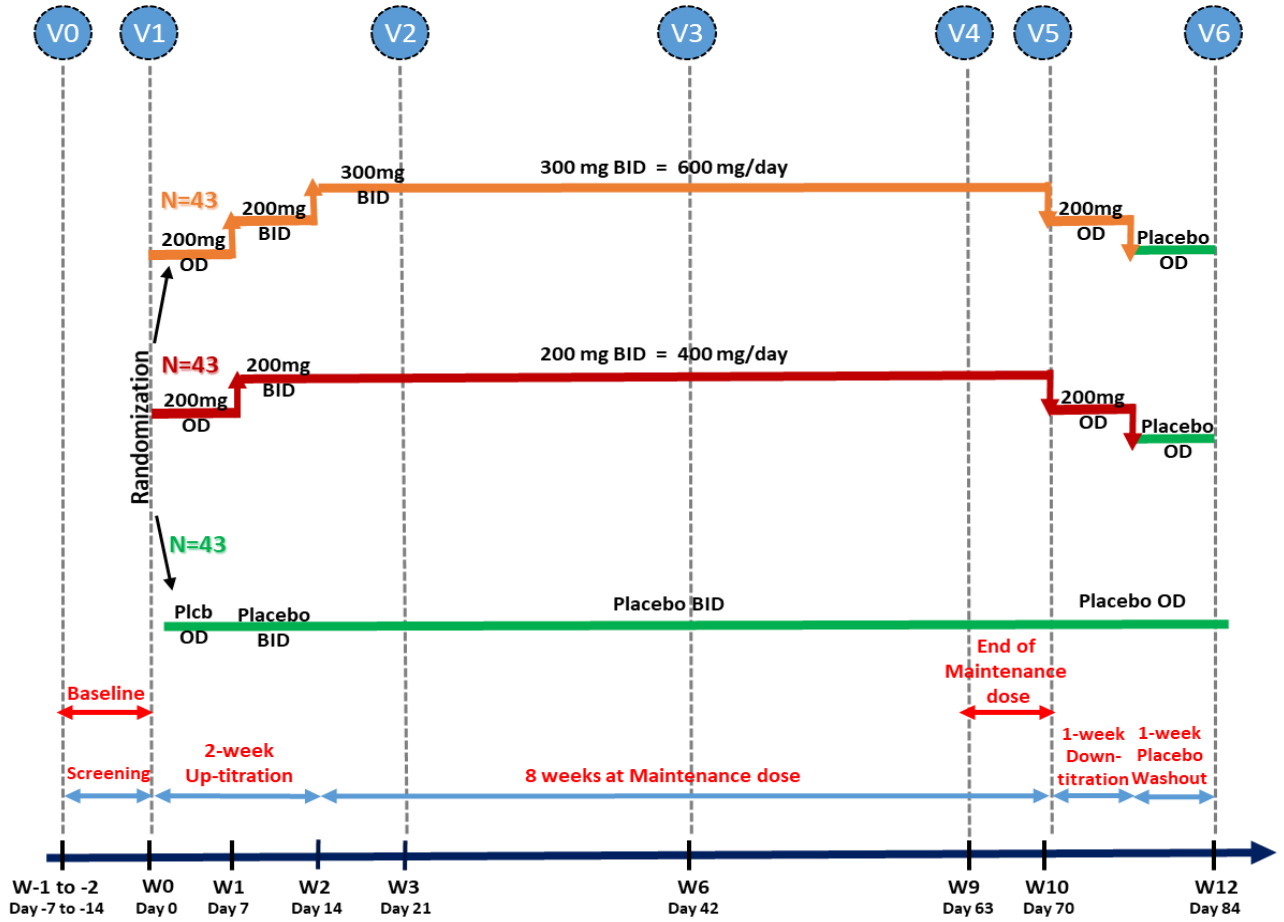
(France, Germany, Italy, Poland, Spain, Switzerland and the UK)

Study duration : **12 weeks** (+ 1-2 w for screening), and **7 visits**

Treatment: **SOM3355 (200 mg BID and 300 mg BID) or placebo** in **oral capsules taken twice daily**

Objectives: To assess the **efficacy to reduce chorea** in HD patients and the **safety of the 2 doses of SOM3355 compared to placebo**

PK sub-study in 24 patients to assess the PK profile and PK/PD in 6 selected sites - PK sampling for 12 hours at V2 (end of titration)



Total study duration 12 weeks (+1 or 2 weeks for screening) – 11 weeks under SOM3355 active drug

22 sites in Europe will enroll patients

The study will be conducted in 7 European Countries :

France, Germany, Italy, Poland, Spain, Switzerland, and UK

3 sites in Germany :

Country	City	HOSPITAL
Germany	Münster	George Huntington Institut
	Berlin	Charité – Universitätsmedizin Berlin
	Ulm	Hospital of University of Ulm

- ✓ First Patient enrolled in August 2022
- ✓ All Sites initiated by mid October
- ✓ Recruitment expected until end of March 2023
- ✓ Study completion by end of June 2023

If you need more information you can contact:

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