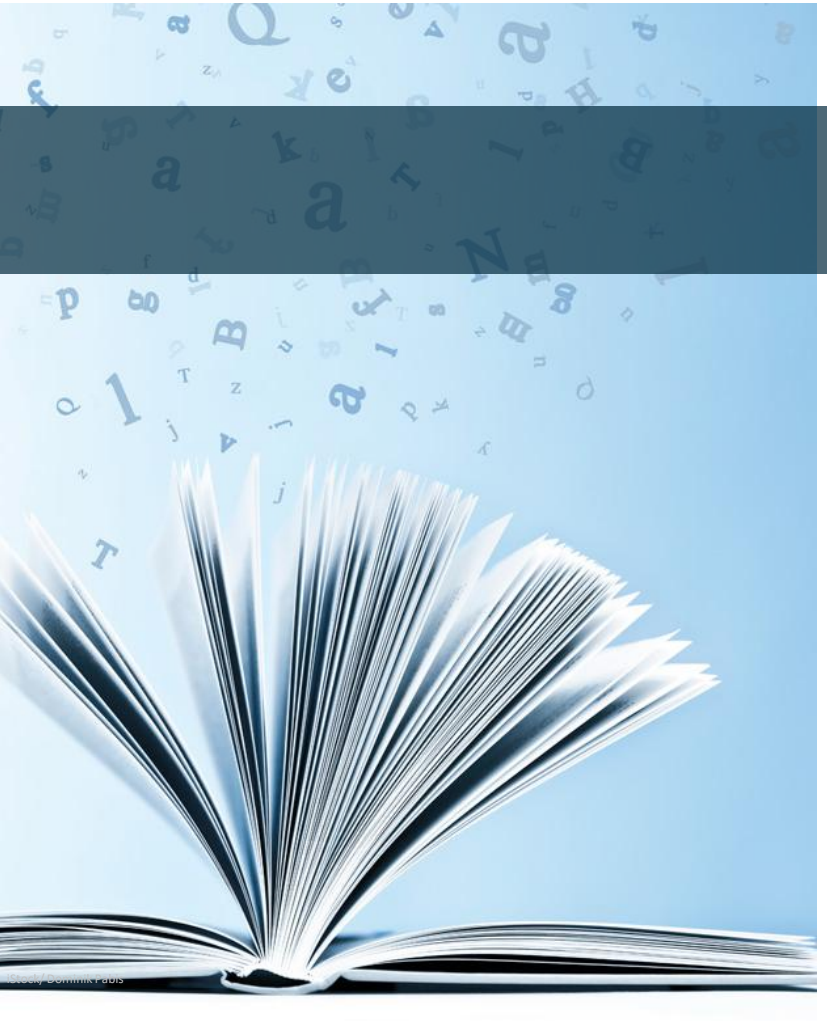
Clinical-stage biopharmaceutical company focused on neurological and psychiatric diseases, with a successful partnership-driven business model

Saniona company deck, March 2026

Table of Contents



Click to go to section

saniona

About Saniona

- **Saniona AB share February 27, 2026**
  - Market Cap: 2.6 BSEK (285 MUSD)
  - AVG Vol 2025: 10.7 MSEK (1.2 MUSD)
  - Share Price: SEK 18.62 ($2.05 USD)
  - Ticker: SANION
  - Exchange: NASDAQ Stockholm

- **Strong Financials Position as of year-end 2025**
  - 581 MSEK ($64 million) in cash
  - 820 MSEK ($90 million) in total including
    - 72 MSEK ($7.5 million) in property subject to sale-lease-back
    - 167 MSEK ($17.5 million) in near-term milestones

saniona™ is a **clinical-stage pharmaceutical company focused on neurological and psychiatric disease**, with a successful strategic partnership-driven business model

saniona

Saniona is well-positioned to capitalise on market growth[1] and unmet medical needs in CNS, with strong financial position and a differentiated pipeline advancing towards clinical milestones

Three core pillars of Saniona

Clinical-stage CNS innovator and leader in ion-channel drug discovery

- **Deep and proven ion-channel expertise** built over decades of innovation
- **Platform and scientific approach validated** through numerous research collaborations and licensing deals
- **Well-positioned to benefit from renewed industry interest** in neurological and psychiatric disorders

Strong financial position and a proven partnership business model

- **~$60M in cash** and **$17.5M** in near-term milestones
- **Multiple ongoing partnerships** with three strategic clinical collaborations and three research partnerships
- **Flexible business model** enabling selective partnerships while preserving key programs internally to capture greater long-term value

Differentiated CNS pipeline with best-in-class potential entering clinic

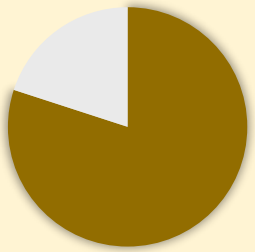
- **SAN2668: Rare paediatric epilepsies (ESES) / DEE** ⟶ Phase 1 prep. ongoing
- **SAN2219: Refractory focal onset epilepsy** ⟶ Phase 1 prep. ongoing
  Exp. potential in movement disorders
- **SAN2465: MDD incl. treatment-resistant depression** ⟶ Phase 1 prep. ongoing
  Exp. potential within rare genetic disease (Dup15q syndrome)

[1]CNS market resurgence: a decade-long slump ends with $80bn milestone - Pharmaceutical Technology

Saniona focuses on targeting two key CNS disease indications with a significant unmet medical need and high-value commercial potential

EPILEPSY

Share of Total Cost for Epilepsy



~80% of the total epilepsy treatment cost is driven by the ~30% drug-resistant patients

- Epilepsy is the 5th cause of disability among neurological disorders
- €20B estimated annual cost in the EU_1
- High commercial value for new therapies
- Strong strategic fit for differentiated $GABA_A$ modulation

Major Depressive Disorder

Share of Total Mental Health Care Cost

Depression accounts for **~56%** of total mental healthcare-related cost

- Depression is the largest contributor to mental disability and mortality
- >€100B estimated total annual cost of depression in the EU_2
- ~60% of all suicides occur in MDD patients
- Multiple lifecycle expansion opportunities

1 -Baulac et al Epilepsy priorities in Europe: A report of the ILAE-IBE Epilepsy Advocacy Europe Task Force. 2015 28;56(11):1687-1695

2 - Sobocki P, Jönsson B, Angst J, Rehnberg C. Cost of depression in Europe. The Journal of Mental Health Policy and Economics. 2006 Jun;9(2):87-98. PMID: 17007486.

saniona

Saniona has a robust pipeline of differentiated CNS entering clinical development

Internal programs

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status and upcoming milestones
SAN2668 $GABA_A$ **(α1),α2, α3**	Ped Epilepsy (DEE)					Phase 1 initiation (Q4/ Q1 2027)
SAN2465 $GABA_A$ **α5** NAM	Major Depressive Disorder					Phase 1 initiation (Q4)
SAN2219 $GABA_A$ **α2, α3**	Refractory Focal Epilepsy					Phase 1 initiation (Q4)

Partner programs

Product Candidate	Partner	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status and upcoming milestones
ACP-711 $GABA_A$ **α3**	**Acadia**	Essential tremor					Acadia to sponsor and initiate Phase 2 clinical trial
SAN2355 Kv7.2/3	**Jazz**	Epilepsy					Jazz Pharmaceuticals to sponsor and initiate Phase 1 clinical trial

Saniona's three prioritized assets are designed for subtype-selective, differentiated pharmacology to address specific medical needs while minimizing the limitations of benzodiazepines

$GABA_A$ positive allosteric modulators (PAMs)

- **GABA acts as the brain's main inhibitory signal by activating $GABA_A$ receptors (α1, α2, α3, α5)**, which are targeted by benzodiazepines
- **While benzodiazepines are effective anti-epileptics and anti-anxiolytics, their non-selective action leads to side effects** like sedation, cognitive impairment, and tolerance
- **Subtype-selective modulation enables targeted clinical effects while reducing adverse events associated with non-selective $GABA_A$ PAMs**

Symptoms can be differentially addressed by subtype selective $GABA_A$ PAMs

Effect/Subtype	GABA α1	GABA α2	GABA α3	GABA α5
Seizure control	++	++	+	+
Anxiolysis		++	+	++
Analgesia		++	++	+
Sedation	++			
Cog. Impair.	++			+
Addiction	++	+		

Seizure control

Benzodiazepine limitations

NAM improve cognition

PAM: Positive Allosteric Modulator

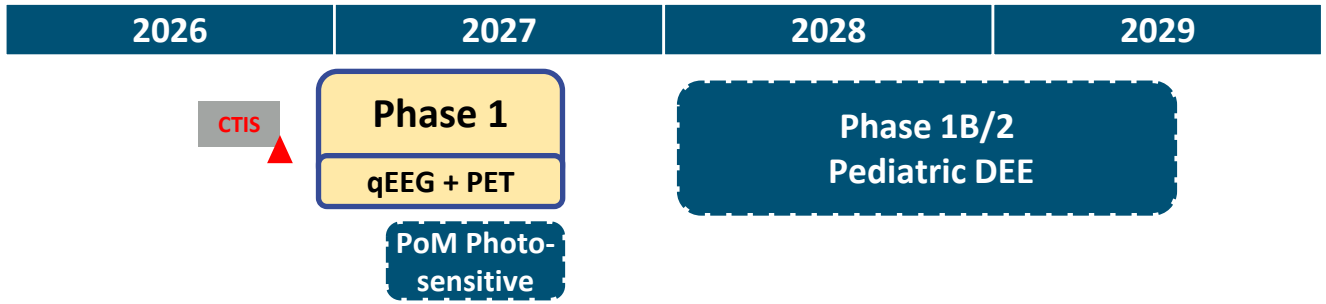
Mohler H Diversity in neuronal inhibition, Dial. Clin. Neurosci. 2002; Knabl J, Reversal of pathological pain through specific spinal GABAA receptor subtypes, Nat. Lett. 2008 ; Rudolph U et al., Beyond classical benzodiazepines, novel therapeutic potential of GABAA receptor subtypes, Nat.Rev. Drug Discov. 2012

saniona

The three prioritized assets are advancing toward Phase 1

SAN2668 - Paediatric Epilepsy (DEE)

- **Phase 1 start expected late 2026**
- **Phase 1B/2 Ped DEE basket study 2028**
- **Photosensitive PoM in epilepsy patients**

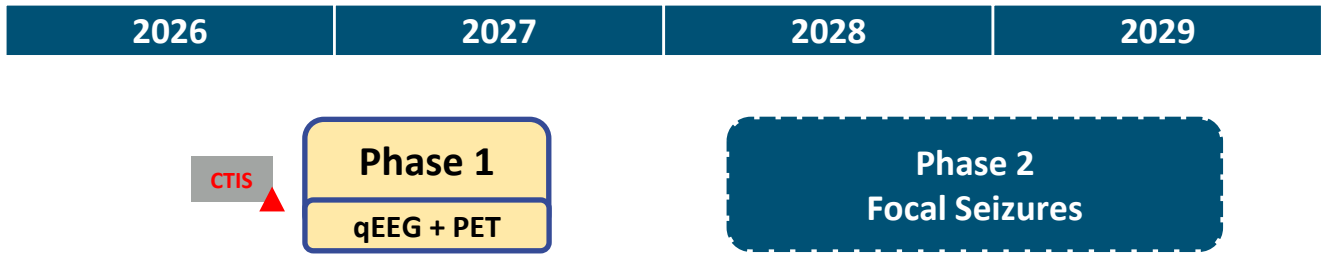


SAN2465 – MDD / TRD

- **Phase 1 start expected in late 2026**
- **Phase 2 study 2028**

SAN2219 - Refractory Focal Epilepsy

- **Phase 1 start expected late 2026**
- **Phase 2 study 2028**



Healthy volunteers Patients

Saniona is on a trajectory similar to Longboard, Karuna, and Cerevel, all acquired in multi-billion-dollar Phase 2/3 CNS deals

	Lundbeck acquired Longboard (Oct 2024)	**BMS acquired Karuna** (Mar 2024)	**AbbVie acquired Cerevel** (Aug 2024)
Deal value	**US $2.6 billion**	**US $14 billion**	**US $8.7 billion**
Lead asset(s)	**One Phase 2 asset** ➢ **Bexicaserin** (Ph2) for **developmental & epileptic encephalopathies** (DEEs) ▪ Phase 2 trial comprised **52 DEE patients** (43 on bexicaserin/9 placebo) with DS (4), LGS (29) and other DEEs (19)	**One Phase 3 asset** and **One Phase 1 asset** ➢ **KarXT** (Ph3) **for schizophrenia**; also evaluated in Alzheimer's disease psychosis and adjunctive therapy in schizophrenia ➢ **KAR-2618** (Ph1) **for mood and anxiety disorders**	**Two Phase 3 assets** and **Two Phase 2 assets** ➢ **Tavapadon** (Ph3) **for Parkinson's disease** ➢ **Emraclidine** (Ph3) **for schizophrenia** ➢ **Darigabat** (Ph2) **for anxiety and epilepsy** ➢ **CVL-871** (Ph2) **for dementia-related apathy**
Additional pipeline	***n/a*** *- Bexicaserin was the only key asset in the Longboard acquisition*	***Four preclinical assets*** *- undisclosed programs focused on neuropsychiatric and neurodegenerative disorders*	***Multiple early-stage CNS assets*** *- incl. programs targeting major depressive disorder, substance use disorder, and Parkinson's disease progression*

Table of Contents

Click to go to section

ACP-711 is a highly selective $GABA_A$ α3 PAM that enabled a substantial development partnership with Acadia Pharmaceuticals

ACP-711 for essential tremor

- **ACP-711 modulates the $GABA_A$ α3** receptor without impact on other $GABA_A$ subtypes affected by benzodiazepines
- **Phase 1 study demonstrating safety and tolerability completed**
  - Single-ascending and multiple-ascending dose cohorts
  - Biomarkers for target engagement and functional EEG read outs

Strategic partnership with Acadia Pharmaceuticals Nov 2024 for future clinical and commercial development in neurological diseases

- **Phase 2 clinical trial in essential tremor expected to initiate in 2026**, sponsored by Acadia
- **$28m upfront payment** received
- **Potential additional milestones:**

  + **$147m** in development and regulatory milestones

  + **$435m** in commercial milestones

  + **Tiered royalties**, up to low double digits

SAN2335 is a novel potassium channel activator that enabled a significant development and commercial partnership with Jazz Pharmaceuticals

SAN2335 for epilepsy

- **Unique mechanism of action** - activates the Kv7.2/7.3 potassium channel only, avoiding dose limiting side effects common with less selective, similar drugs
- **Preclinical studies confirms one-of-a-kind drug profile and potential best in class**, demonstrating superior seizure control and favourable side effect profile compared to less selective Kv7 activators

Strategic partnership with Jazz Pharmaceuticals Aug 2025 for future clinical and commercial development in epilepsy

- **Jazz will sponsor all future of preclinical and clinical development** for this assets
- **$42.5m upfront payment** received
- **Potential additional milestones:**

  + **$192.5m** in development and regulatory milestones

  + **$800m** in commercial milestones

  + **Tiered royalties**, up to low double digits

Saniona's Strategic Partnerships Set to Generate Significant Value

Upfront payments received:

- ✓ ACP-711: **$28m**
- ✓ SAN2355: **$42.5m**

$70.5m

Potential development and regulatory milestones:

- ➢ ACP-711: **$147m**
- ➢ SAN2355: **$192.5m**

$410m

Potential commercial milestones:

- ➢ ACP-711: **$435m**
- ➢ SAN2355: **$800m**

>$1.6B

Tiered royalties

ACADIA®

ACP-711 - essential tremor

Jazz

SAN2355 - epilepsy

saniona™

Table of Contents

Click to go to section

Executive summary - SAN2668

SAN2668 is a next-generation, oral, subtype selective $GABA_A$ PAM advancing toward phase 1

- **Targets rare, difficult-to-treat paediatric epilepsies** with potential for broad DEE label
- **Designed for robust seizure control - retain benzodiazepine efficacy level with improved safety and tolerability** through predominant modulation of $GABA_A$ $\alpha2/\alpha3$ with balanced $\alpha1$ contribution for optimal seizure protection
- **Highly potent and brain penetrant molecule:** low nM affinity to the target (human recombinant receptors)
- **Phase 1 planned for 2026**, potentially with photosensitivity POM targeted for 2027

SAN2668 has demonstrated potent seizure control:

- **Strong efficacy in acute generalized- and focal seizure models** (PTZ, MEST, 6Hz)
- **Profiling in chronic epilepsy models** ongoing:
  - GAERS (Absence/Spike-wave-Discharges) ✓
  - Amygdala kindling (focal-to-generalized seizures) ✓
  - MTLE (kainic acid): mesial temporal lobe epilepsy
- **Lack of motor impairments or sedative effects**
- **qEEG study in rodents confirms preserved vigilance** and no evidence of sedation
- **Patent protection through 2045**

saniona

Developmental Epileptic Encephalopathies (DEEs) represent a persistent unmet need

- Developmental epileptic encephalopathies (DEEs) remain largely treated with broad ASMs and benzodiazepines
- Benzodiazepines provide seizure control but are limited by **sedation, cognitive impairment, and tolerance**, restricting chronic use
- Therapies capable of controlling seizures and suppressing **spike-wave EEG pathology while preserving development and cognition** remain limited

saniona

SAN2668 – Value proposition

SAN2668 has the potential to become the Anti Seizure Medication of choice for difficult to treat paediatric epilepsy syndromes with robust efficacy and improved safety and tolerability profile

Key value messages

- **SAN2668 is designed to deliver benzodiazepine-class efficacy without benzodiazepine-class liabilities**
- **SAN2668 differentiated pharmacology has the potential to control seizures and Spike-Wave EEG abnormalities** with reduced cognitive liability and reduced developmental burden and polypharmacy in developmental epileptic encephalopathies (DEEs)

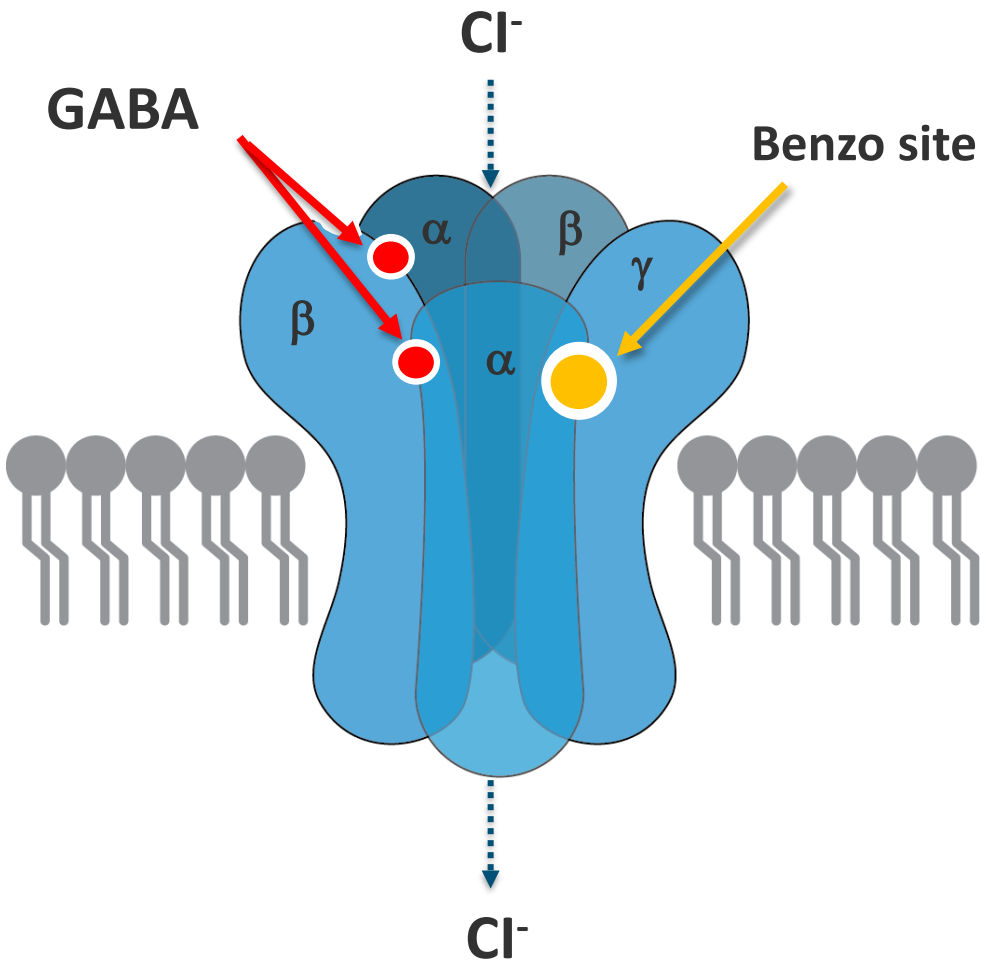
Mechanistically designed to combine robust efficacy with improved tolerability

- Positive allosteric modulator of **$GABA_A$ receptors with activity across α1, α2, and α3 subunits**
- **α3-mediated modulation** targets thalamocortical circuits implicated in spike-wave discharges
- Moderate **α1 engagement** intended to preserve benzodiazepine-class antiseizure efficacy
- Structurally **distinct from benzodiazepines**

saniona

The $GABA_A$ receptor is the molecular target for SAN2668

- **$GABA_A$ receptor is a ligand-gated ion-channel activated by GABA**
- **The channel consists of 5 subunits, various subtypes** (typically 2α, 2β and 1g, e.g., α2β3γ2)
- **The functional properties of each receptor subtype are primarily determined by the specific α-subunit composition** (α1, α2, α3 or α5)

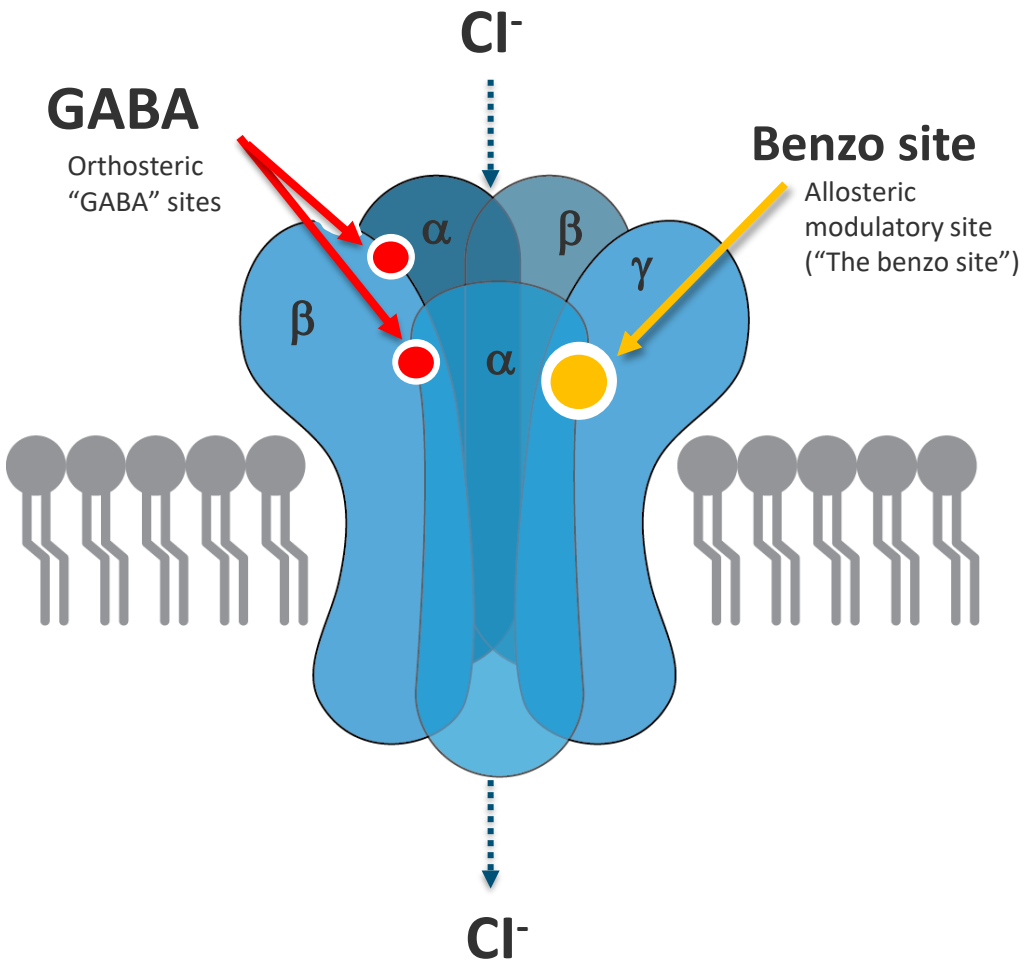


Mohler H., Dial. Clin. Neurosci. 2002

saniona

Benzodiazepines exert their pharmacological effects through positive allosteric modulation of The $GABA_A$ receptor

- **Orthosteric ("GABA") site - α/β interface**
  - Primary binding site where GABA binds
  - GABA binding opens the chloride channel, allowing Cl^- influx
  - Chloride influx hyperpolarizes the postsynaptic neurons, reducing excitability and suppressing action potentials
- **Allosteric modulatory site ("the benzo site") - α/γ interface**
  - Saniona's GABA PAMs bind here, similar to benzos
  - Saniona PAMs are structurally distinct from benzodiazepines
  - Located away from the GABA binding site, enabling modulation of GABAs effect
  - Ligands at this site do not open the channel on their own, but enhance GABA's effect (positive allosteric modulation; "PAM")
  - Likely responsible for the safer mode-of-action vs. barbiturates

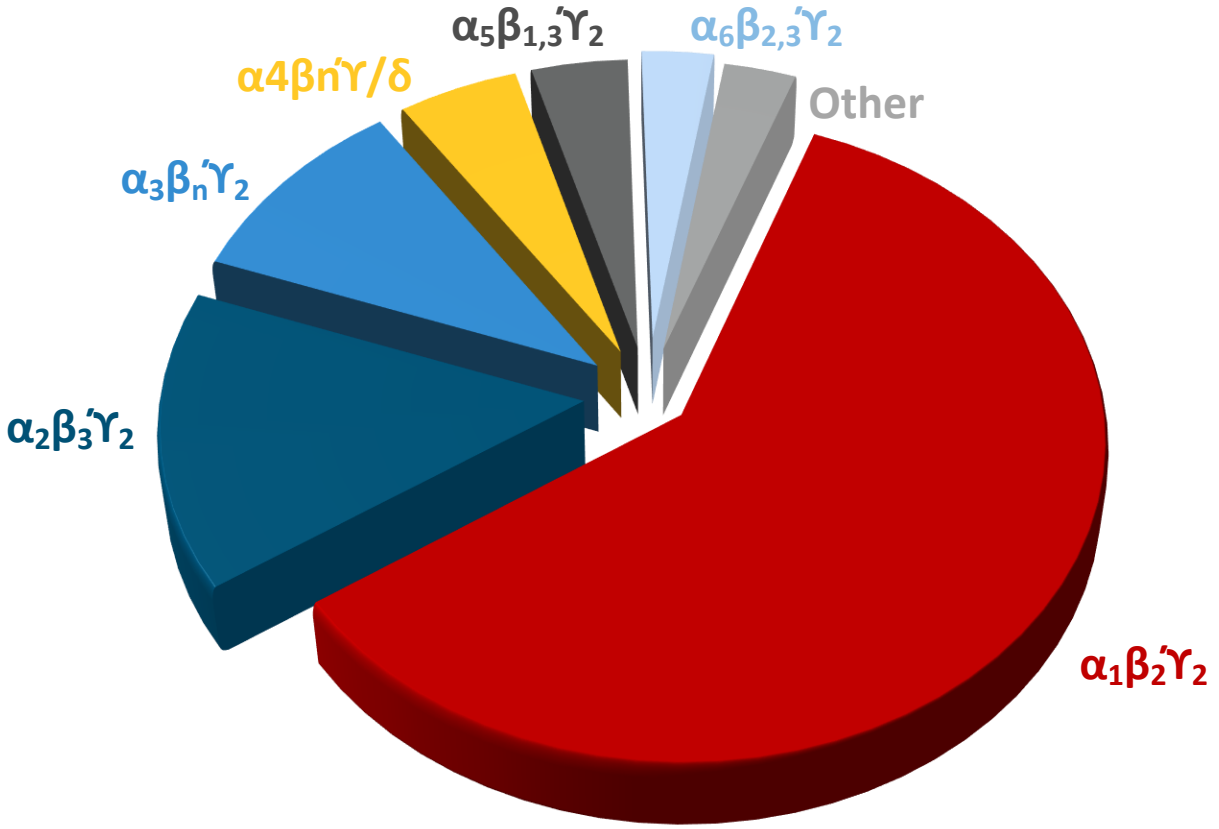


Vinkers et al., Expert. Opin. Investig. Drugs (2010) 19: 1217-1221, Rudolph & Knoflach, 2011, Nat. Rev. Drug Disc. 10:1-13

saniona

The majority of all $GABA_A$ receptors contain a BDZ site, and most of them contains the α1 subtype

- ~90% of all $GABA_A$ receptors contains a benzodiazepine binding site
- The vast majority of benzodiazepine binding sites in the human brain contains the $GABA_A$ α1 subtype (~60%)
- Followed by $GABA_A$ α2 (15-20%), $GABA_A$ α3 (10-15%) and $GABA_A$ α5 (< 5%)

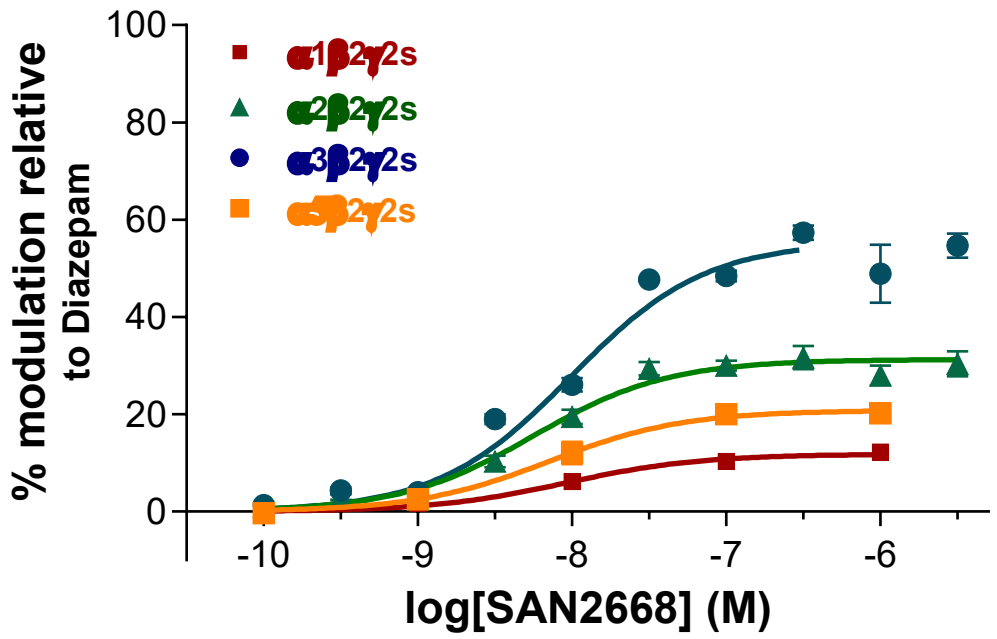


Mohler H., Dial. Clin. Neurosci. 2002

saniona

SAN2668 delivers selective modulation of key $GABA_A$ subtypes to target the seizure types most relevant in difficult-to-treat paediatric epilepsy

SAN2668 differentially modulates $GABA_A$ receptors



Targeting different $GABA_A$ receptors for different seizure types:

- $GABA_A$ α3: prevention of non-convulsive seizures with potential cognitive benefit
- $GABA_A$ α2: robust activity against convulsive seizures
- $GABA_A$ α1: additional seizure control

SAN2668 is ideally suited to prevent seizures in difficult-to-treat paediatric epilepsy

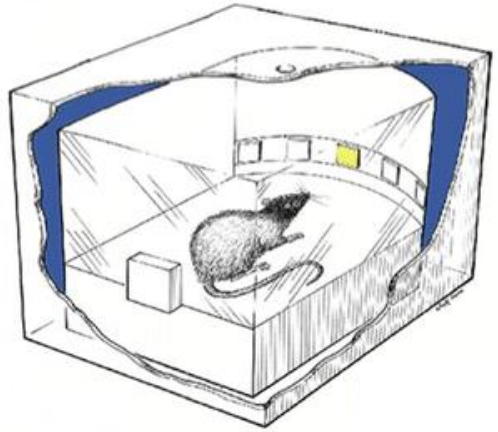
saniona

In the five-choice serial reaction time test, selective α3 modulation with ACP-711/SAN711 improves attention and vigilance, whereas non-selective GABA PAMs impair these functions, such as diazepam

Targeting GABAA a3 containing receptors confers additional cognitive benefit
Data obtained with SAN711 - selective $GABA_A$ a3 PAM

Five-choice serial reaction time test		ACP-711/SAN711 GABA α3	Diazepam GABA α1, α2, α3, α5
Percent correct choices	Attention	⊕ Increased	✕ Decreased
Omissions	Adverse effects, motivation, attention	= No effects	✕ Increased
Premature responding	Task engagement/ impulse control	⊕ Increased	✕ Decreased
		Improved attentional functions and task engagement	**Deleterious effects on attentional functions and task engagement**

Five-choice serial reaction time task is used to assess sustained- and selective attention, vigilance and impulse control

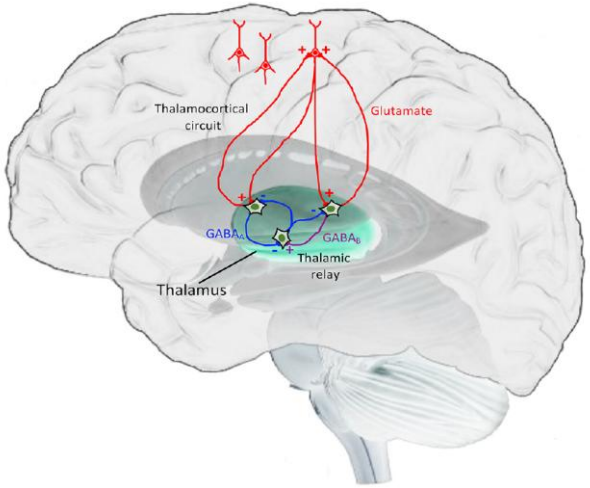


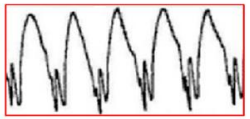
- Rodents are trained to respond to an unpredictable stimulus in one of the five locations
- After training, their ability to select the correct target to achieve food reward is evaluated

Higgings G et al., Society for Neuroscience 2025 Characterisation_of_Gaba2_3_positive_allosteric_modeulars_PAMS_in_tests_of_anxiety_and_side_effect_10babfd883.pdf

Spike-and-wave discharges are the abnormal EEG rhythms the drive absence seizures and define the EEG signature of severe paediatric epilepsies such as ESES

- **SPIKE AND WAVE DISCHARGES** is due to abnormal interaction in the cortico-thalamic (TRN) system
- GABA α3 subunit show a **dense expression in TRN**, where α3 is exclusively expressed, among $GABA_A$ subunits (in humans as well as rodents)[1]
- Spontaneous rat model for absences (WAG/Rij rats) show **selective reduction** in α3 subunit protein in TRN[2]
- The anti-absence compound, **Clonazepam**, reduce SWDs in wildtype mice, but effect is lost in α3 point mutated mice rendered insensitive for BDZs[3]
- $GABA_A$ α3 subtype selective PAM **SAN711 suppresses SWDs** in GAERS rats[4] providing pharmacological evidence for α3-mediated suppression of SWDs





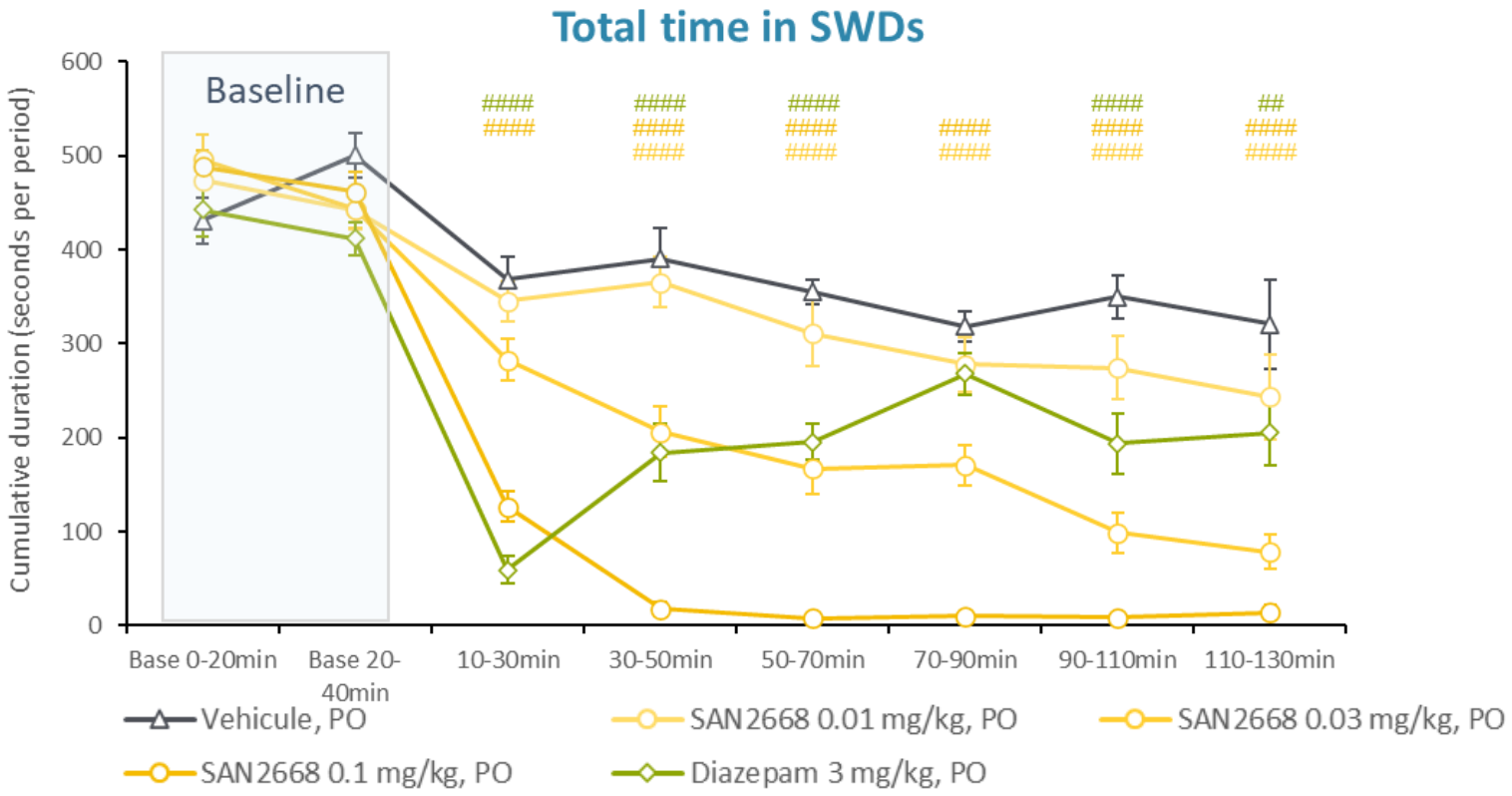
Spike and wave EEG

1Pirker et al., Neurosci. 2000, Waldwogel et al., J. Chem. Neuroanat. 2017
2Liu X et al., PNAS 2007
3Sohal VS, J. NeuroSci. 2003
4Crunelli V et al.,Soc.for Neurosci. 2023, PSTR526.08

saniona

SAN2668 fully suppresses pathological spike-wave-discharges in GAERS rats suggesting potent efficacy in DEEs with generalized SWDs

- **GAERS rats demonstrated multiple spontaneous spike-wave-discharges (SWDs) leading to increased time in SWDs**
- **SAN2668 potently suppresses SWDs in GEARS rats after oral administration, attaining the minimal efficacious dose level at ~25% receptor occupancy (RO) and full suppression achieved at ~50 % RO**
- Plasma bioanalysis and final report pending



Dose (mg/kg)	Projected receptor occupancy
0.01	< 25%
0.03	25 %*
0.1	48 %*

*Based on Saniona internal rodent receptor occupancy study

Vehicle: n = 10; Diazepam and all doses of SAN2668: n = 11.
#, ##, ### and #### indicate significance versus vehicle ($p < 0.05$, 0.01, 0.001 and 0.0001, respectively).

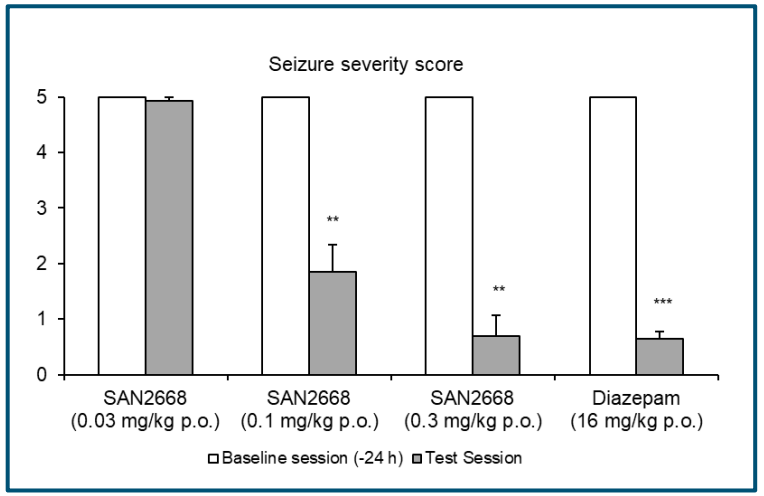
SAN2668 potently suppresses epileptiform activity and reduces seizure severity in amygdala kindled rats indicating potent efficacy in focal and focal-to-generalized seizures

- **Amygdala kindling induced prolonged epileptiform afterdischarges with secondary cortical propagation**
- **SAN2668 robustly suppresses both amygdala and cortical afterdischarge duration**
- **Seizure severity is markedly reduced**, reflected by lower Racine scale scores
- **A minimal efficacious dose of 0.1 mg/kg is achieved across all endpoints** (~50% receptor occupancy)
- **Plasma bioanalysis** and final report pending

Dose (mg/kg)	Projected receptor occupancy*
0.03	~ 25 %
0.1	~ 48 %
0.3	~ 80 %

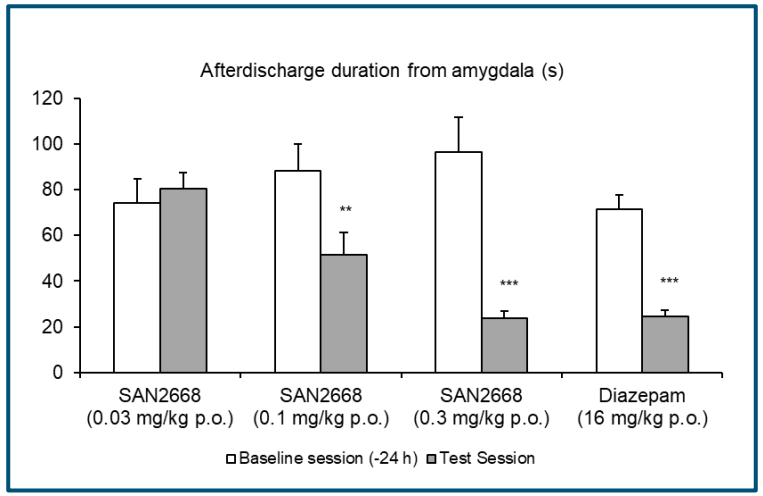
*Based on Saniona internal rodent receptor occupancy study

SAN2668 potently suppresses **seizure severity**



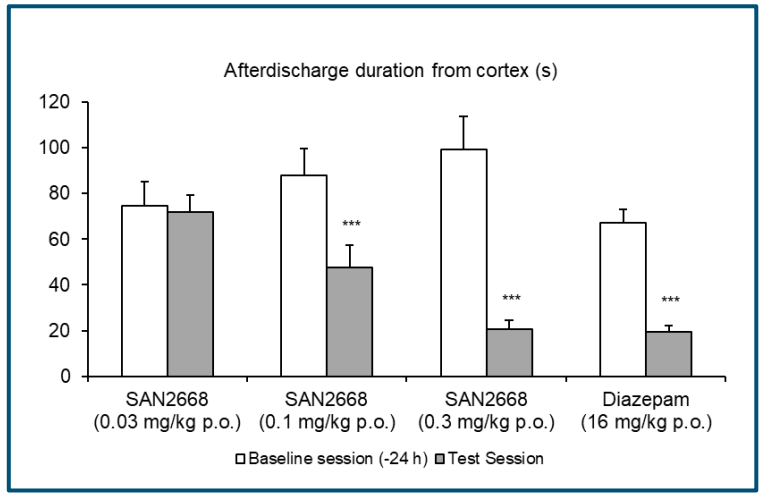
Wilcoxon test (compared with Baseline session):
no indication = not significant;
* = p < 0.05; ** = p < 0.01; *** = p < 0.001.

SAN2668 potently suppresses **amygdala afterdischarge duration**



Paired Student's t test (compared with Baseline session):
no indication = not significant;
* = p < 0.05; ** = p < 0.01; *** = p < 0.001.

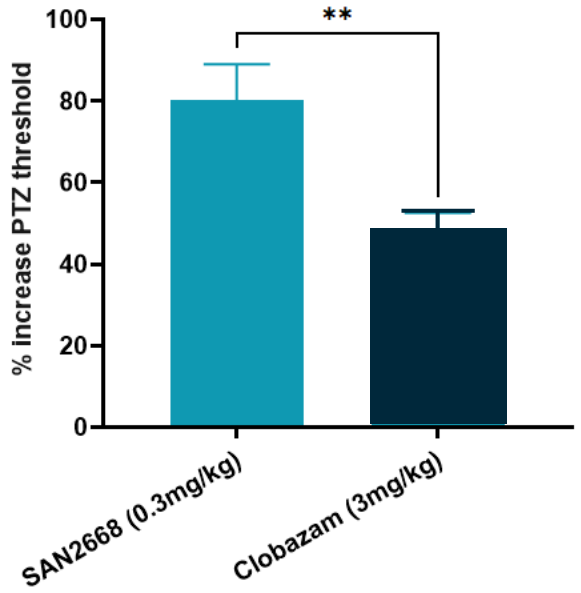
SAN2668 potently suppresses **cortex afterdischarge duration**



Paired Student's t test (compared with Baseline session):
no indication = not significant;
* = p < 0.05; ** = p < 0.01; *** = p < 0.001.

SAN2668 demonstrates superior seizure control vs. non-selective $GABA_A$ PAMs, such as Clobazam, likely due to achievement of higher receptor occupancy

Generalized seizures: SAN2668, at a dose achieving 70 % receptor occupancy, demonstrates superior seizure control compared with Clobazam at clinically efficacious plasma exposure (~40 % receptor occupancy)*



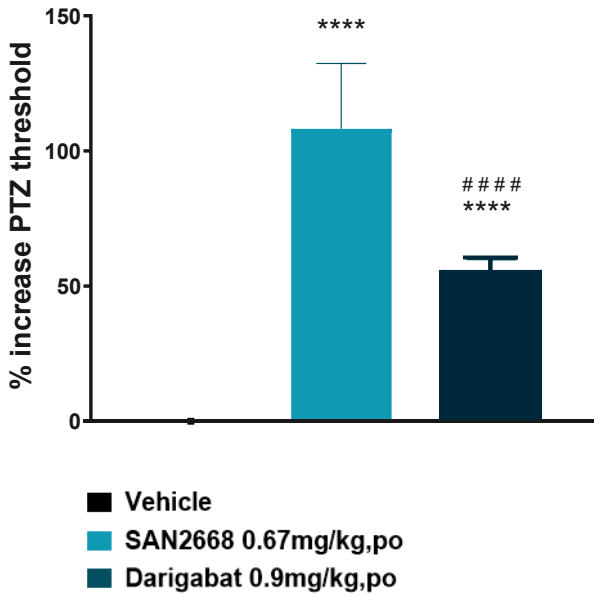
**: p=0.0058, n=10 (Welch's unpaired t-test)

Clobazam	Mouse	Human	RO (%)
Dose	3 mg/kg	40 mg tablet	
Cpl (free) (nM)	318	243**	~ 40

A clobazam dose of 3 mg/kg in mice achieves plasma concentrations comparable to those observed in humans after a 40 mg dose (maximum human dose) after correcting for species differences in plasma protein binding. This concentration corresponds to ~40% receptor occupancy (RO).
*Calculated based on plasma samples from study B11047
**Tolbert et al., J. Clin. Pharmacol. 2019.

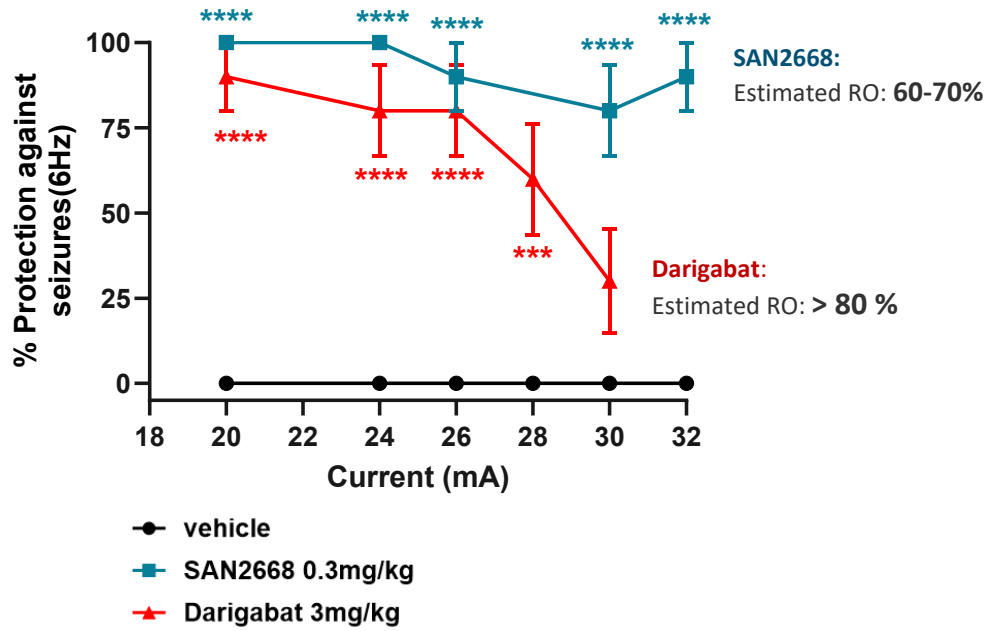
SAN2668 demonstrates superior seizure control vs. clinical subtype selective $GABA_A$ PAMs, such as Darigabat, likely due to additional marginal α1 modulation

Generalized seizures: SAN2668 demonstrates superior seizure control compared to Darigabat at equal calculated receptor occupancies[1]



[1]: dose levels calculated to result in 80% receptor occupancy
***: p < 0.001 vs. vehicle, #### p<0.001 vs. SAN2668 (one way ANOVA)

Focal onset seizures: SAN2668 maintains seizure protection at higher current intensities and lower receptor occupancy compared to Darigabat

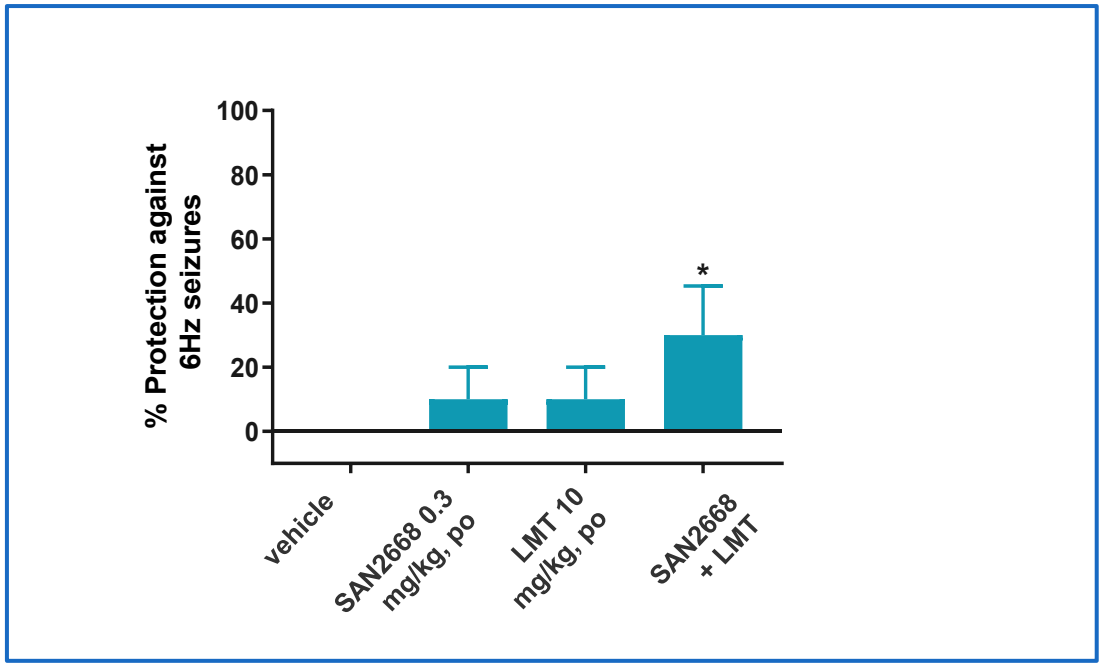


/*: p < 0.001/0.0001 vs. vehicle, Mann Whitney U test
Darigabat and SAN2668 were tested on two different testdays

SAN2668 shows additive effects when combined with standard of care

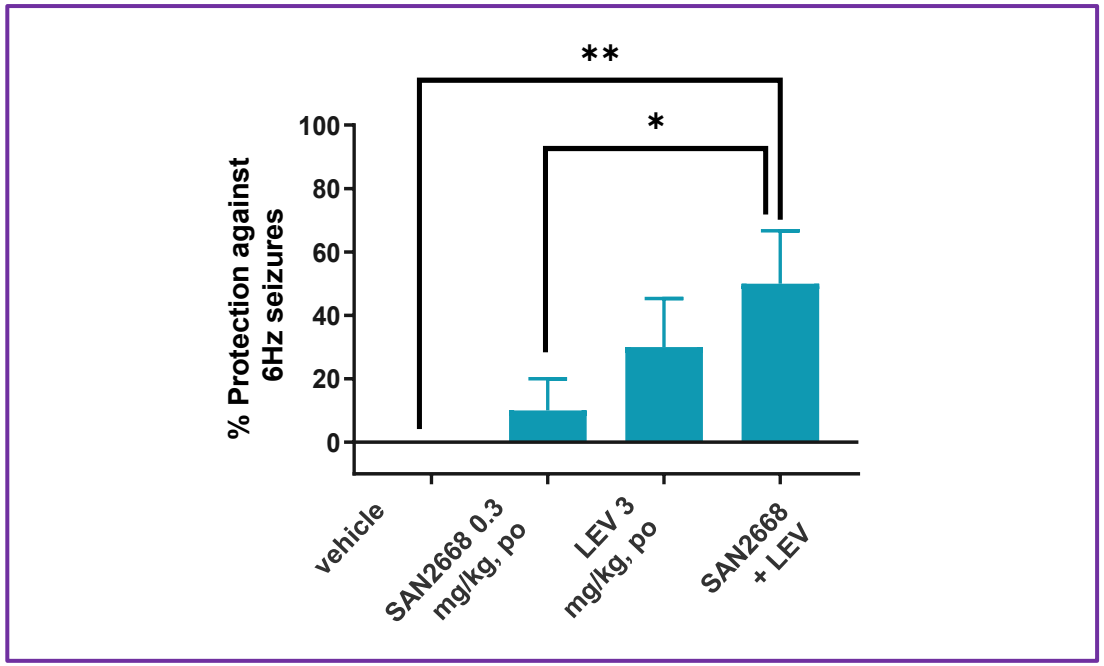
- At sub-therapeutic dose levels, **SAN2668 produces additive protection in the 6-Hz focal-seizure model when co-administered** with sub-therapeutic dose of different anti-seizure medications:
  - **Lamotrigine** (sodium-channel blocker)
  - **Levetiracetam** (SV2A modulator)

With Lamotrigine



*p<0.05 vs vehicle, Kruskal-Wallis test, n=10

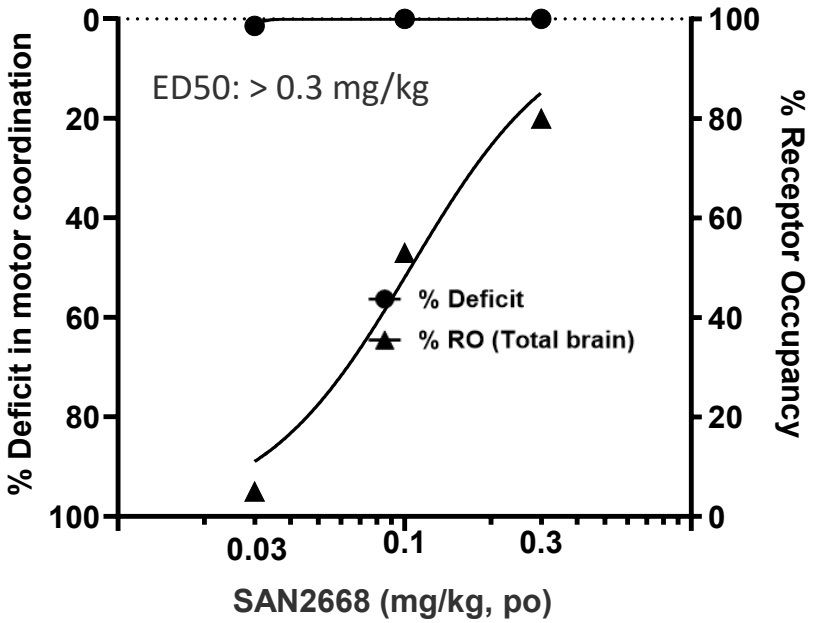
With Levetiracetam



*p<0.05,**p<0.01 Kruskal-Wallis test, n=10

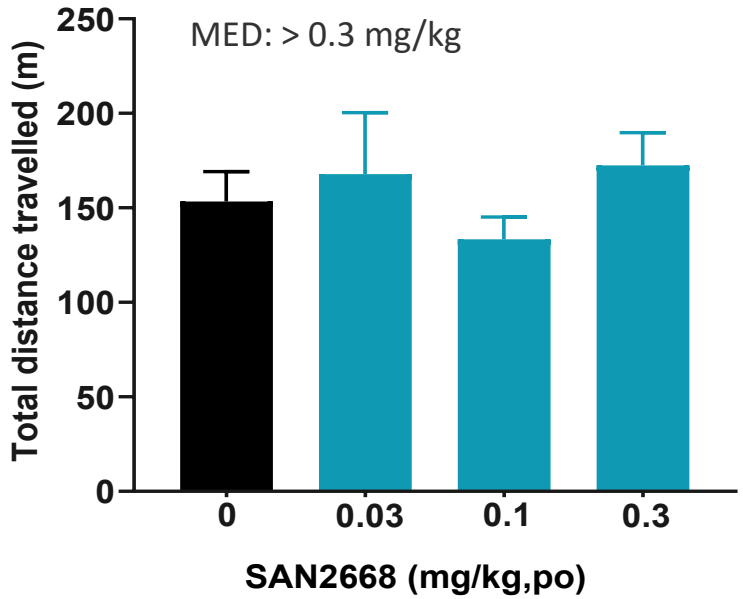
SAN2668 does not adversely affect motor performance or cause sedation in rodents in clinically relevant dose levels

Adverse effects, Rotarod: SAN2668 does not cause motor impairments in rodents at pharmacologically relevant dose levels which contrasts with benzodiazepines



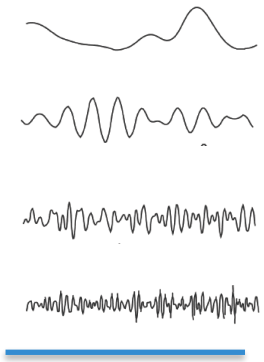
Motor impairments is assessed by placing rodents on an accelerating rotarod and measuring the latency to fall. The test drug is administered according to Tmax. A minimal effective dose and the ED50 are determined. *ED50 is the estimated dose producing 50% motor impairment relative to vehicle-treated rats.*

Adverse effects, locomotor activity: SAN2668 does not cause sedation in rodents at pharmacologically relevant dose levels which contrasts with benzodiazepines



Sedation is assessed by placing rodents in a novel environment that promotes exploratory locomotor activity and measuring the distance travelled over 30 minutes. The test drug is administered according to Tmax. A minimal effective dose (MED) is established.

EEG provides a non-invasive and interpretable pharmacodynamic biomarker for GABAergic compounds and enable translation of preclinical readouts into humans

EEG signal over time		Frequency Band	Functional Meaning	Effects of known MoA	Interpretation
 1 sec	δ	**Delta (1-4 Hz)**	Dominant during deep sleep	Typically **increased by benzodiazepines**[1] and reduced by activating drugs (stimulants like caffeine[2])	Enhancement associated with sedation Reduction might indicate improved attention
	α	**Alpha (8-12 Hz)**	Prominent in relaxed wakefulness, eyes closed	Typically **decreased by benzodiazepines**[1] (15-40%) and by α2,3,5 selective compounds (i.e., darigabat)[4]	Diminishment associated with reduced alertness and drowsiness
	β	**Beta (13-30 Hz)**	Linked to active thinking, sensorimotor processing	Typically **increased by benzodiazepines**[1] (15-40%), SSRIs[5] and darigabat[3]	Enhancement associated with anxiolytic effect
	γ	**Gamma (>30 Hz)**	High-order cognitive integration	Typically **increased by ketamine**[6] and to a less extent by BDZ[1]	Enhancement associated with increased information processing and perception

Clear EEG fingerprints during wakefulness for different $GABA_A$ receptor subunits

Compound	MoA	γ Gamma	β Beta	α Alpha	θ Theta	δ Delta	Ref
AZD7325 (BAER-101)	a2,3 PAM	-	-	-	↓	↓	Chen et al 2014
NS11821	a2,3,5 PAM	-	↑	-	-	-	Zuicker et al 2016
PF-06372865 (Darigabat)	a2,3,5 PAM	↑	↑	↓	↓	↓	Nichols et al 2018
ENX-102	a2,3,5 PAM	-	↑	↓	↓	↓	Nettesheim et al., Cells 2025
Lorazepam	a1,2,3,5 PAM	↑	↑	↓	↓	↑	Chen et al 2014
SAN711	a3 PAM	↑	-	↑	-	↓	Internal Saniona data
Basmisanil	a5 NAM	-	↓	↑ (low alpha)	↑	-	Hipp et al 2021

EEG fingerprints to confirm target-specific pharmacology:

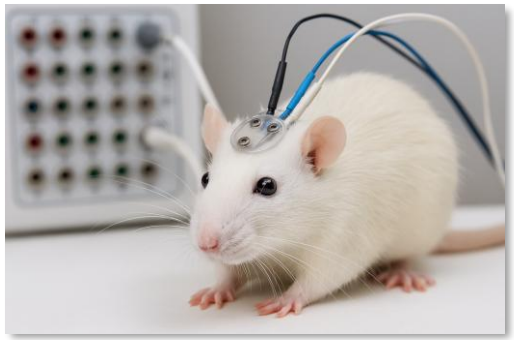
- ➢ Enable translation of preclinical pharmacodynamic readout into humans
- ➢ Provide objective readout of clinical observations
- ➢ Increase probability of success

1.Chen et al 2014; 2. Baur et al 20204; 3.Prashad et al 2018; 4. Nickolls et al 20184 5. Dumont et al 2004, 6. Nottage et al 2022

saniona

SAN2668 shows a distinct qEEG signature characterized by robust beta/gamma enhancement and no increases in delta activity, indicating preserved vigilance and no propensity for sedation

- **SAN2668 exhibits a unique qEEG profile** that is distinct from non-selective benzodiazepines
- **Produces a robust, dose-dependent increase in beta (β) and gamma (γ) power** during wakefulness - EEG markers associated with active cognition and vigilance
- **The magnitude of β and γ enhancement is stronger** than that typically observed with diazepam, supporting a differentiated pharmacology



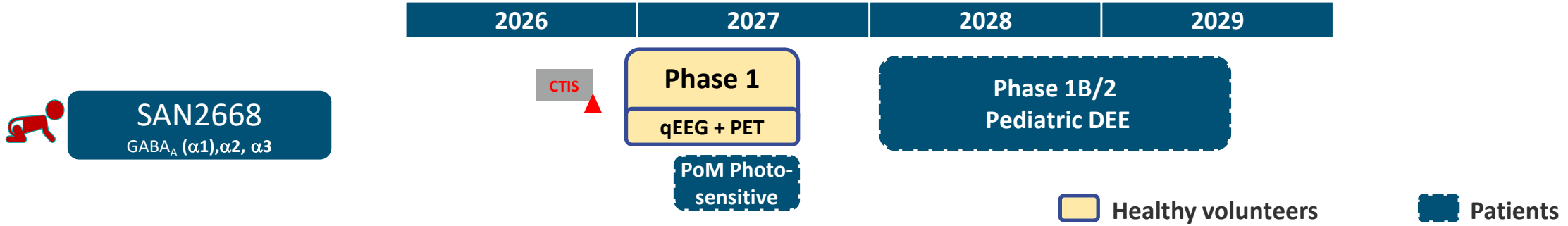
- **Lack of delta elevation and alpha suppression differentiates SAN2668 from non-selective GABAergic modulators** and sedative-hypnotic compounds and suggests preservation of vigilance
- **Overall sleep structure remains intact**, further supporting a favourable non-sedating profile

Unique qEEG signature in rodents with robust beta/gamma enhancement indicates preserved vigilance and no propensity for sedation

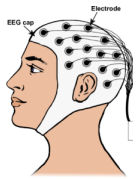
saniona

Phase 1 for SAN2668 will establish target engagement and pharmacodynamic biomarkers using qEEG and PET imaging to enable dose selection and support progression into Phase 1B/2 in paediatric DEE

SAN2668 Phase 1 expected late 2026 with Phase 1B/2 Ped DEE basket study late 2027

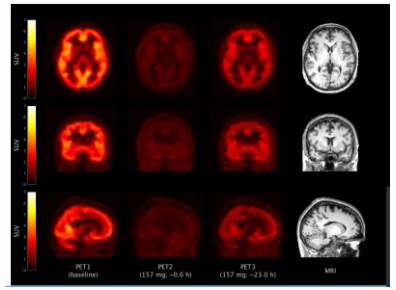


qEEG biomarkers will be used to confirm the expected GABA$_A$ α2/α3-selective pharmacology (i.e., reduced delta power) and to demonstrate lack of sedative effects

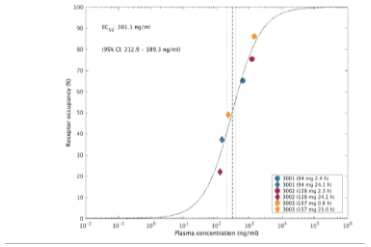


Compound	Gamma	Beta	Alpha	Theta	Delta	Ref
Benzodiazepines (lorazepam)	↑	↑	↓	↓	↑	Chen et al 2014
ACP-711 (alpha 3)	-	-	↑	-	↓	

PET imaging with [^{11}C] flumazenil will characterize receptor occupancy and establish exposure/RO correlation to support rational Phase 2 dose selection



Receptor Occupancy



Plasma Exposure

saniona

Table of Contents

Click to go to section

Executive summary - SAN2219

SAN2219 is a next-generation, oral, subtype selective $GABA_A$ PAM advancing toward phase 1

- **Targets refractory focal onset and generalized seizures** with anticipated high tolerability
- **Designed for robust seizure control** through predominant modulation of $GABA_A$ $\alpha2/\alpha3$ with no $\alpha1$-driven adverse effects for high tolerability
- **Highly potent and brain penetrant molecule:** low nM affinity to the target (human recombinant receptors)
- **Phase 1 planned for 2026, with PET study and established EEG biomarkers**
- **Patent protection through 2043**

SAN2219 has demonstrated potent seizure control:

- **Strong efficacy in acute focal- and generalized seizure models** (PTZ, MEST, 6Hz)
- **Additive effects when combined with standard AED**
- **Profiling in chronic epilepsy models ongoing:**
  - GAERS (Absence/Spike-Wave-Discharges) ✓
  - Amygdala kindling (focal-to-generalized seizures)
  - MTLE (mesial temporal lobe epilepsy)
- **Lack of motor impairments or sedative effects**
- **qEEG study to confirm lack of sedation ongoing**

saniona

The Burden of Drug-Resistant Epilepsy

- Despite the multitude of approved anti seizure medications there is a **sustained unmet need in epilepsy**
- **30% of patients are considered drug resistant**[1] - 1.5 million patients in G7
- Mortality rate in epilepsy patients is **10 times higher**[2]
- Every year 2,000 epilepsy patients die of **Sudden Unexpected Death**[3]
- **Uncontrolled Seizures**: Physical and Psychological Consequences, Lack independence [4]
- There is the **need of high efficacy ASM** with improved safety and tolerability profile

1 – Drug resistance defined according to ILAE (International League Against Epilepsy), i.e. fail to control seizures after two ASM
2 – Fazel et al 2013; Holst et al 2013; Hesdorfer et al 2013
3 – Laxer at al 2014
4 – Baker et al 1997; Taylor et al 2001; Azuma et al 2014

saniona

SAN2219 – Value proposition

SAN2219 has the potential to become a highly differentiated, broad-spectrum robust anti-seizure medication (ASM) for patients with focal and generalized seizures, designed to deliver high efficacy while minimizing the CNS tolerability limitations associated with currently available ASMs

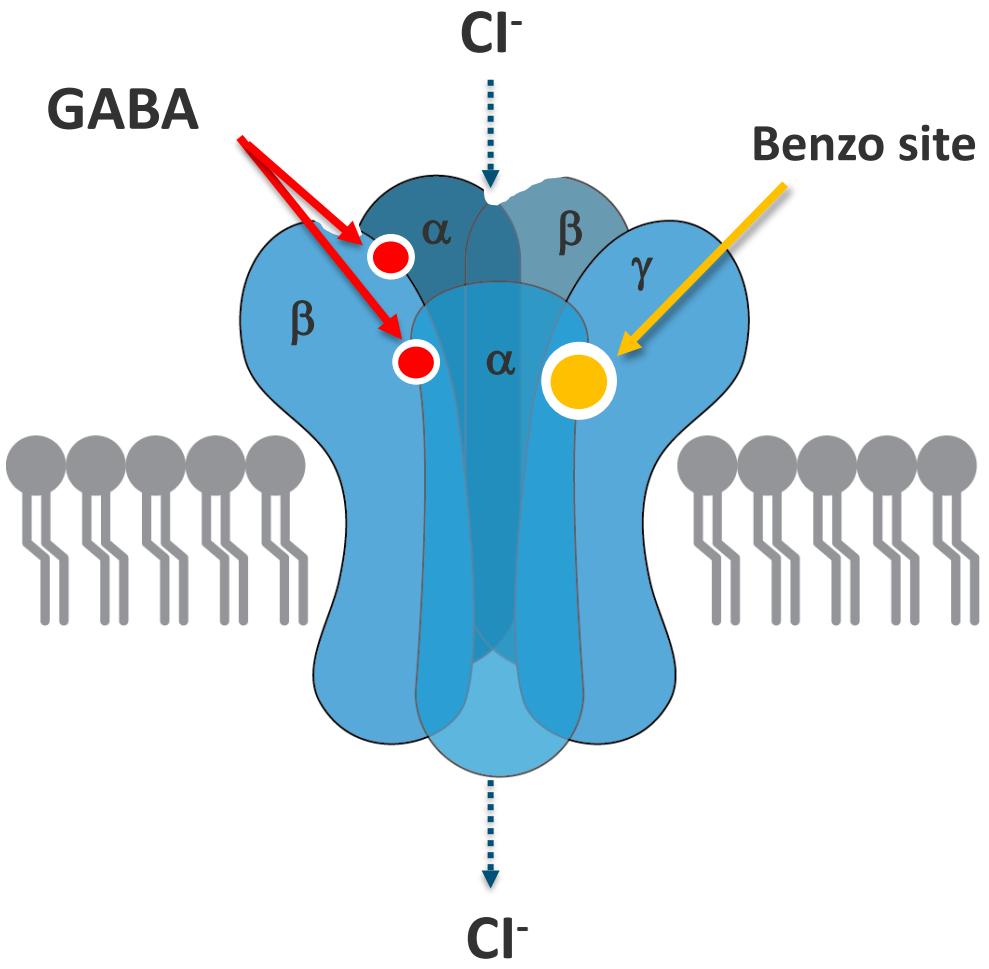
Key value messages

- **SAN2219 is a next-generation $GABA_A$ modulator designed to deliver the proven efficacy of benzodiazepines** with a safety and tolerability profile suitable for chronic use in epilepsy
- While benzodiazepines remain among the most effective antiseizure drugs, their **clinical utility is constrained by sedation**, cognitive impairment, and tolerance due to non-selective activation of α1-containing $GABA_A$ receptors
- SAN2219 was specifically engineered to overcome this limitation through functional selectivity for α2/α3/α5 receptor subtypes **with minimal α1 activity, enabling seizure control without the liabilities** that limit benzodiazepines in chronic therapy

saniona

The $GABA_A$ receptor is the molecular target for SAN2219

- **$GABA_A$ receptor is a ligand-gated ion-channel activated by GABA**
- **The channel consists of 5 subunits, various subtypes** (typically 2α, 2β and 1g, e.g., α2β3γ2)
- **The functional properties of each receptor subtype are primarily determined by the specific α-subunit composition** (α1, α2, α3 or α5)

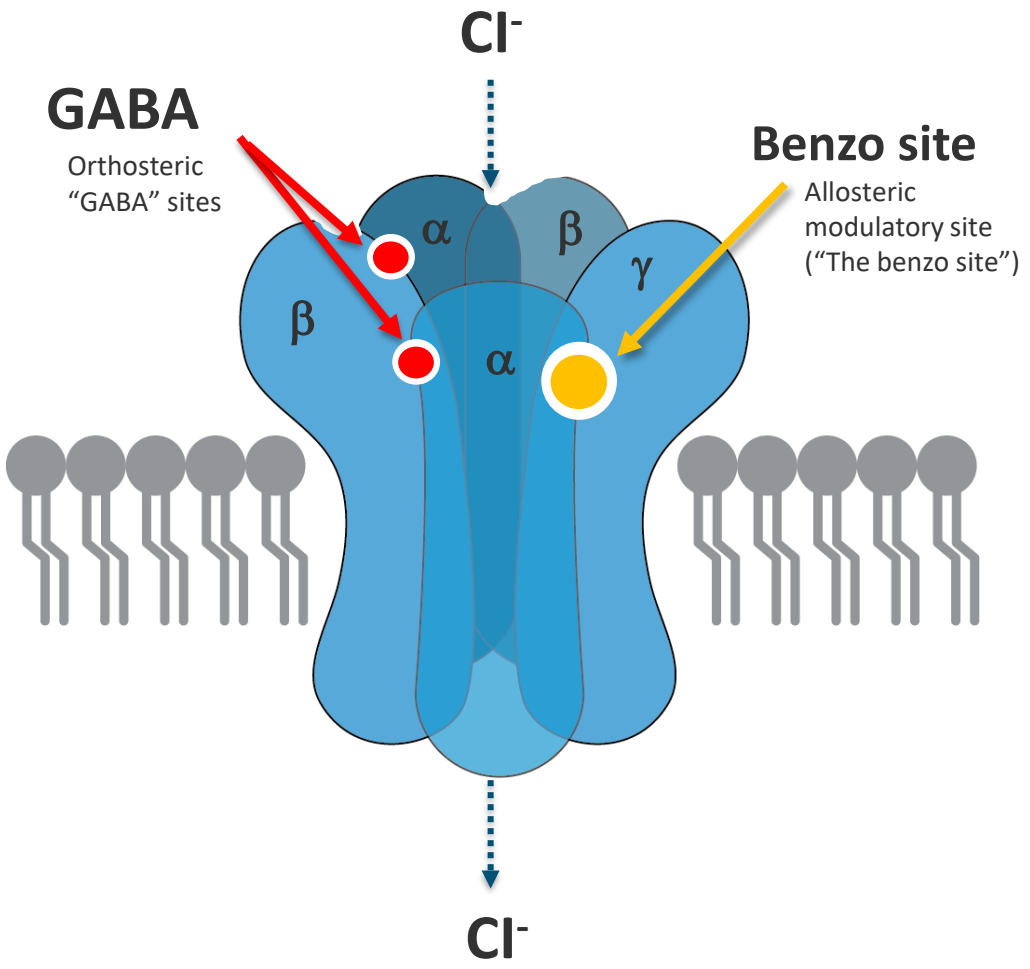


Mohler H., Dial. Clin. Neurosci. 2002

saniona

Benzodiazepines exert their pharmacological effects through positive allosteric modulation of The $GABA_A$ receptor

- **Orthosteric ("GABA") site - α/β interface**
  - Primary binding site where GABA binds
  - GABA binding opens the chloride channel, allowing Cl^- influx
  - Chloride influx hyperpolarizes the postsynaptic neurons, reducing excitability and suppressing action potentials
- **Allosteric modulatory site ("the benzo site") - α/γ interface**
  - Saniona's GABA PAMs bind here, similar to benzos
  - Saniona PAMs are structurally distinct from benzodiazepines
  - Located away from the GABA binding site, enabling modulation of GABAs effect
  - Ligands at this site do not open the channel on their own, but enhance GABA's effect (positive allosteric modulation; "PAM")
  - Likely responsible for the safer mode-of-action vs. barbiturates

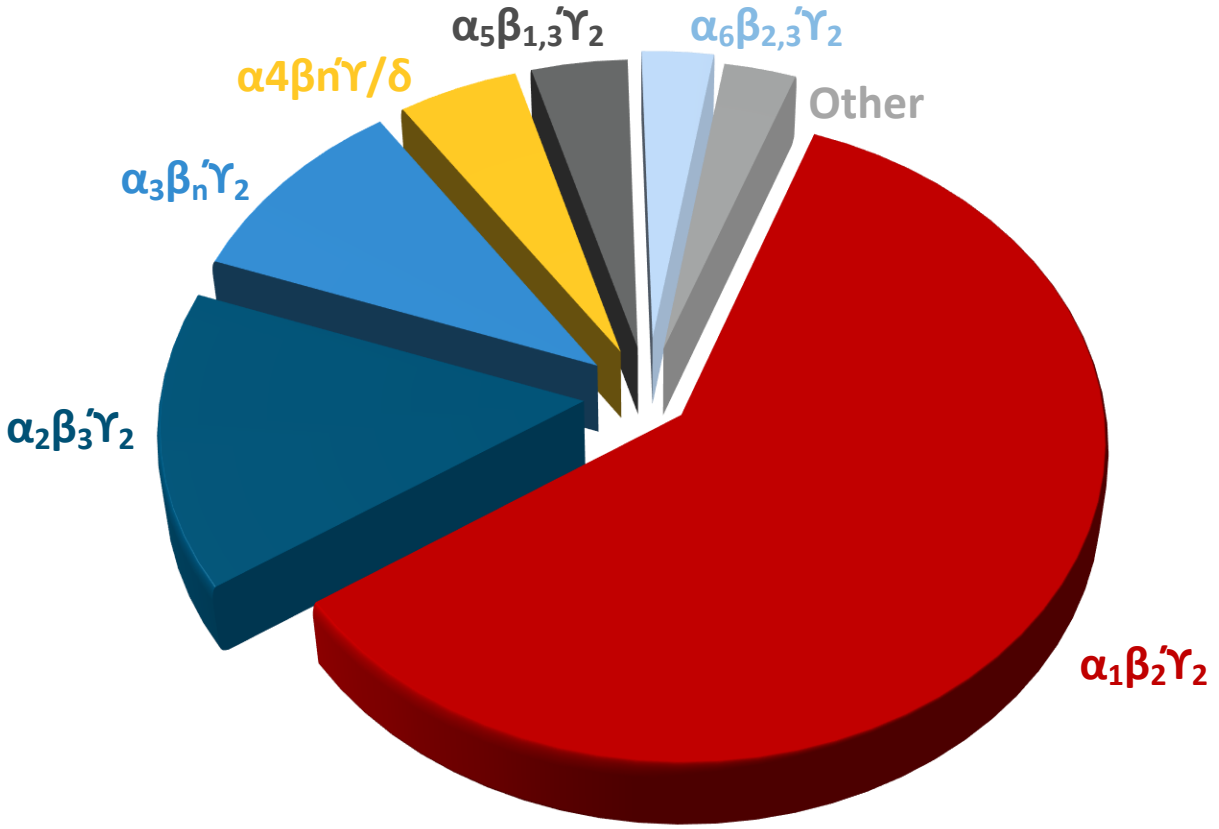


Vinkers et al., Expert. Opin. Investig. Drugs (2010) 19: 1217-1221, Rudolph & Knoflach, 2011, Nat. Rev. Drug Disc. 10:1-13

saniona

The majority of all $GABA_A$ receptors contain a BDZ site, and most of them contains the α1 subtype

- ~90% of all $GABA_A$ receptors contains a benzodiazepine binding site
- The vast majority of benzodiazepine binding sites in the human brain contains the $GABA_A$ α1 subtype (~60%)
- Followed by $GABA_A$ α2 (15-20%), $GABA_A$ α3 (10-15%) and $GABA_A$ α5 (< 5%)

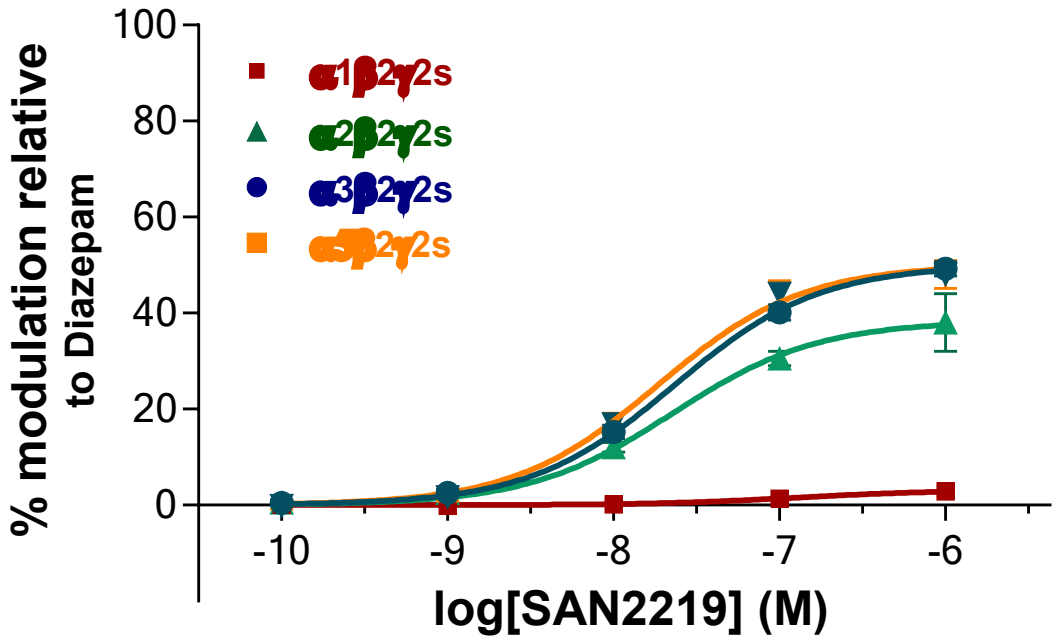


Mohler H., Dial. Clin. Neurosci. 2002

saniona

SAN2219 selectively modulates $GABA_A$ subtypes to suppress focal and generalized seizures while minimizing α1-driven adverse effects

SAN2219 differentially modulates $GABA_A$ receptors



Selective targeting $GABA_A$ receptors for strong seizure control and high tolerability

- $GABA_A$ α3: prevention of non-convulsive seizures with potential cognitive benefit
- $GABA_A$ α2: robust activity against convulsive seizures

SAN2219 is ideally suited to prevent focal and generalized seizures with high tolerability

saniona

SAN2219 shows stronger positive modulation of $GABA_A$ α2/α3 subtypes than competitor compounds, while maintaining negligible activity at the α1 subtype associated with sedation

	SAN2219 $GABA_A$ α2, α3, α5	Darigabat $GABA_A$ α2, α3, α5	ENX102 (TPA023B) $GABA_A$ α2, α3, α5
$GABA_A$ α1 (%)	3.2	4.1	5.0
$GABA_A$ α2 (%)	**38**	27	24
$GABA_A$ α3 (%)	**50**	36	37
$GABA_A$ α5 (%)	**50**	38	44

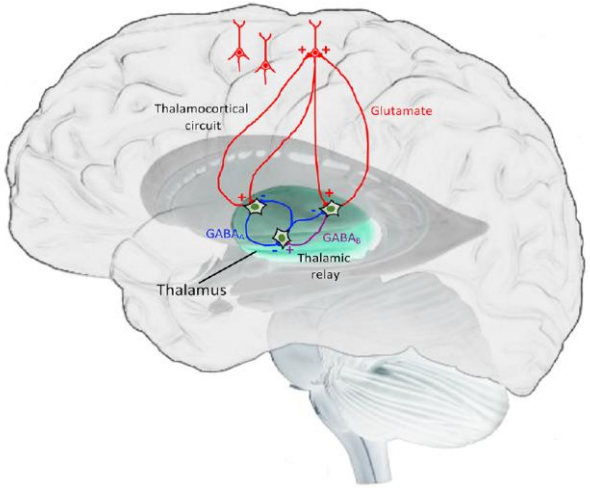
- **SAN2219 shows stronger positive modulation of efficacy-linked $GABA_A$ α2/α3/α5 subtypes** than competitor compounds, supporting a differentiated pharmacology profile
- **Minimal activity at the sedative-linked $GABA_A$ α1 subtype**, reducing the risk of benzodiazepine-like side effects

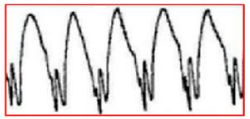
Saniona data on file: modulatory effect of SAN2219, Darigabat and TPA023B on $GABA_A$ receptors composed of $\alpha_1\beta_2\gamma_2$, $\alpha_2\beta_2\gamma_2$, $\alpha_3\beta_2\gamma_2$ and $\alpha_5\beta_2\gamma_2$ expressed in Xenopus oocytes. The percent modulation is indexed relative to the potentiating effects of 0.5 mM diazepam on the same oocytes

saniona

Spike-and-wave discharges are the abnormal EEG rhythms the drive absence seizures and define the EEG signature of severe paediatric epilepsies such as ESES

- **SPIKE AND WAVE DISCHARGES** is due to abnormal interaction in the cortico-thalamic (TRN) system
- $GABA_A$ α3 subunit show a **dense expression in TRN**, where α3 is exclusively expressed, among $GABA_A$ subunits (in humans as well as rodents)[1]
- Spontaneous rat model for absences (WAG/Rij rats) show **selective reduction** in α3 subunit protein in TRN[2]
- The anti-absence compound, **Clonazepam**, reduce SWDs in wildtype mice, but effect is lost in α3 point mutated mice rendered insensitive for BDZs[3]
- $GABA_A$ α3 subtype selective PAM **SAN711 suppresses SWDs** in GAERS rats[4] providing pharmacological evidence for a3-mediated suppression of SWDs





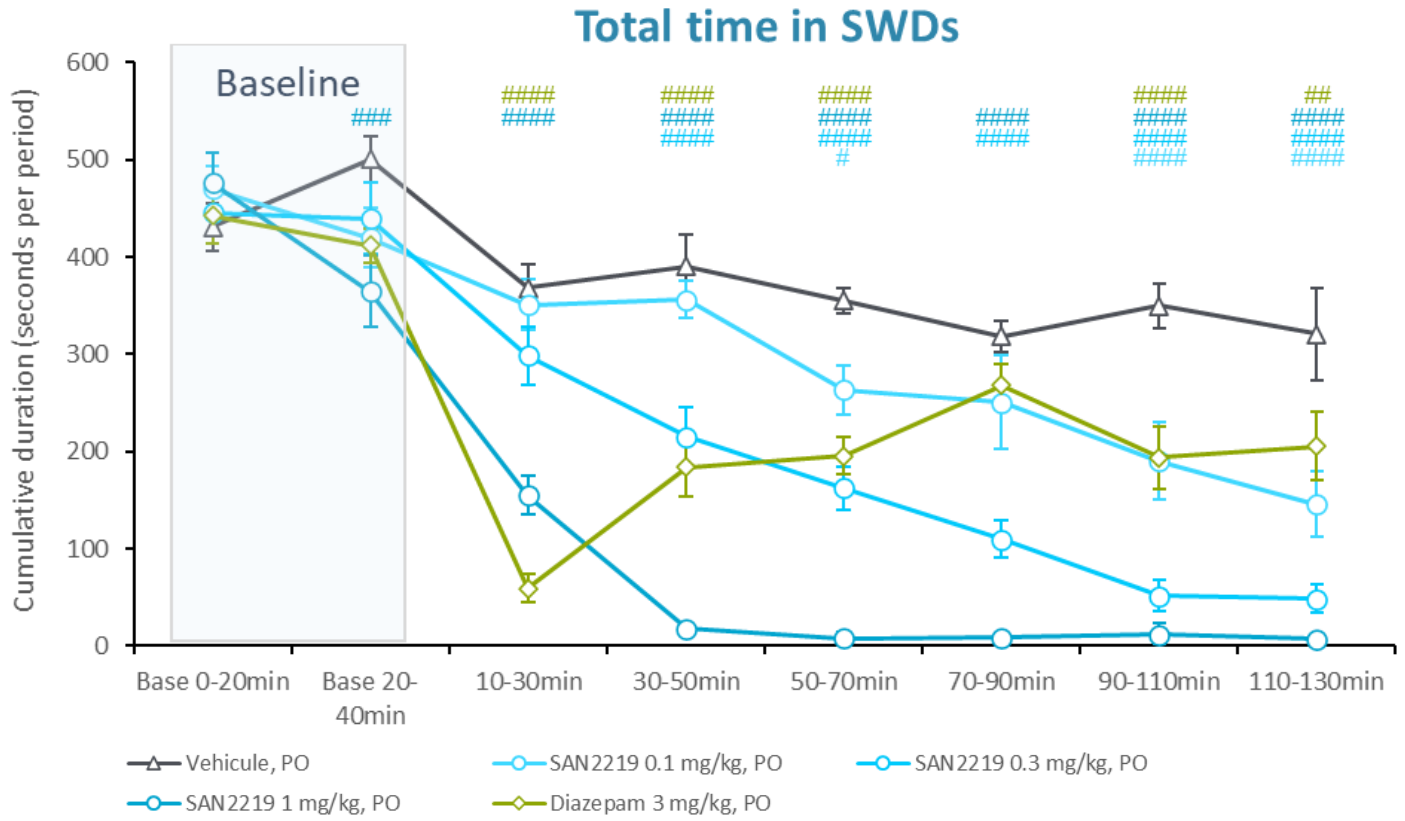
Spike and wave EEG

1Pirker et al., Neurosci. 2000, Waldwogel et al., J. Chem. Neuroanat. 2017
2Liu X et al., PNAS 2007
3Sohal VS, J. NeuroSci. 2003
4Crunelli V et al.,Soc.for Neurosci. 2023, PSTR526.08

saniona

SAN2219 fully suppresses pathological spike-wave-discharges in GAERS rats suggesting potent efficacy against absence seizures

- **GAERS rats demonstrated multiple spontaneous spike-wave-discharges (SWDs), reflected by increased time spent in SWDs**
- **SAN2219 potently suppresses SWDs in GEARS rats after oral administration, attaining the minimal efficacious dose level at ~20% receptor occupancy (RO) and full suppression achieved at ~80% RO**
- Bioanalytical analysis of plasma samples from study ongoing and final report pending



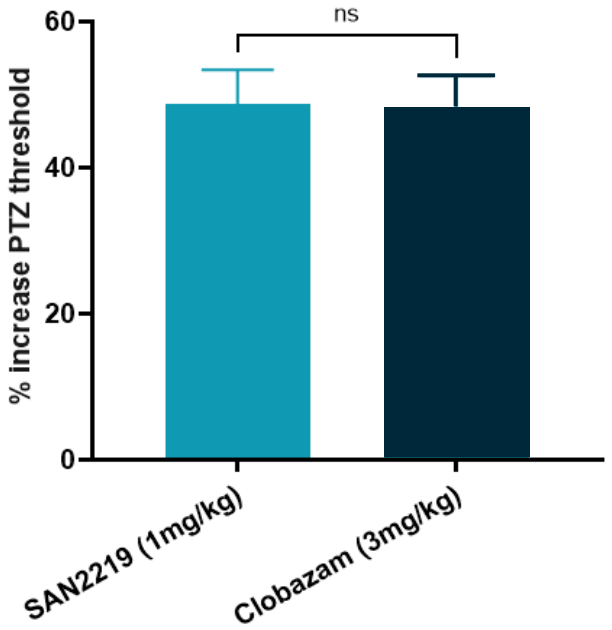
SAN2219 dose (mg/kg)	Projected receptor occupancy*
0.1	~ 20 %
0.3	~ 50 %
1.0	~ 80 %

*Based on Saniona internal rodent receptor occupancy study in rats

Vehicle: n = 10; Diazepam and all doses of SAN2219: n = 11. #, ##, ### and #### indicate significance versus vehicle ($p < 0.05$, 0.01, 0.001 and 0.0001, respectively).

SAN2219 demonstrates equal seizure control vs. non-selective Benzodiazepines, such as Clobazam, at high receptor occupancy

Generalized seizures: SAN2219, at a dose achieving >80% receptor occupancy, demonstrates comparable seizure control compared with Clobazam at clinically efficacious plasma exposure (~ 40 % receptor occupancy)*



Clobazam	Mouse	Human	RO
Dose	3 mg/kg	40 mg tablet	%
Cpl (free) (nM)	318	243**	~ 40

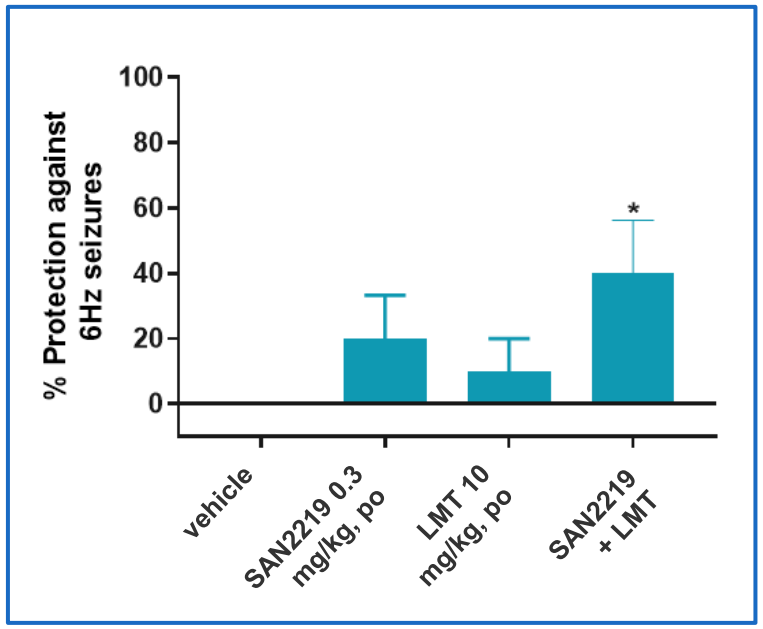
A clobazam dose of 3 mg/kg in mice achieves plasma concentrations comparable to those observed in humans after a 40 mg dose when correcting for species differences in plasma protein binding. This concentration corresponds to ~40% receptor occupancy (RO).
*Calculated based on plasma samples from study B11047
**Tolbert et al., J. Clin. Pharmacol. 2019.

saniona

SAN2219 shows additive effects when combined with standard of care

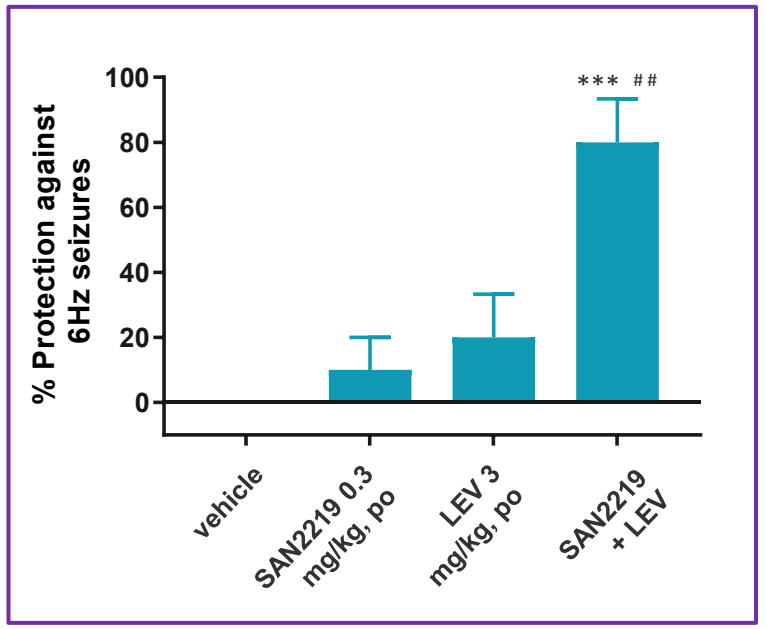
- At sub-therapeutic dose levels, **SAN2219 produces additive protection in the 6-Hz focal-seizure model when co-administered** with sub-therapeutic dose of different anti-seizure medications:
  - **Lamotrigine** (sodium-channel blocker)
  - **Levetiracetam** (SV2A modulator)
  - **Valproic acid**

With Lamotrigine



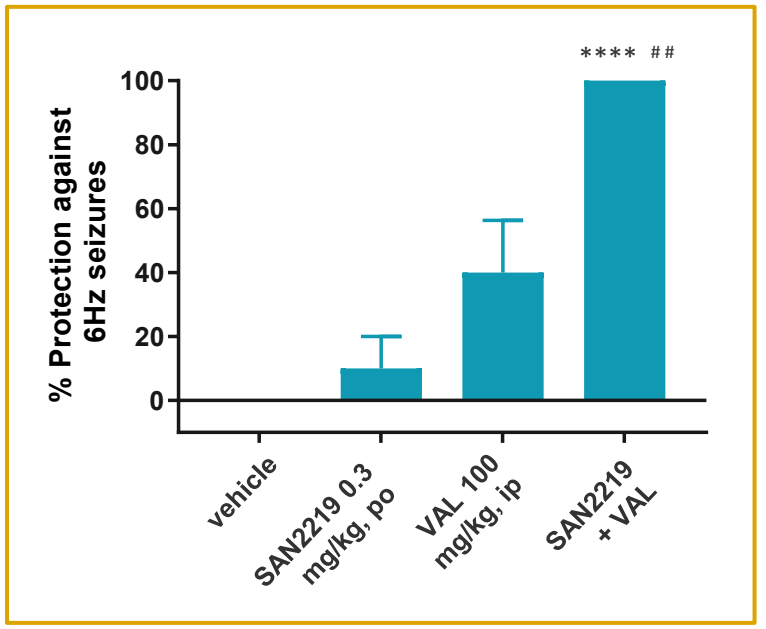
*/**: p < 0.05/0.01 vs. vehicle

With Levetiracetam



***: p < 0.001 vs. SAN2219, # #: p < 0.01 vs. Levetiracetam

With Valproic acid

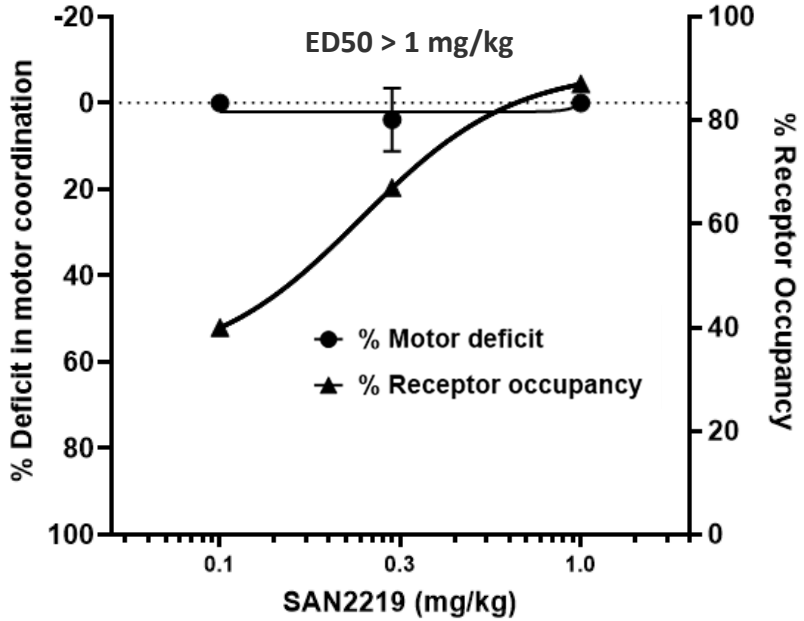


****: p < 0.0001 vs. SAN2219, # #: p < 0.01 vs. Valproic acid

saniona

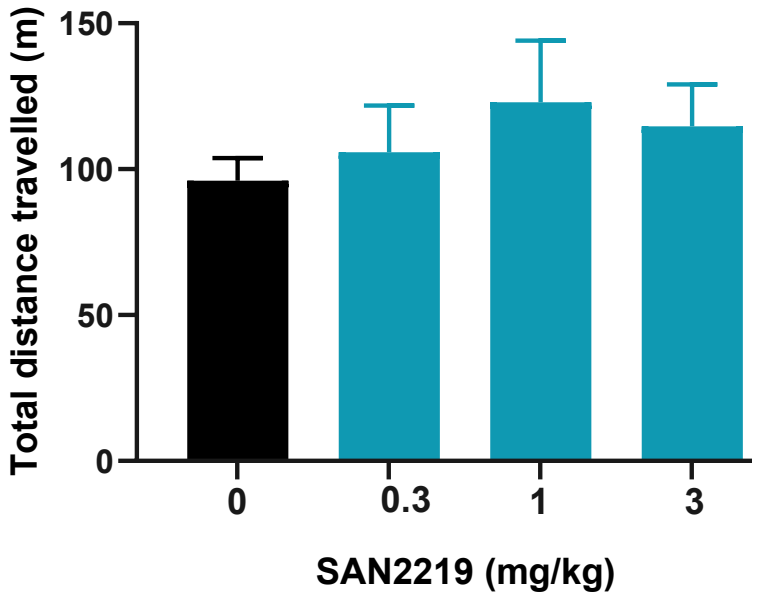
SAN2219: does not adversely affect motor performance or cause sedation in rodents in pharmacological relevant dose levels

Adverse effects, Rotarod: SAN2219 does not cause motor impairments in rodents at pharmacologically relevant dose levels which contrasts with benzodiazepines



Motor impairments is assessed by placing rodents on an accelerating rotarod and measuring the latency to fall. The test drug is administered according to Tmax.
A minimal effective dose and the ED50 are determined. *ED50 is the estimated dose producing 50% motor impairment relative to vehicle-treated rats.*

Adverse effects, locomotor activity: SAN2219 does not cause sedation in rodents at pharmacologically relevant dose levels which contrasts with benzodiazepines

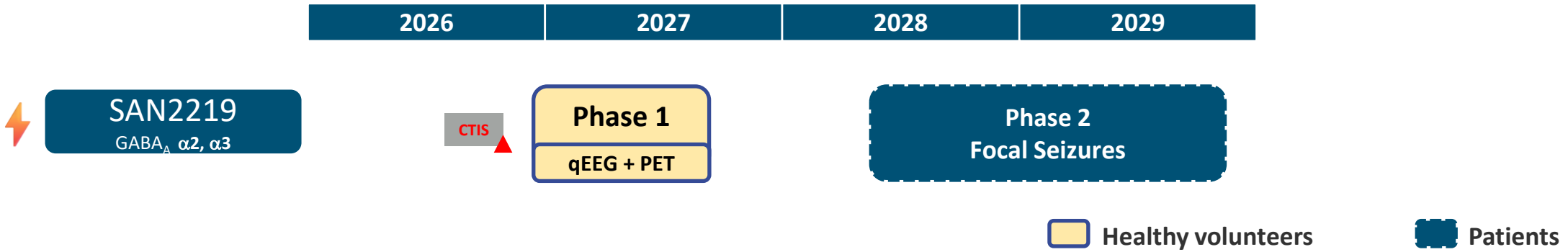


Sedation is assessed by placing rodents in a novel environment that promotes exploratory locomotor activity and measuring the distance travelled over 30 minutes.
The test drug is administered according to Tmax.
A minimal effective dose (MED) is established.

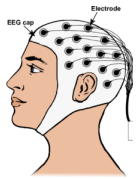
saniona

Phase 1 for SAN2219 will establish target engagement and pharmacodynamic biomarkers using qEEG and PET imaging to enable dose selection and support progression into Phase 2 in 2028

SAN2219 Phase 1 expected late 2026 with Phase 2 study 2028

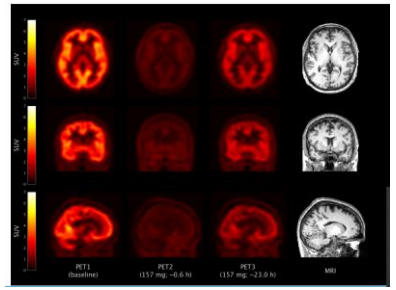


qEEG biomarkers will be used to confirm the expected GABA$_A$ α2/α3-selective pharmacology (i.e., reduced delta power) and to demonstrate lack of sedative effects

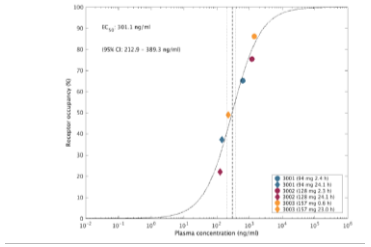


Compound	Gamma	Beta	Alpha	Theta	Delta	Ref
Benzodiazepines (lorazepam)	↑	↑	↓	↓	↑	Chen et al 2014
ACP-711 (alpha 3)	-	-	↑	-	↓	

PET imaging with [^{11}C] flumazenil will characterize receptor occupancy and establish exposure/RO correlation to support rational Phase 2 dose selection



Receptor Occupancy



Plasma Exposure

saniona

Table of Contents

Click to go to section

saniona

Executive summary - SAN2465

SAN2465 is a novel, oral, subtype selective $GABA_A$ α5 NAM advancing toward phase 1

- **Fast onset of action antidepressant** not requiring intensive in-clinic monitoring with **additional benefit in patients with cognitive dysfunction**
- **Highly selective GABAA α5 NAM,** mode of action differentiated from conventional antidepressants and novel investigational psychedelics
- **Improved adverse effects profile** through restricted expression of $GABA_A$ α5 receptors in the brain
- **Highly potent and brain penetrant molecule:** low nM affinity to the target (human recombinant receptors)
- **Phase 1 planned for 2026, with PET study and established EEG biomarkers**
- **Patent protection through 2041**

SAN2465 has demonstrated rapid onset efficacy in gold standard model, the chronic mild stress model:

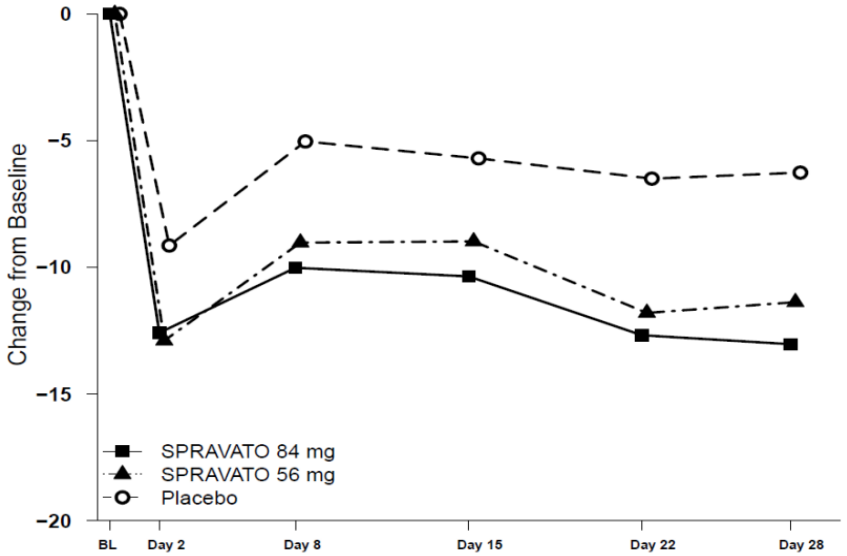
- **Rapid, full- and sustained reversal of chronic stress-induced depressive-like symptoms** including anhedonia, anxiety, and cognitive impairment
- **Onset and effect-size** comparable to ketamine
- **Cognitive improvement** additionally confirmed in working memory test
- **qEEG study in rodents** ongoing
- **Opportunity within rare neurodevelopmental disorder** (Dup15q syndrome)

saniona

Unmet need in MDD: Fast onset of action & cognitive impairment remain significant unmet needs

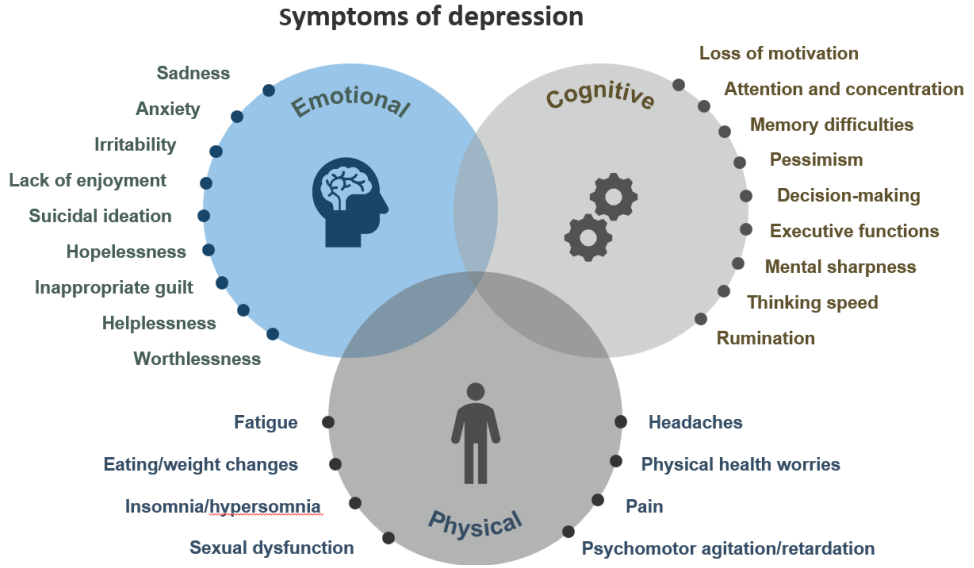
Onset of action

- Traditional antidepressants take 4-8 weeks to onset of effect
- Industry has pursued faster onset for decades
- Ketamine breakthrough demonstrated possibility to achieve faster onset
- Use of (es)ketamine restricted to in-clinic administration
- Many patients not eligible for ketamine treatment, high cost



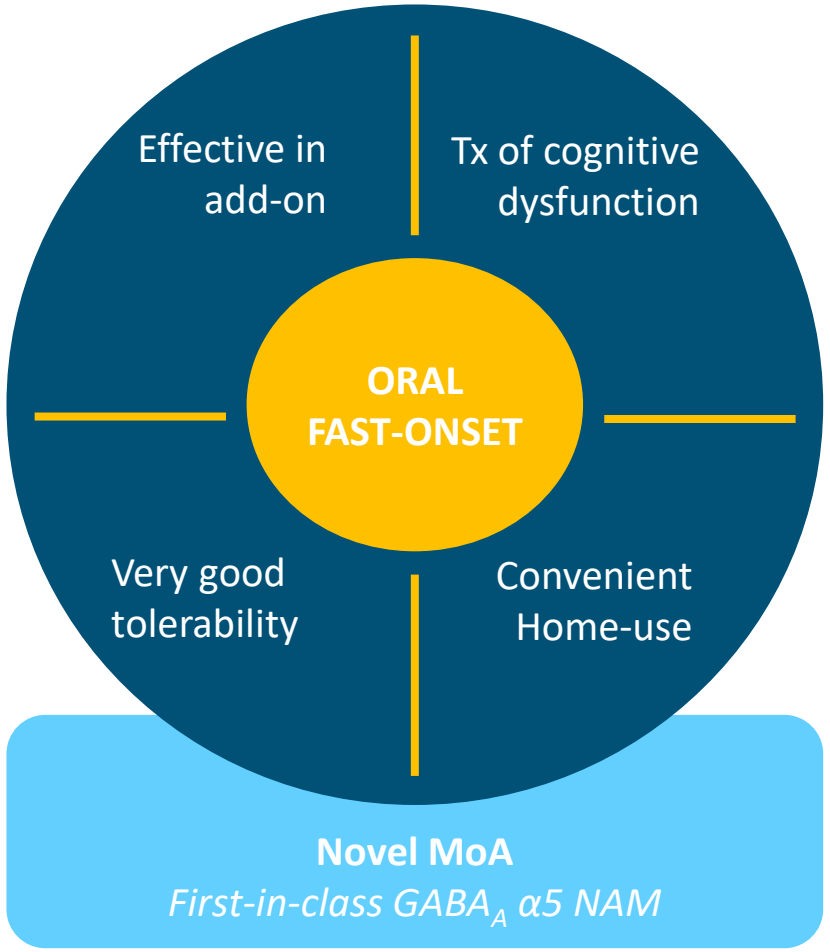
Cognitive impairment

- Cognitive symptoms in patients with MDD are common, persistent, and often debilitating
- Cognitive impairment occurs during and between episodes of MDD
- The persistence of cognitive deficits after remission of depressive symptoms has been shown to contribute to the failure in achieving full functional recovery



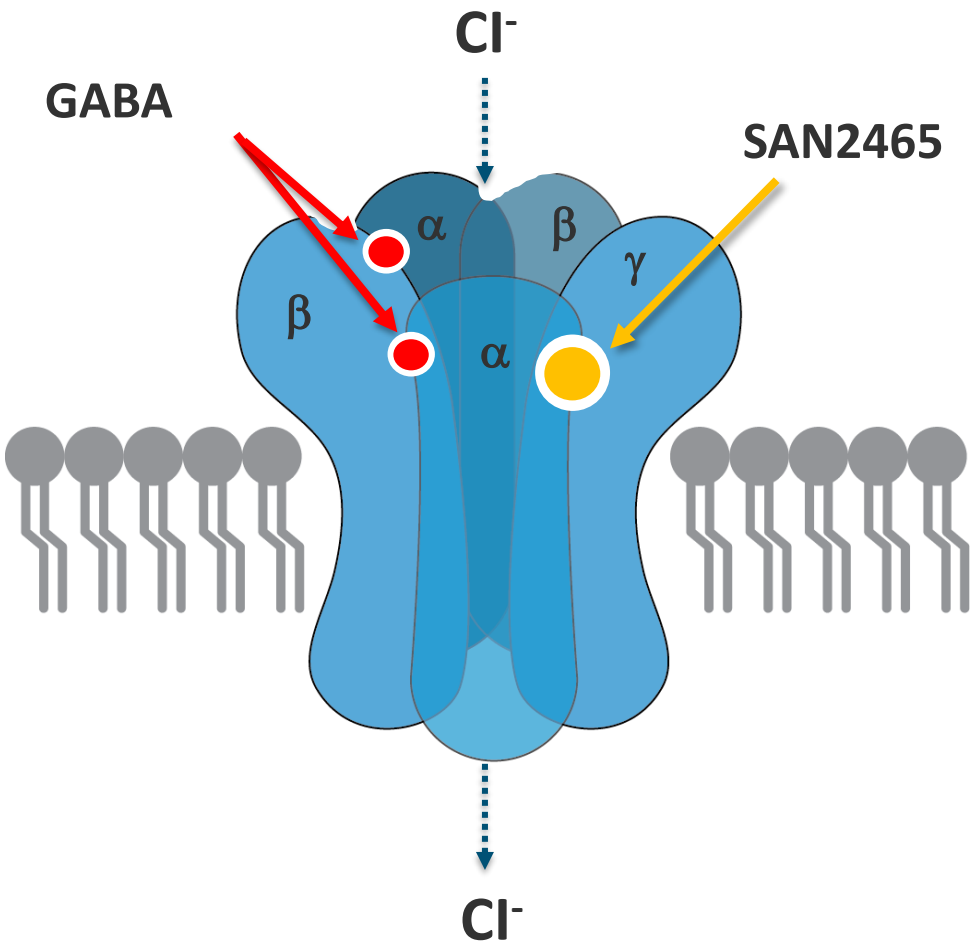
SAN2465 – Value Proposition

- SAN2465 has the potential to become a **differentiated fast onset of action**, orally administered **antidepressant** not requiring intensive in-clinic monitoring
- Add-on of choice for both MDD **patients with inadequate response OR treatment resistance**
- **Pro-cognitive benefit potential**, a positive prognostic factor for antidepressant efficacy and improvement on activity of daily living and and quality of life



The molecular target for SAN2465 is the $GABA_A$ receptor

- **$GABA_A$ receptor is the molecular target for SAN2465**
- **The $GABA_A$ receptor is a hetero-pentameric chloride-conducting channel**; when activated by $GABA_A$ induces hyperpolarization of the postsynaptic membrane and reduces neuronal excitability
- **SAN2465 binds at the allosteric modulatory site** (”Benzodiazepine (BDZ) binding site”) in the α–γ interface
- **The majority of human (and rodent) brain $GABA_A$ receptors contain a benzodiazepine** binding site (~90%)
- **$GABA_A$ α5 containing receptors** are enriched in the hippocampus:
  - $GABA_A$ α5 comprise < 5% of total BDZ sites in the brain but approximately 20% in the hippocampus

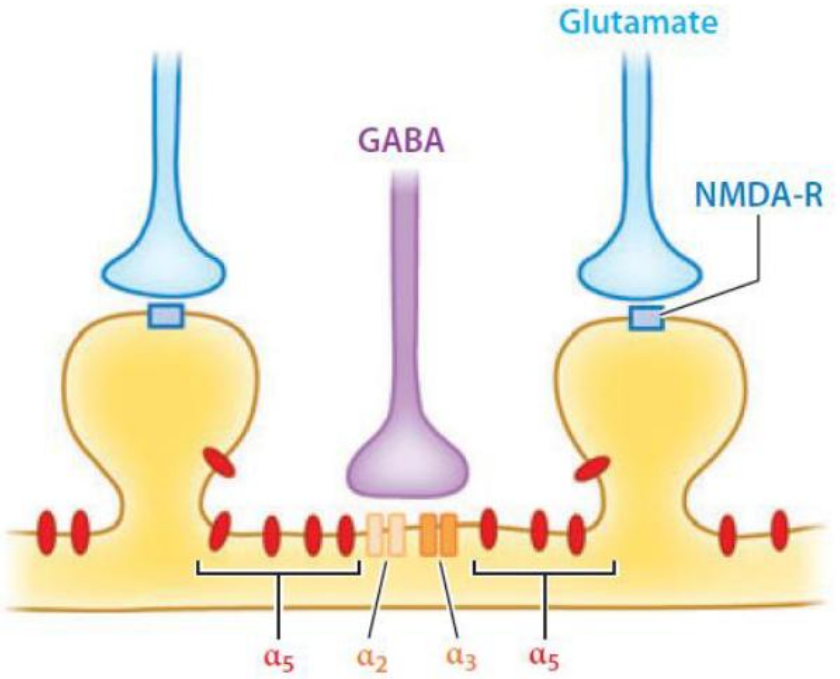


Mohler, Dial.Clin.Neurosci. (2002) 4(3): 261-269 , Vinkers et al., Expert. Opin. Investig. Drugs (2010) 19: 1217-1221

saniona

$GABA_A$ α5 containing receptors are localized on hippocampal pyramidal neurons and mediate tonic inhibition

- **The $GABA_A$ α5 containing receptors** are localized extrasynaptically on dendritic spines of pyramidal neurons in CA1/CA3 region, **mediating tonic inhibition of excitatory output**
- **Negative allosteric modulation (NAM**) of $GABA_A$ α5 containing receptors will lead to hippocampal *disinhibition* and increased excitatory output to target structures
- **Comparable to ”releasing-the-brake”**

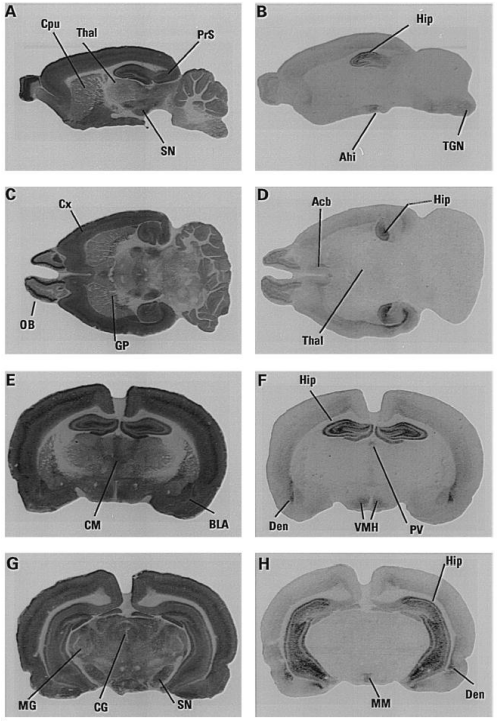


Rudolph & Mohler, Annu. Rev. Pharmacol. Toxicol., (2014) 54:483-507

$GABA_A$ α5 containing receptors are preferentially expressed in hippocampal/limbic areas
The expression pattern is conserved across species

Rat

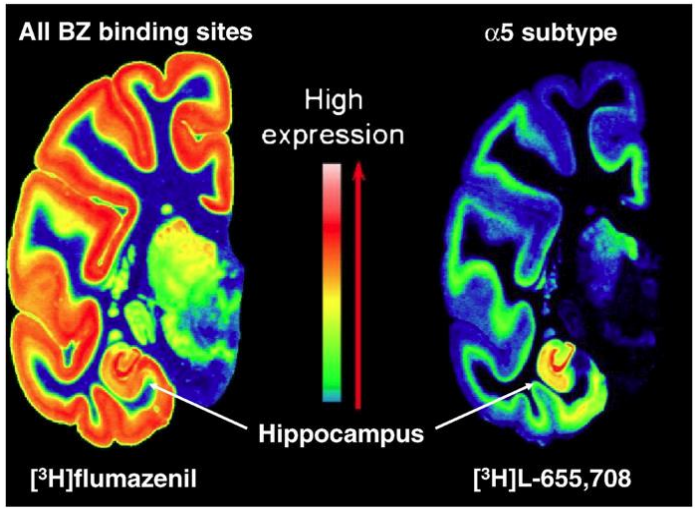
^{3}H-Ro15-1788 ^{3}H-L655,708



Sur et al., Brain Res. (1999) 822: 26-270

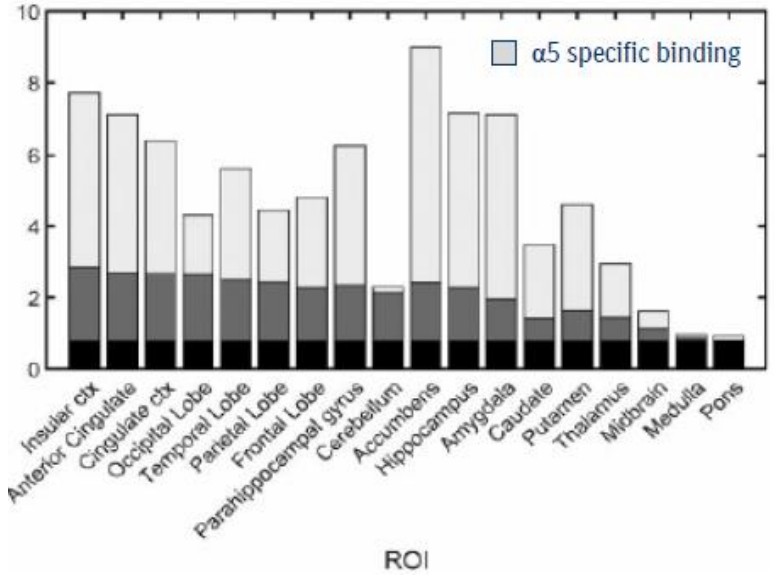
Primate

^{3}H-Ro15-1788 ^{3}H-L655,708



Human

^{11}C-Ro15-4513 in humans



^{3}H-Ro15-1788 (Flumazenil) binds to all $GABA_A$ receptors while ^{3}H-L655,708 only binds to $GABA_A$ α5 containing receptors

^{11}C-Ro15-4513 shows preferential binding to $GABA_A$ α5 containing receptors and can be used for human target engagement studies

Atack J, Pharmacol. Therapeutics (2010) 125: 11-26, Myers et al., JCBFM (2016): 1-12, Sur et al., Brain Res. (1999) 822: 26-270

saniona

$GABA_A$ α5 NAM Mode of Action in Depression - the hypothesis[1]:

- **Ketamine presumably works by inhibiting the NMDA receptors localized on GABAergic interneurons**. This results in disinhibition of the principal neurons, increased glutamate neurotransmission, increased AMPA signalling and triggering of several activity dependent synaptic strengthening processes (e.g., LTP, expression of Immediate Early Genes etc.)

- **This ultimately leads to the rapid induction of neuroplastic changes in the reward circuitry** responsible for the fast- and sustained resolution of depressive signs and symptoms

$GABA_A$ α5 receptors are localized directly on the principal neurons and a $GABA_A$ α5 NAM will - by "releasing the brake" - reduce the inhibition of the principal neurons directly resulting in comparable neuroplastic changes in the reward circuitry and fast-onset resolution of anhedonia

- **As the expression of $GABA_A$ α5 receptors are mainly restricted to limbic areas**, the adverse effects experienced by ketamine, is not anticipated

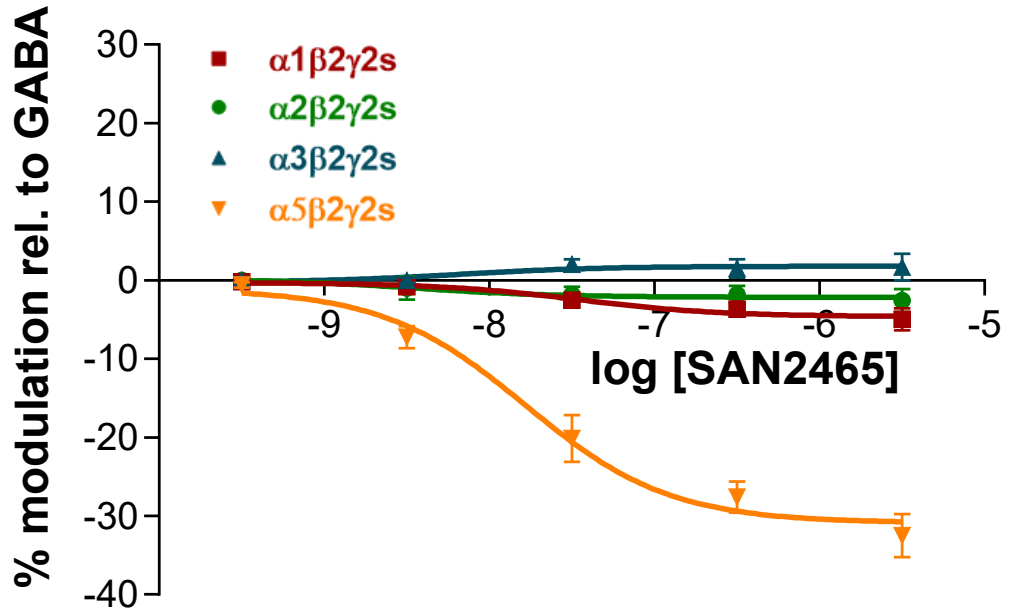
- **A very benign safety profile is confirmed by published data on Basmisanil**, that was reported to be safe and well tolerated at receptor occupancies > 90 %[2]

[1]*Fischell et al. Neuropsychopharmacol., 2015, 40(11): 2499-509); Zanos P et al., eNeuro 2017, Trippoli T.A et al., Biol. Psychiat. 2021*
[2]*Hipp J.F et al., Sci. Report 2021*

saniona

SAN2465 selectively modulates $GABA_A$ α5 subtypes for specific modulation of limbic circuitry and rapid onset antidepressant efficacy

SAN2465 selectively modulates $GABA_A$ α5 receptors



Selective targeting $GABA_A$ α5 receptors for rapid onset antidepressant efficacy combined with cognitive improvement

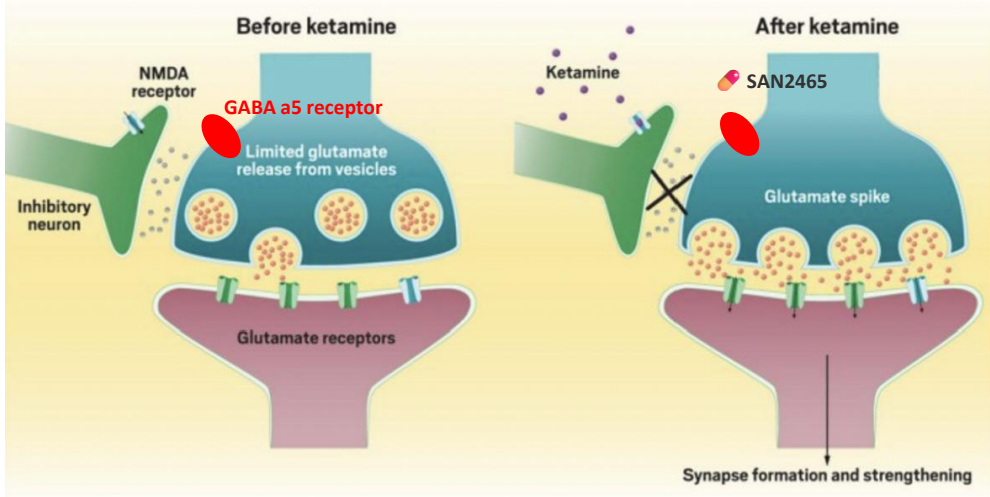
- $GABA_A$ α5: specific modulation of limbic circuitry, including hippocampus, for rapid onset efficacy with additional cognitive benefit
- No modulation of $GABA_A$ α1, α2 or α3 receptors: selective pharmacology to avoid adverse effects

SAN2465 is ideally suited for rapid antidepressant efficacy, devoid of adverse effects, in patients with cognitive impairment

saniona

Innovative mode of action of SAN2465: opportunity for rapid resolution of depressive symptoms devoid of ketamine-induced adverse effects

SAN2465 and Ketamine: Distinct mechanisms but shared downstream pathway to neuronal plasticity and rapid antidepressant effects



- Ketamine indirectly increase glutamate release by inhibiting inhibitory neurons, promoting neural plasticity and rapid antidepressant efficacy
- SAN2465, by reducing GABA's influence on glutamate neurons directly ("releasing the brake"), is thought to trigger similar plastic changes

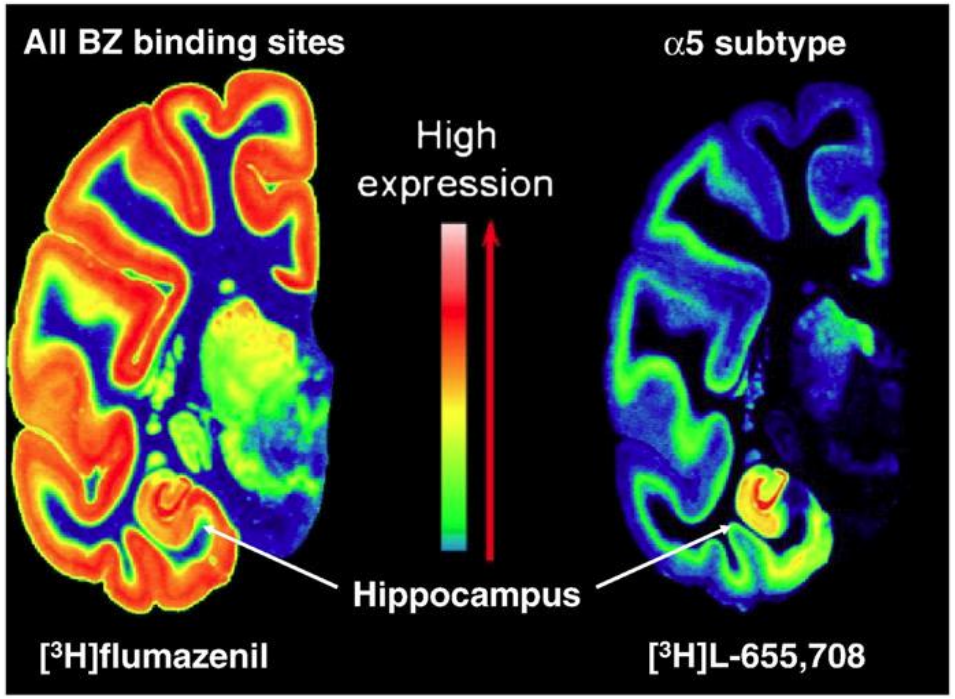
How Ketamine Works Quickly When Other Treatments Have Failed - Heading Health

Fischell et al. Neuropsychopharmacol., 2015, 40(11): 2499-509); Zanos P et al., eNeuro 2017, Trippoli T.A et al., Biol. Psychiat. 2021

SAN2465: Improved side-effect profile through restricted expression of $GABA_A$ α5 receptors in the brain -unlike Ketamine's broad CNS activity

Mapping of all $GABA_A$ receptors by ^{3}H-Ro15-1788

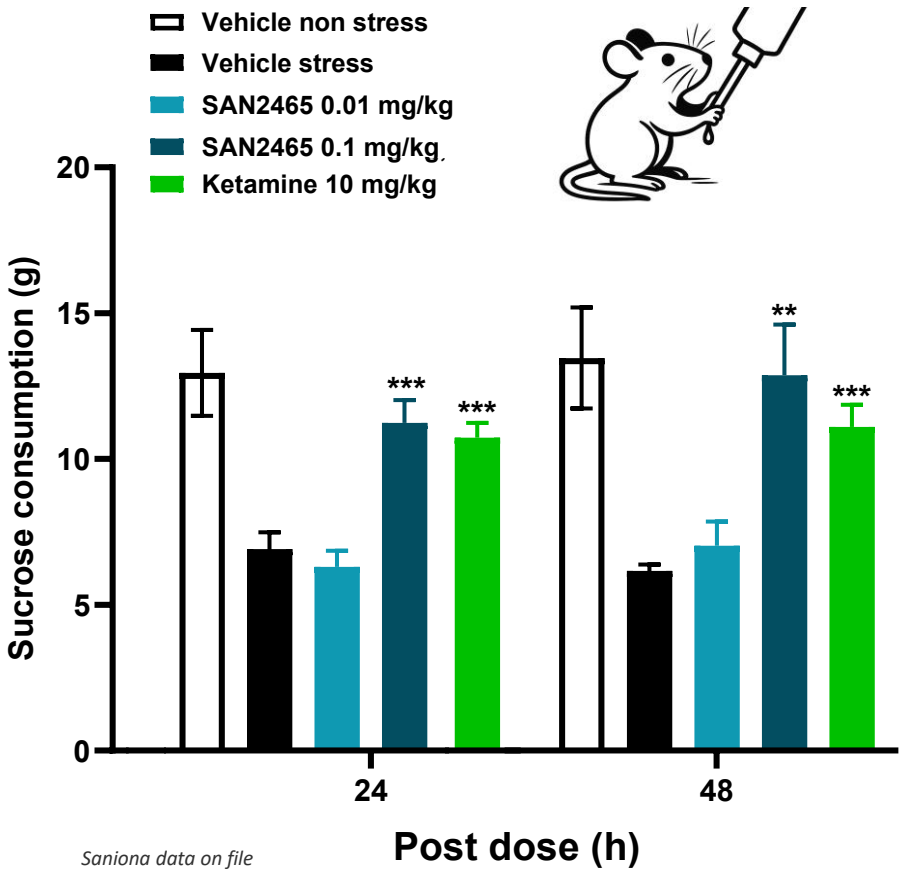
Mapping of $GABA_A$ α5 receptors by ^{3}H-L655,708



Atack J, Pharmacol. Therapeutics (2010) 125: 11-26

saniona

SAN2465 demonstrates rapid and sustained normalization of stress-induced anhedonic-like behavior in the chronic mild stress model



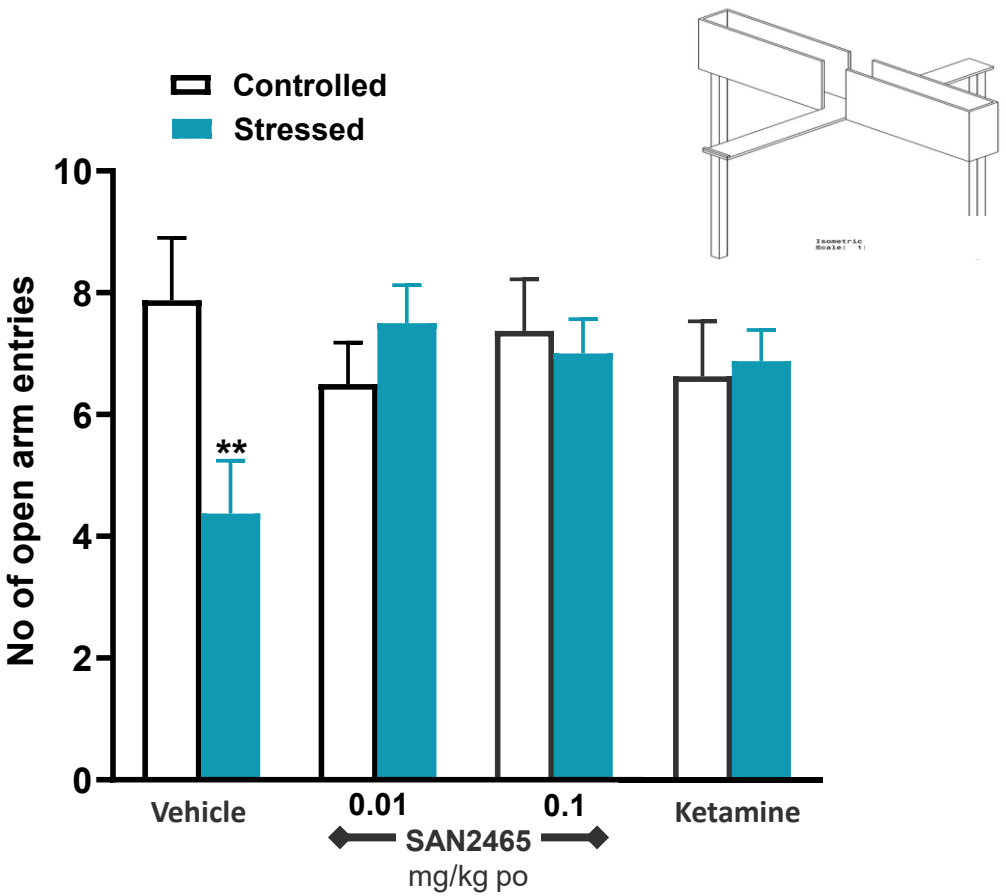
Saniona data on file

SAN2465 0.01 mg/kg, 0.1 mg/kg and ketamine dosed once 24 hours prior to testing
/*P<0.01/0.001 vs. vehicle stress two-way ANOVA (stress/treatment) followed by Fishers LSD test

- **ANHEDONIA:** Core symptom in MDD, is the lack of ability to feel pleasure or to engage in pleasurable activities ("Anhedonia")
- **Anhedonia-like behavior can be measured as a stress-induced reduction of sucrose consumption in rodents** ("reduced engagement in pleasurable activities")
- **SAN2465 demonstrates:**
  - **Dose-related effect with full normalization** of anhedonic-like behavior at 0.1 mg/kg [■] oral administration
  - **The onset is rapid**, within 24 hours post dosing which contrasts with conventional antidepressants, where onset of effect is only observed after 3-5 weeks of daily dosings in the CMS model[1]
  - **The effect is sustained** after a single oral administration, lasting at least 48 hours post dosing
  - **The effect onset and effect size is comparable to that of Ketamine** [■], that has proven rapid-onset antidepressant efficacy in depressed patients[2]
  - **Acute dosing of 0.1 mg/kg 2 hrs prior to sucrose testing, does not significantly affect sucrose consumption,** potentially indicating that reversal of anhedonia requires downstream adaptive mechanisms (data not shown)

1 Papp M., et al., Eur. J. Psychopharmacol. 1996
2. Berman RM et al., Biol. Psychiat. 2000

SAN2465 demonstrates full reversal of stress-induced anxiogenic-like behaviors when dosed 48 hours prior to test

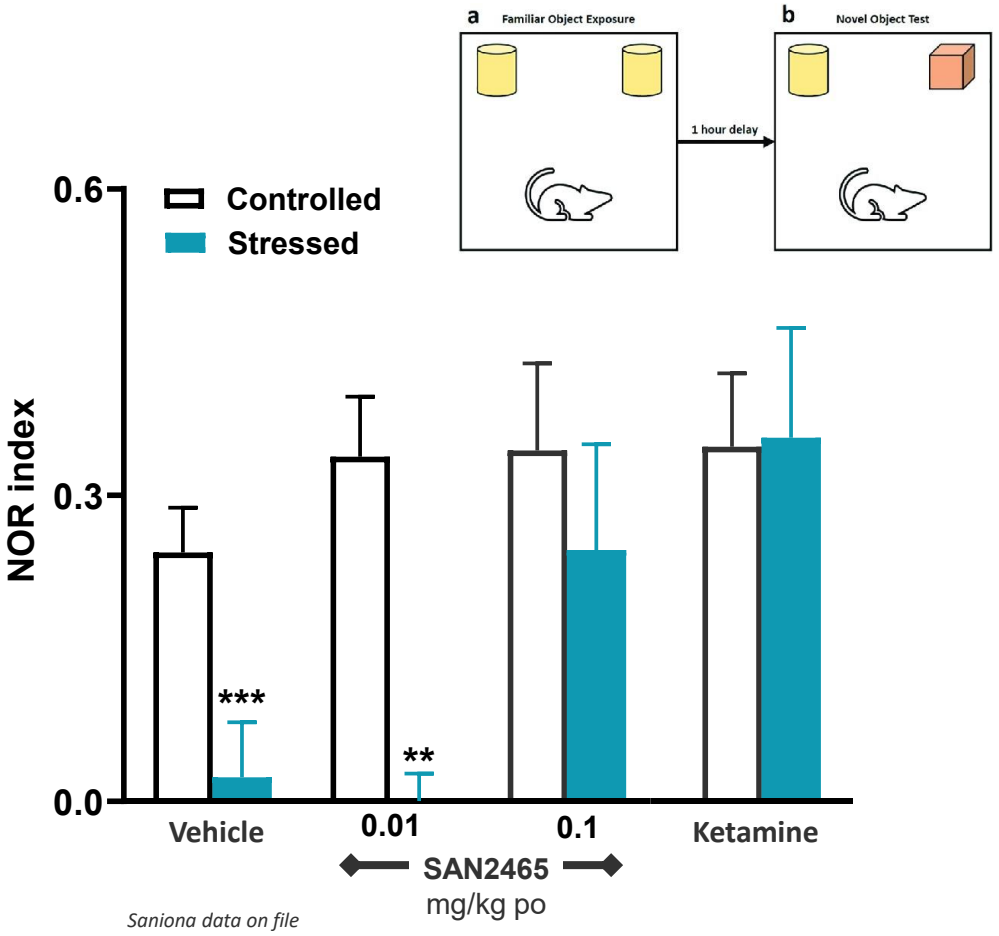


Saniona data on file

SAN2465 0.01 mg/kg, 0.1 mg/kg and ketamine dosed once 48 hours prior to testing
**: $p < 0.01$ vs. non-stressed control group
Ketamine: 10 mg/kg

- **ANXIETY:** Comorbid symptom in MDD, can present as generalized anxiety characterized by persistent excessive worry that is difficult to control
- **Generalized anxiety-like behaviour can be assessed in rodents** in the **elevated plus maze** by measuring stress-induced avoidance of open arms and preference for closed arms, reflecting a shift from natural exploratory tendencies.
- **SAN2465 demonstrates:**
  - **Chronic stress results in avoidance of open arms** vs. non-stressed control group
  - **Full reversal of stress-induced avoidance of open arms** at all doses tested (0.01, 0.1 mg/kg, po) when dosed 48 hours prior to testing.
  - **The effect size is comparable to that of ketamine**
  - **Acute dosing** of 0.1 mg/kg 2 hrs prior to testing, **significantly ameliorates stress-induced anxiogenic-like behaviours** (data not shown)

SAN2465 demonstrates full reversal of stress-induced cognitive impairment when dosed 72 hours prior to test in the Novel Object Recognition Test



Saniona data on file

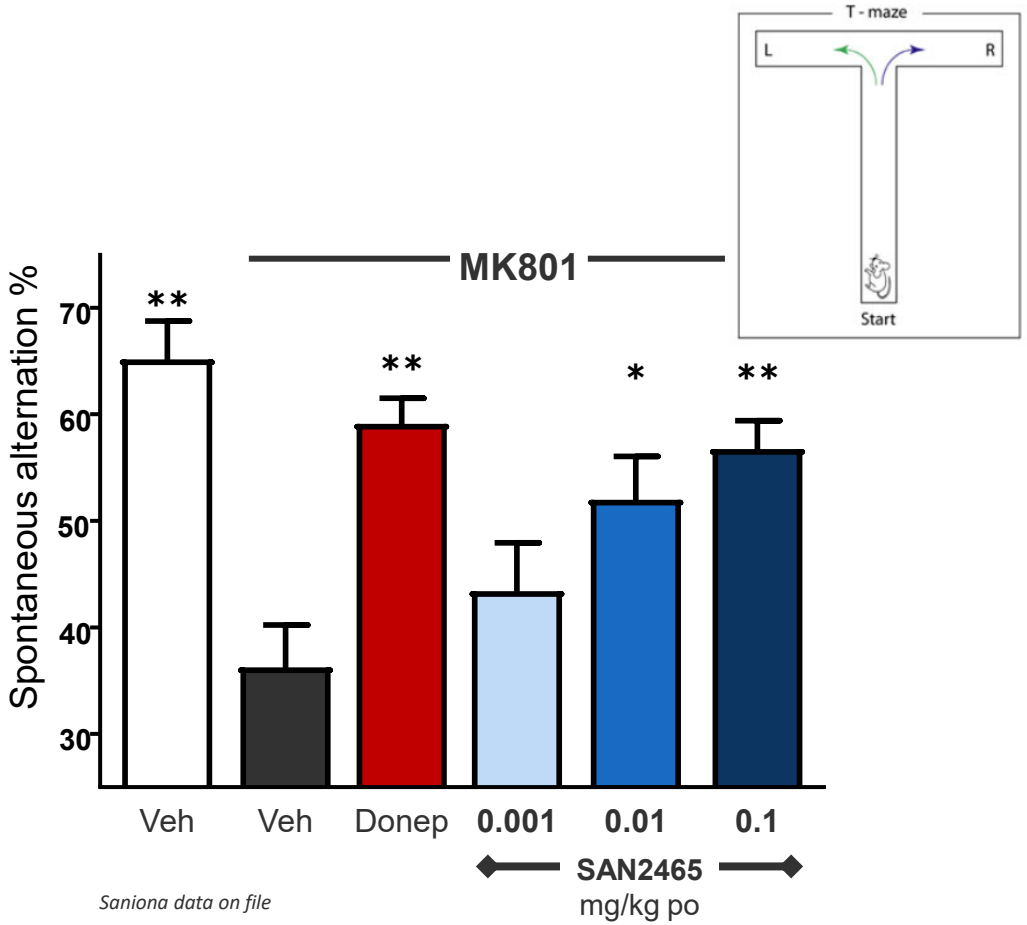
SAN2465 0.01 mg/kg, 0.1 mg/kg and ketamine dosed once 72 hours prior to testing
SAN2465 0.1 mg/kg acute group dosed 2 hours prior to testing
/*: p < 0.01/p<0.001 vs. non-stressed control group
Ketamine: 10 mg/kg

- **COGNITIVE IMPAIRMENT**: Difficulty concentrating, poor attention, impaired learning and memory and executive functions. In about 20-30% of MDD patients, cognitive impairment is an independent and negative prognostic factor for antidepressant response
- **Impaired learning and memory-like behavior** can be measured as stress-induced reduction of novelty index in Novel Object Recognition test ("NOR index"[1])
- **SAN2465 demonstrates:**
  - **Dose-related effect** with full normalization of stress induced impairment in recognition index at a dose level of 0.1 mg/kg, oral administration
  - **Rapid onset** within 72 hours post-dosing, and comparable effect size to that of Ketamine.
  - **Acute dosing** of 0.1 mg/kg 2 hrs prior to testing, **significantly ameliorates stress-induced reduction of novelty index** (data not shown)
  - There was **no effects of any treatments on number of crossings** signifying lack of effect on locomotor activity (data not shown)

[1] I **NOR index**: time spend exploring novel object + time spend exploring familiar object during second trial divided by total time spend exploring both objects

Lam et al., CanJPsy 2014; Bennabi et al., Psychopramacology 2019

SAN2465 acutely reverses pharmacologically induced cognitive deficits in the T-maze in mice



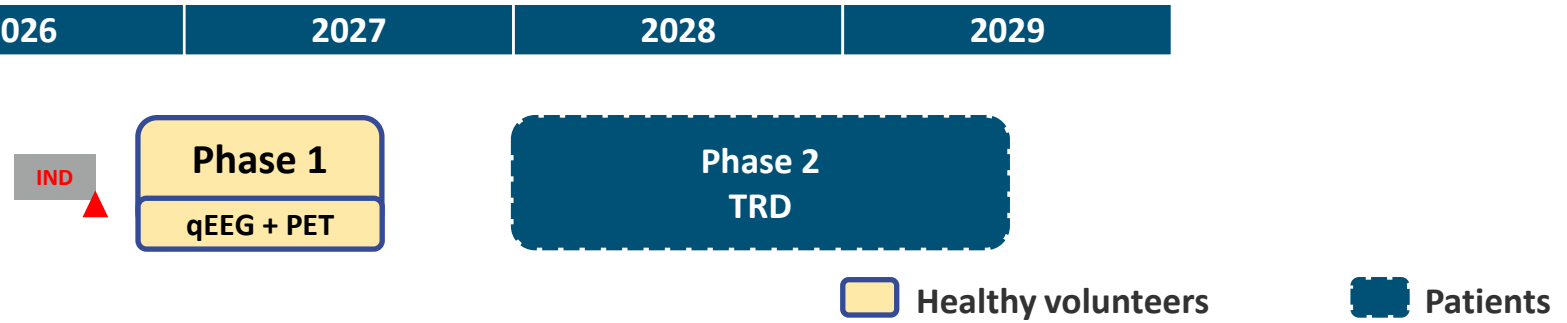
MK-801 was administered at 0.075 mg/kg s.c. 30 min before test,
SAN2465 was administered p.o. 60 min before test
Donepezil (2 mg/kg) was administered p.o. 60 min before test (n=9-15 pr dose group)
*/**: p<0.05/0.01 vs vehicle (ANOVA followed by Fishers LSD test for pairwise comparisons)

- **WORKING MEMORY**: Part of the cognitive domains known to be impaired in MDD[1]
- **Working memory-like behaviour** in mice can be evaluated in the **T-maze** by measuring spontaneous alternation. MK801 pharmacologically impairs this pattern, and reversal of the impairment indicates improved working memory.
- **SAN2465 demonstrates**:
  - **Dose-related reversal of MK-801 induced deficit** at 0.01- and 0.1 mg/kg (PO) (RO ~ 66%-97%)
  - **The effect size of the reversal is comparable** to the positive control, Donepezil
  - The **data indicates that SAN24565 effectively improves deficits in working memory-like behavior** suggesting benefit in treatment of cognitive deficits associated with MDD

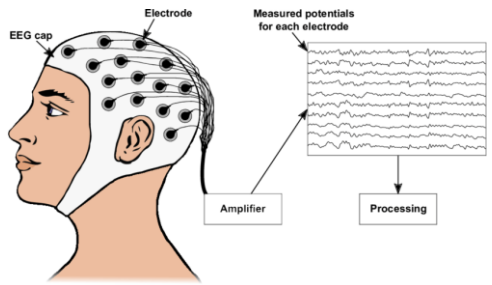
[1]Lam et al., CanJPsy 2014; Bennabi et al., Psychopramacology 2019

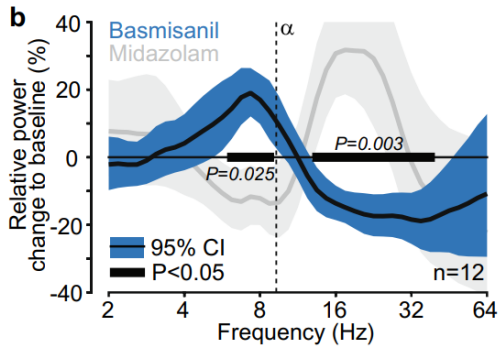
SAN2465 Phase 1 will establish target engagement and pharmacodynamic biomarkers through qEEG and PET to enable informed Phase 2 dose selection by 2027

SAN2465 Phase 1 expected late 2026 with Phase 2 study late 2027

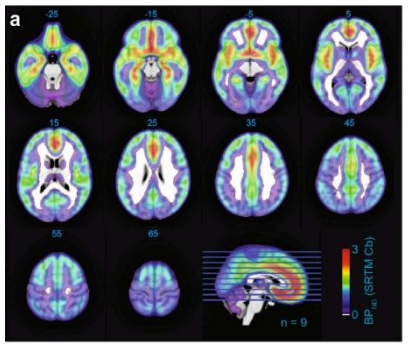


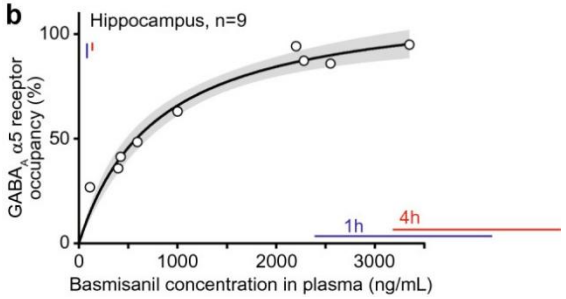
Quantitative EEG biomarkers will be used to detect the expected $GABA_A$ α5 NAM effect (a decrease in β-power), establishing the pharmacology-exposure relationship





PET imaging with [^{11}C]-Ro15-4513 will be used to define the exposure-receptor-occupancy correlation needed for rational Phase 2 dose selection





saniona

saniona™

Thank You