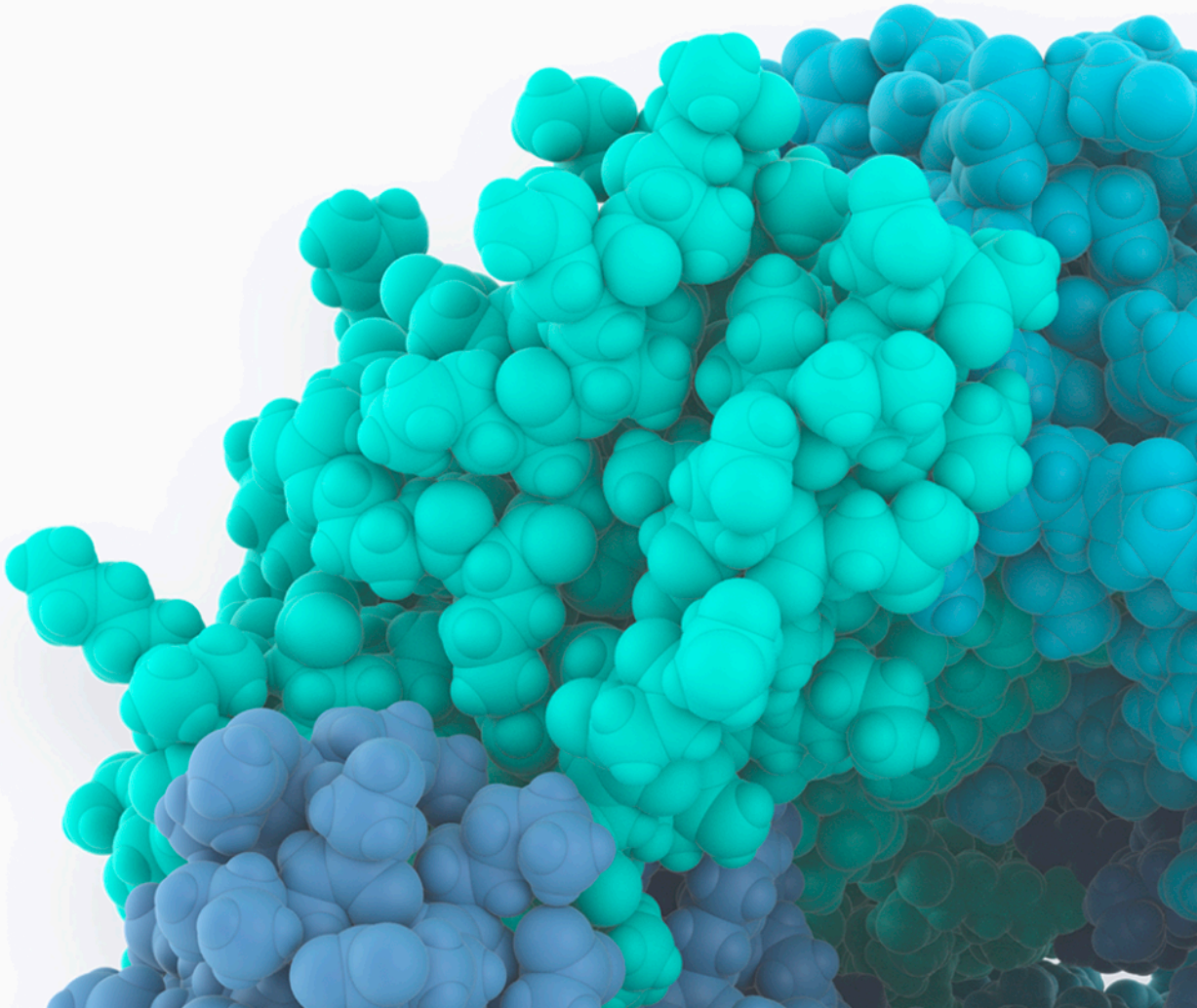
Lactocore

CNS peptide technologies



September 2020

Non-confidential slide deck

Company highlights

Peptide therapeutics for depression and anxiety

Lactocore is a preclinical stage company that discovers **novel peptide drugs** for key CNS targets using 3D modeling and scoring algorithms.

We address tremendous unmet need for new drugs with distinct mechanisms of action and better safety profiles in the areas of **depression and anxiety**, a $17 bln global market.

Leading candidate, **LCGA-17,** is a GABA-A and voltage-gated calcium channels (VGCC) modulator with both rapid-onset and long-lasting anxiolytic and antidepressant activity.

LCGA-17 is entering IND-enabling studies, with **4 other candidates in the pipeline.**

PCT and provisional USA patent applications filed in March 2020.

Raising $24M to bring LCGA-17 through proof-of-concept Phase II clinical trials, as well as advance the pipeline. **Smaller round $9M** available for development up to Phase II. **Current investor commitment: $3M.**

Addressed problems

13% of Americans take antidepressants

68%
of them take these drugs **for > 2 years**

33 mln people est. in 2023
with major depressive disorder

8 mln people
with comorbid anxiety

46 mln people
overall anxiety disorders

$210 bln
cost to the US per year (loss in productivity and healthcare needs)

$17 bln est. in 2020
global revenue for antidepressants

Source: Mordor Intelligence ; report by Reports and Data 2019; NCHS Data Brief No. 283, August 2017

A tremendous unmet need for **novel, superior therapies** for depression and anxiety

Majority of currently used drugs are old generics

Depression: **SSRIs, developed in 80's.**

Anxiety: **BDs, developed in 60's**.

Bipolar: **AAPs, developed in 90's, lithium from 1949.**

Problems with existing drugs

Unreliable efficacy

30% of depressed patients never realize any benefit.

Unacceptable side effects

SSRIs and AAPs: sexual problems, metabolic abnormalities, indented fatigue, cardiovascular risks.

BDs: sedation, addiction and abuse potential, tolerance.

Delayed onset of benefit

4-6 weeks for all approved antidepressants to date to take effect.

SSRIs - selective serotonin reuptake inhibitors; BDs – benzodiazepines; AAPs - atypical antipsychotics

Recently approved antidepressants have severe side effects and major barriers to utilization

Spravato™ (esketamine) C III nasal spray

enantiomer of ketamine

can only be used in certified medical facility

Esketamine by Jannsen Pharmaceuticals (J&J).
Approved for TRD on 03.05.2019 / NMDA receptor antagonist
Rapid-acting / AEs: sedation, hallucinations, dissociation.

Zulresso™ (brexanolone) injection C IV

allopregnanolone

intravenous infusion for 60 hours in certified medical facility

Brexanolone by SAGE Therapeutics.
Approved for PPD on 03.19.2019 / GABA-A receptor modulator
Rapid-acting / AEs: sedation, loss of consciousness.

TRD: treatment-resistant depression; PPD: post-partum depression; AE: adverse events

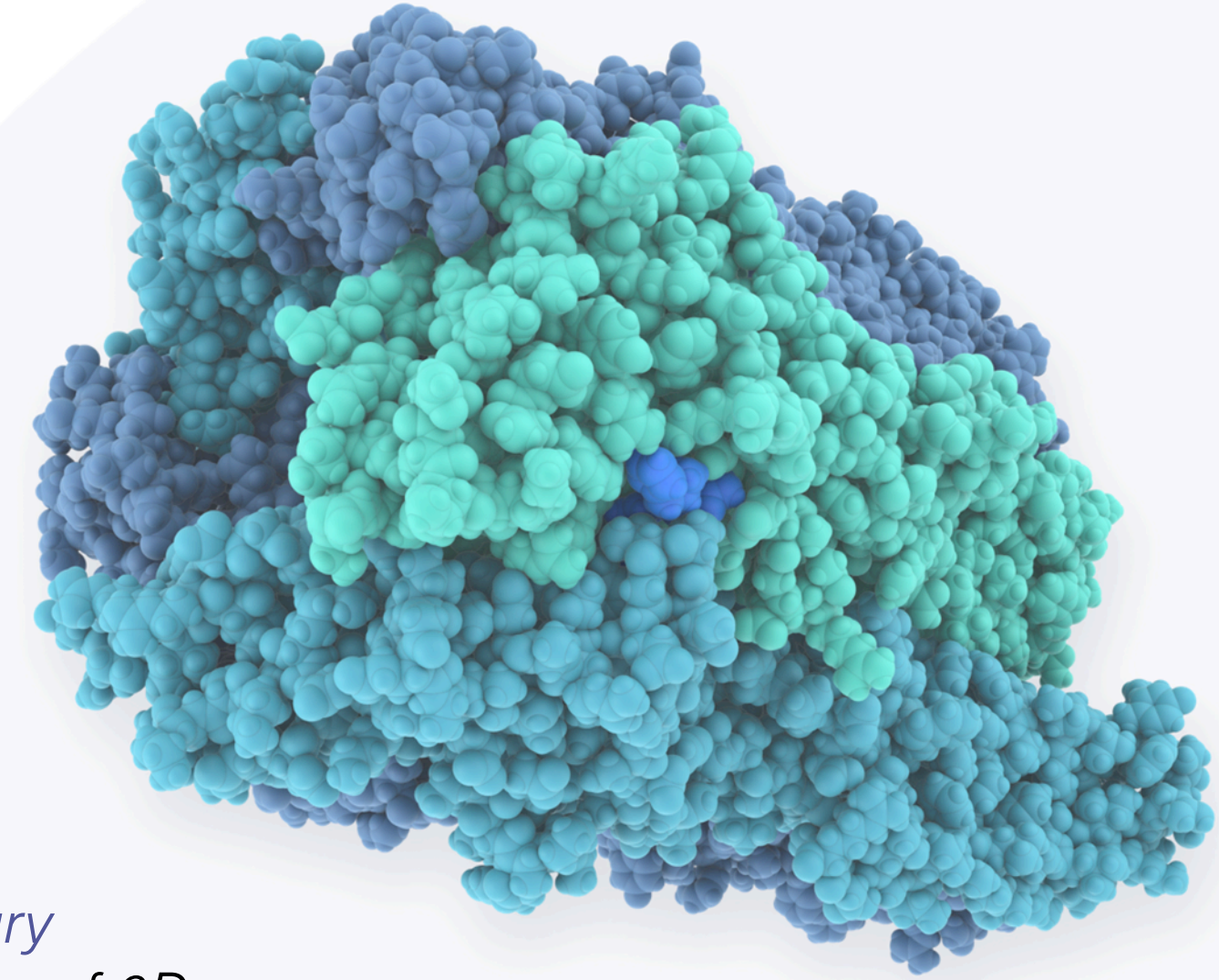
Lactocore solution

Computer-aided drug discovery

Focus on **peptides** with **new mechanisms** of action

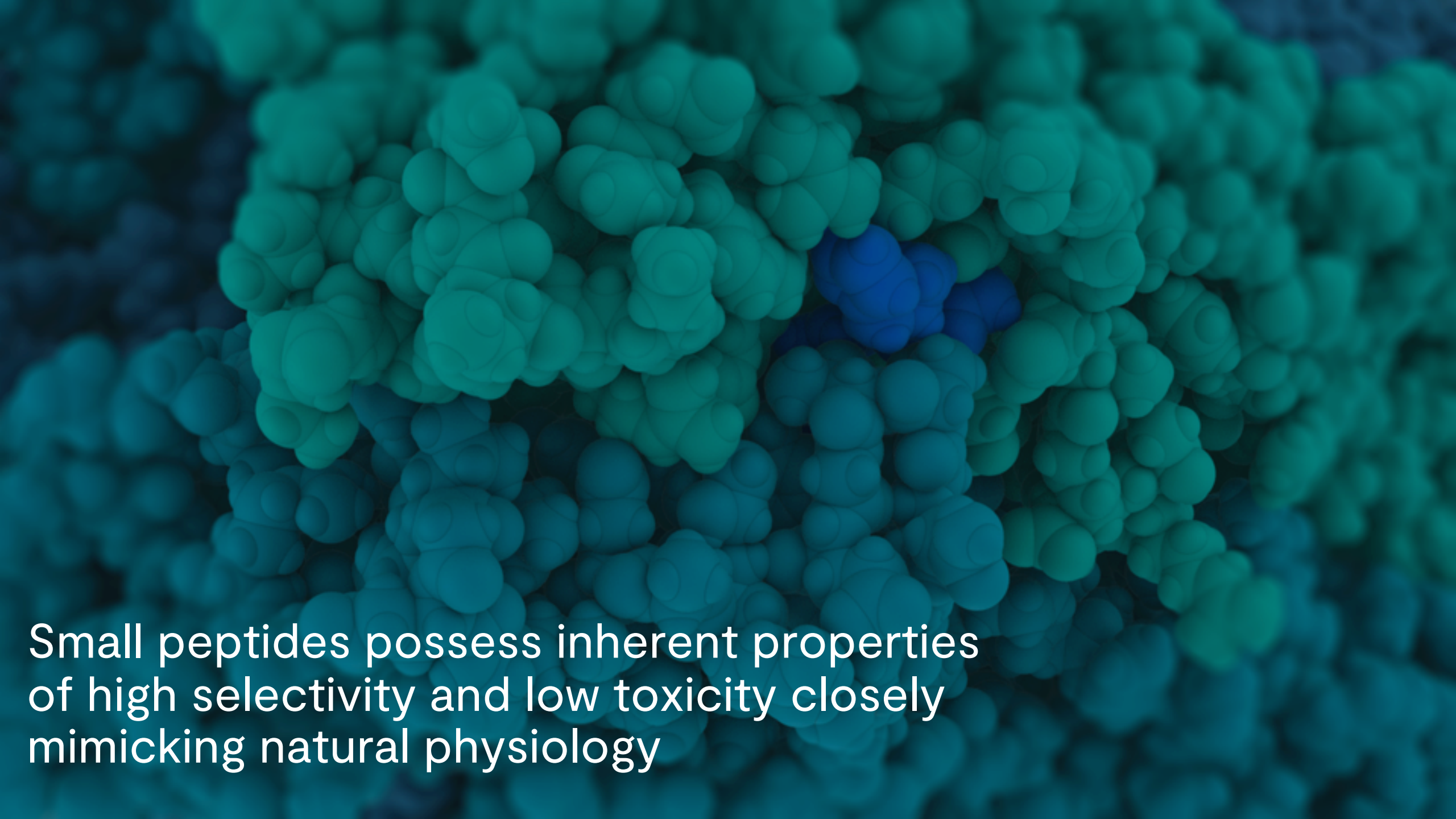
Fast and **effective** early development **engine**

Computer-aided drug discovery



Supercomputer power and proprietary algorithms are used to screen millions of 3D peptide structures for key CNS targets

GABA-A receptor



Small peptides possess inherent properties of high selectivity and low toxicity closely mimicking natural physiology

Fast and cost-efficient early development engine

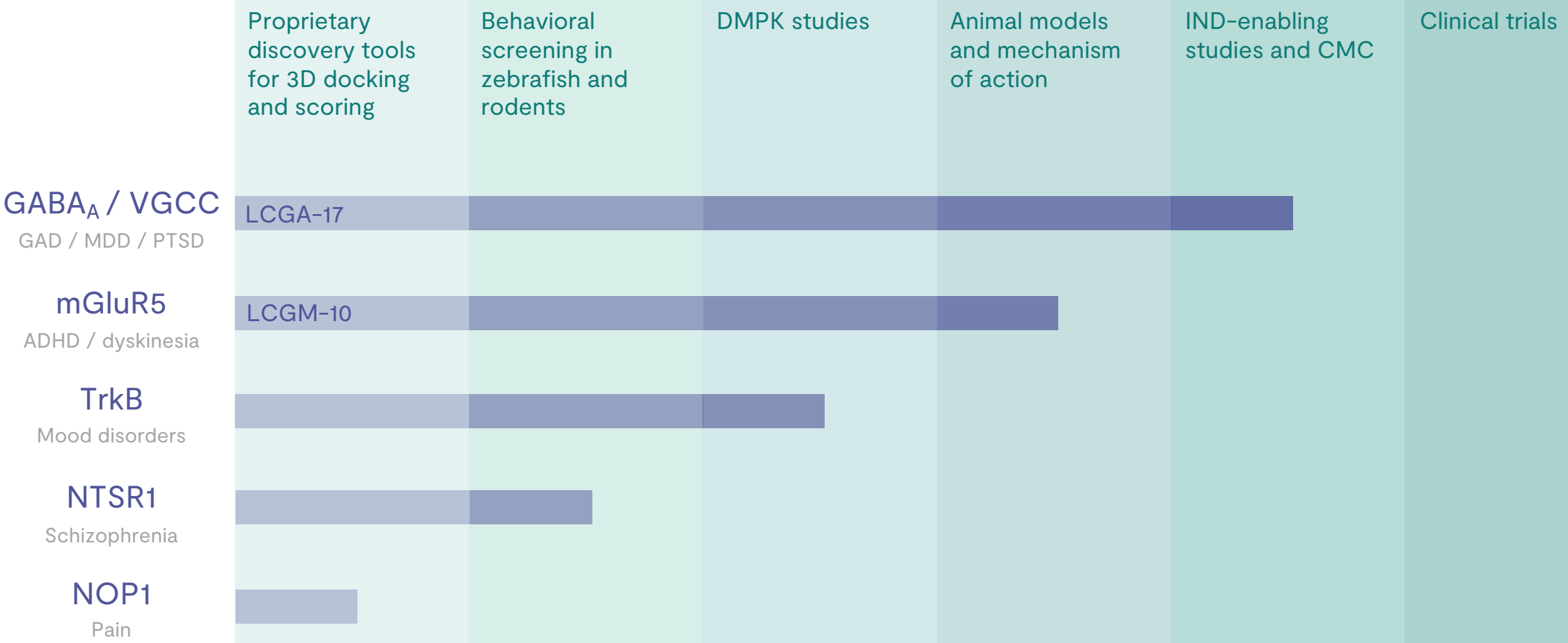
Leads are generated **in silico**

Fast **in vivo** screening in zebrafish

Behavioral rodent models

Experimental validation of in silico leads using zebrafish and rodent behavioral platform generates drug candidates quickly and cost-effectively

Current pipeline



Leading asset

LCGA-17 advantages

Novel mechanism of action

Distinctive multimodal target profile

Clinically relevant targets: GABA-A and VGCC

Rapid onset of action and long-lasting effect

Potential in multiple indications with huge unmet medical need

Robust efficacy in anxiety, depression and PTSD animal models

Intranasal route of administration

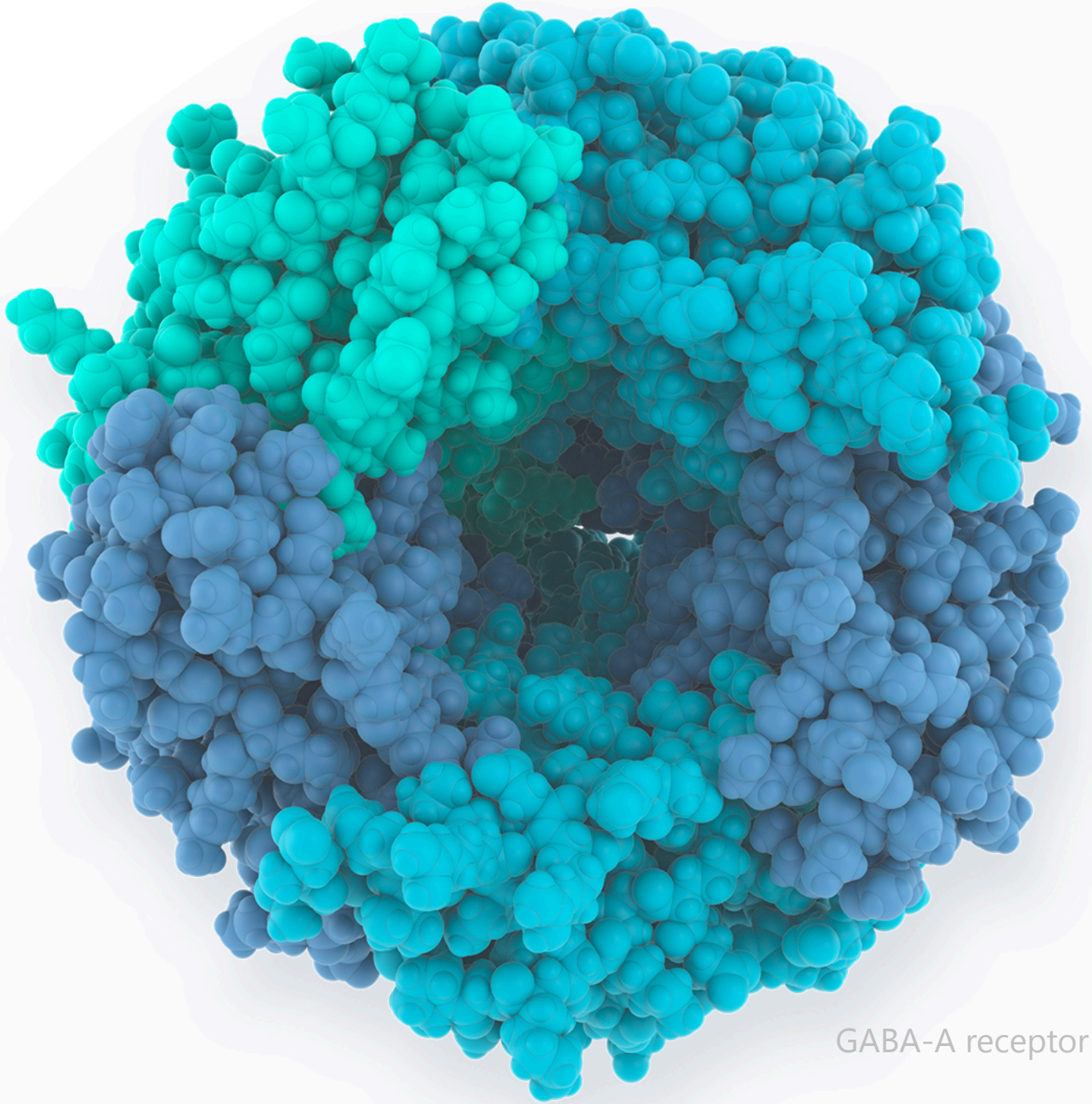
Blood-brain barrier permeability

No adverse effects typical for standard of care drugs

No sedation and no tolerance

No cognitive impairment

No addiction potential

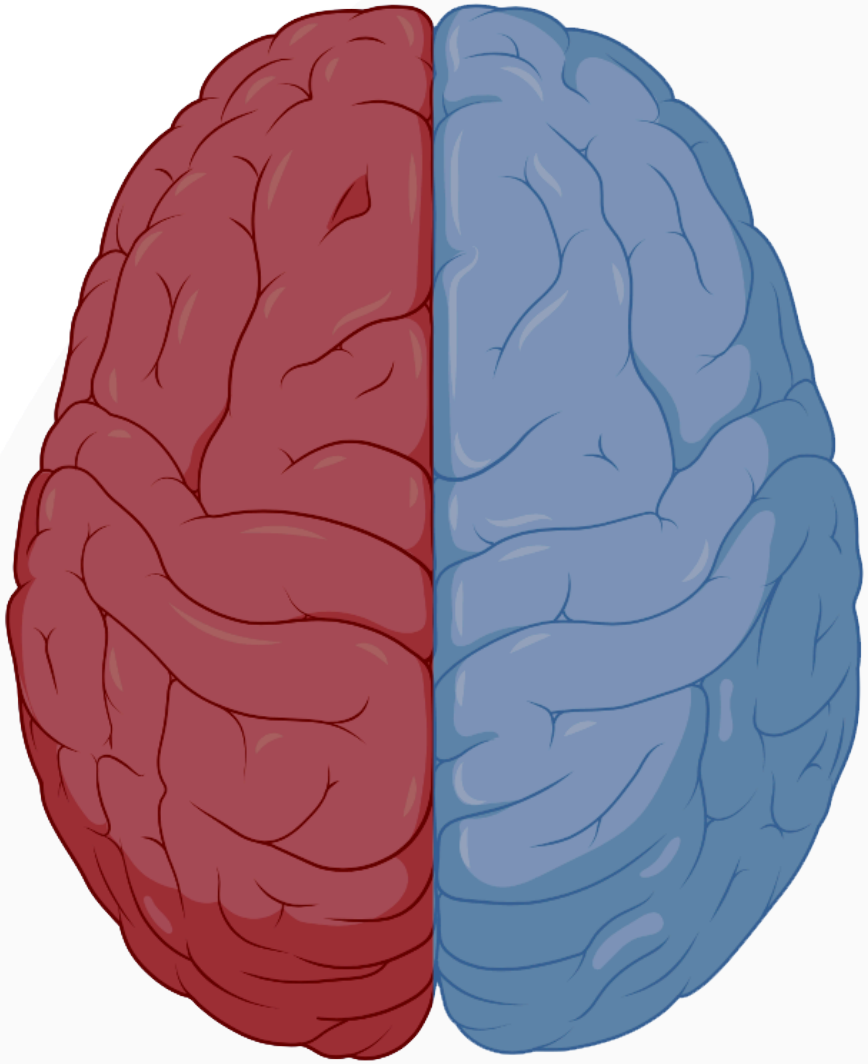


GABA-A receptor

Novel multimodal mechanism of action: silencing GABA-A and VGCC

Mood disorder:

- Disturbed balance of excitation and inhibition
- Neuroplasticity
- Neuroinflammation
- Catecholamines levels
- Glucocorticoid levels
- Excitotoxicity



LCGA-17 treatment:

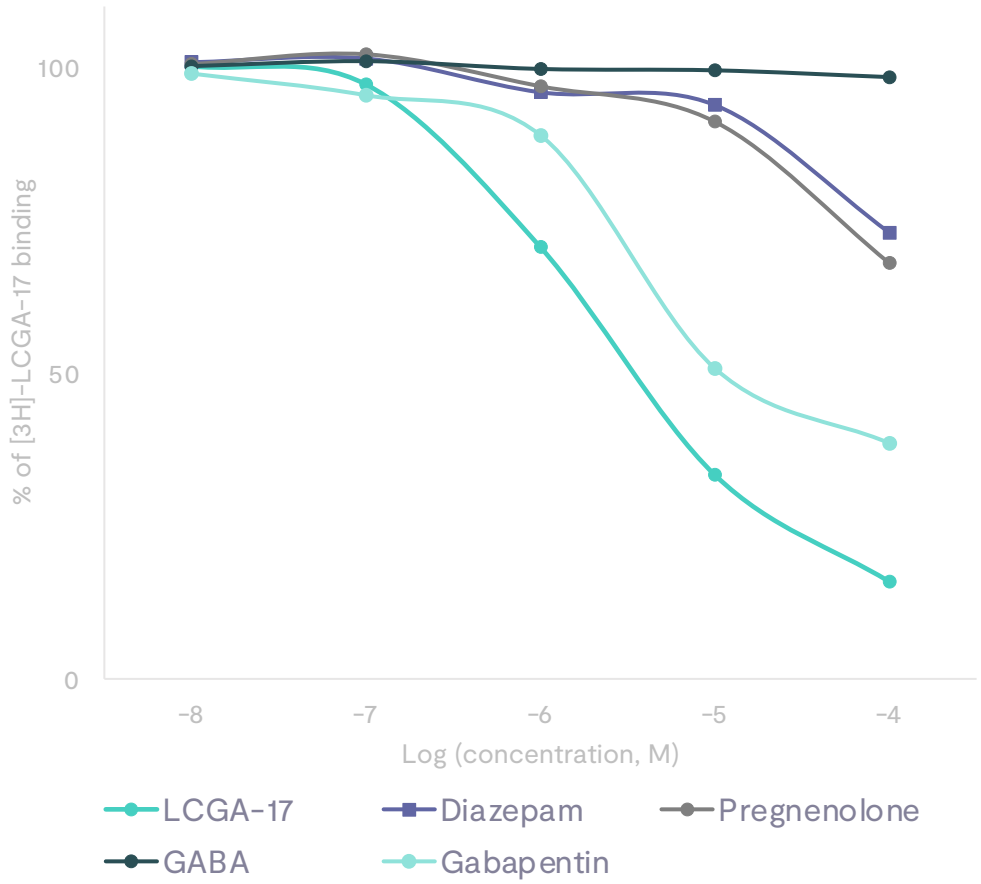
- Normalized balance of excitation and inhibition
- Neuroplasticity
- Neuroinflammation
- Catecholamines levels
- Glucocorticoid levels
- Excitotoxicity

LCGA-17 molecular biomarkers of efficacy demonstrate novel multi-modal action, while also aligning well with clinically validated drugs

Mechanism of action	Anxiolytic effect	Antidepressant effect	Comparable to*
NAM of $\alpha_2\beta_2\gamma_2$, $\alpha_3\beta_2\gamma_2$, $\alpha_4\beta_3\delta$ GABA-A	+	+	Pregnenolone sulfate
Inhibition of $\alpha_2\delta$ VGCC	+	+	Gabapentinoids
Neuroinflammation suppression	N/A	+	SSRI, KET, APN
Neurogenesis induction	N/A	+	SSRI, KET, APN
mTOR signaling	N/A	+	SSRI, KET, APN
Catecholamines levels normalization	N/A	+	SSRI, KET, APN
HPA axis normalization	+	+	SSRI, BD, APN
EEG biomarkers	+	+	N/A

** based on literature data*
NAM – negative allosteric modulator; VGCC – voltage-gated calcium channels;
HPA: hypothalamic–pituitary–adrenal axis; EEG: electroencephalography;
SSRI: selective serotonin reuptake inhibitors; BD: benzodiazepines; APN: allopregnanolone; KET: ketamine

Target validation: competitive radioligand binding assay in $GABA_A$-enriched membranes of the rat cerebral cortex



Results

Unlabeled LCGA-17 specifically replaces [^{3}H]-LCGA-17 at low concentrations.

LCGA-17 interacts with benzodiazepine and NAM neurosteroid sites on $GABA_A$-receptor.

LCGA-17 interacts with alpha2-delta binding site on VGCCs (voltage-gated calcium channels).

No cross-reactivity with targets associated with significant side effects such as serotonin or opioid receptors.

IC_{50}

LCGA-17 = $2*10^{-6}$ M

Diazepam = $52*10^{-6}$ M

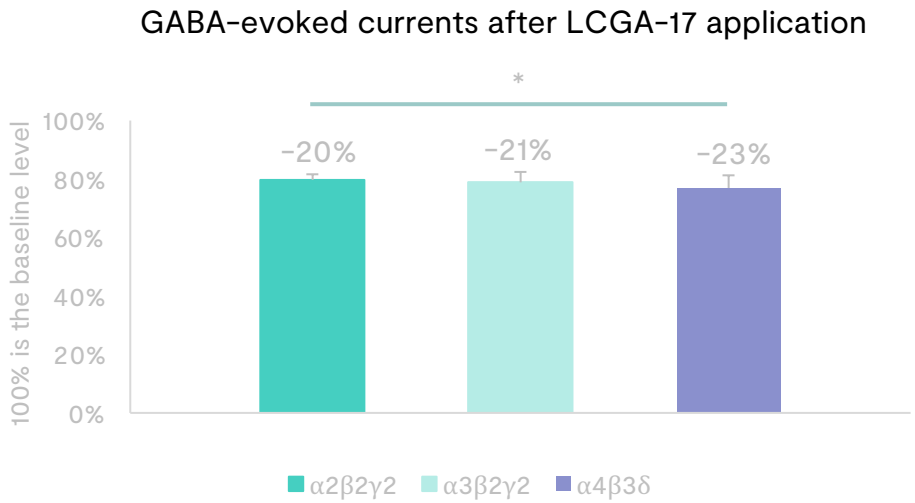
Pregnenolone sulfate = $36*10^{-6}$ M

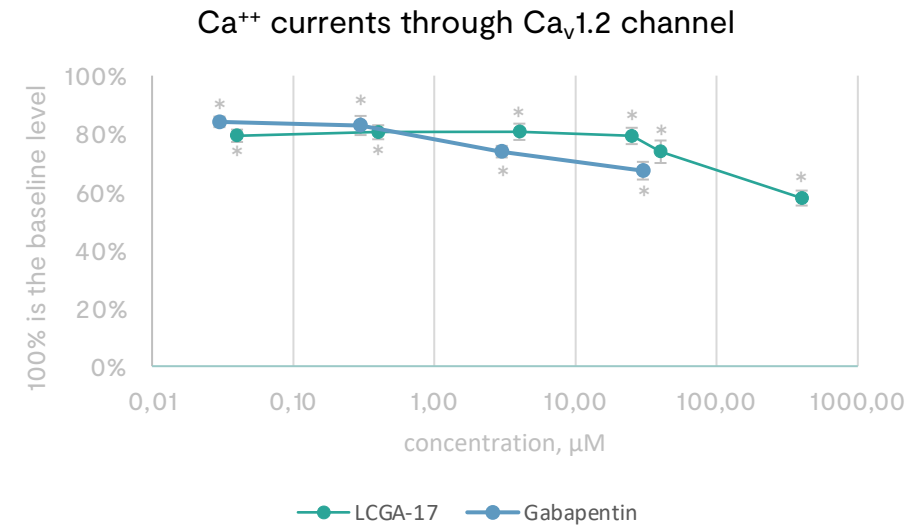
Gabapentin = $11*10^{-6}$ M

No cross-reactivity with

Dopamine receptors (D2, D3, D4)
Serotonin receptors (5-HT1, 5-HT2A)
GABA-B receptors
Glutamate receptors (NMDAR and mGluR2)
Acetylcholine receptors (nACh7)
Glycine receptors (GlyRA1)
Transient receptor potential channels (TRPM3)
Opioid receptors (sigma)
Translocator protein (TSPO)
Cannabinoid receptors (CB1)

LCGA-17 has distinctive binding profile in cortical membrane preparations





*The results are expressed as the mean ± SEM. * p < 0.05 in respect to the baseline current level. Two-tailed paired t-test.*

Target validation: electrophysiological profiling using SyncroPatch platform

Results

LCGA-17 displays inhibitory (NAM) activity against $\alpha_2\beta_2\gamma_2$, $\alpha_3\beta_2\gamma_2$, $\alpha_4\beta_3\delta$ GABA-A receptor cell lines.

LCGA-17 doesn't show activation (PAM) effect against $\alpha_{1\text{-}6}\beta_2\gamma_2$ and $\alpha_4\beta_3\delta$ GABA-A receptor cell lines.

LCGA-17 shows a concentration-dependent inhibition of the $Ca_v1.2$ channel.

Together with binding data, these results position LCGA-17 as a novel, functionally active ligand of the GABA-A NAM site and the $\alpha_2\delta$ VGCC subunit

LCGA-17 has strong potential as a superior, next generation antidepressant and anxiolytic

Animal model	Anxiolytic effect	Antidepressant effect	Superior to*	Comparable to*
Open Field	+	N/A	SSRI	BD, APN
Elevated Plus Maze	+	N/A	SSRI, KET	BD
Acute foot shock-induced stress model	+	+	N/A	SSRI, BD, KET, APN
Single prolonged stress-induced conditioned fear (PTSD model)	+	+	N/A	SSRI, BD, KET, APN
Predator odor-induced place aversion (PTSD model)	+	+	BD	SSRI, KET, APN
Forced Swim	N/A	+	BD	SSRI, KET, APN
Chronic Restraint Stress	N/A	+	BD	SSRI, KET, APN
Chronic Unpredictable Mild Stress	+	+	BD	SSRI, KET, APN
Effects in Dominant and Submissive mice strains (social model)	+ in Sub (antimanic/ antipsychotic in Dom)	+ in Sub (antimanic/ antipsychotic in Dom)	BD	SSRI

** based on literature data*

SSRI: selective serotonin reuptake inhibitors; BD: benzodiazepines; APN: allopregnanolone; KET: ketamine

CUMS – 26 days of stress exposure

Elevated Plus Maze (EPM)	1 (LCGA-17 i.n. adm.)
Social interaction (SI)	4
Female urine sniffing (FUS)	8
Novelty suppressed feeding (NSF)	11
Sucrose preference (SP)	16
Forced swimming (FS)	18
Brain samples collection	22

Test	CUMS			
	Vehicle	Diazepam	LCGA-17 0.05 mg/kg	LCGA-17 0.5 mg/kg
EPM	—	anxiolytic-like and sedative effects	slight anxiolytic-like effect	—
SI	depressive-like behavior	—	antidepressant-like effect	—
FUS	anhedonia, depressive-like behavior	—	antidepressant-like effect	antidepressant-like effect
NSF	—	anxiolytic-like effect	anxiolytic-like effect	—
SP	anhedonia, depressive-like behavior	—	—	—
FS	depressive-like behavior	—	—	antidepressant-like effect

Animal models: chronic unpredictable mild stress (CUMS) model of depression in Wistar male rats

Results

CUMS led to the development of a persistent depressive state in rats.

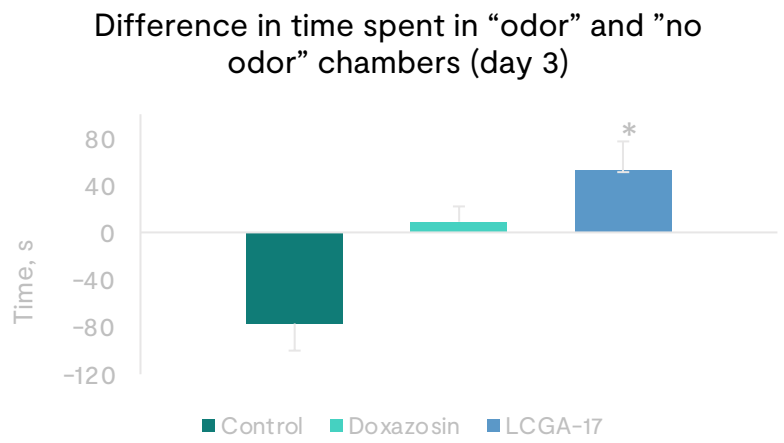
Diazepam had prominent anxiolytic-like and sedative effects.

LCGA-17 showed combined antidepressant-like and anxiolytic-like effects in various behavioral tests.

Data strongly support further development of the LCGA-17 as a potential treatment for anxiety and depression disorders

"–" means no effect

Animal models: predator odor-induced conditioned place aversion model of post-traumatic stress disorder (PTSD) in male Sprague-Dawley rats

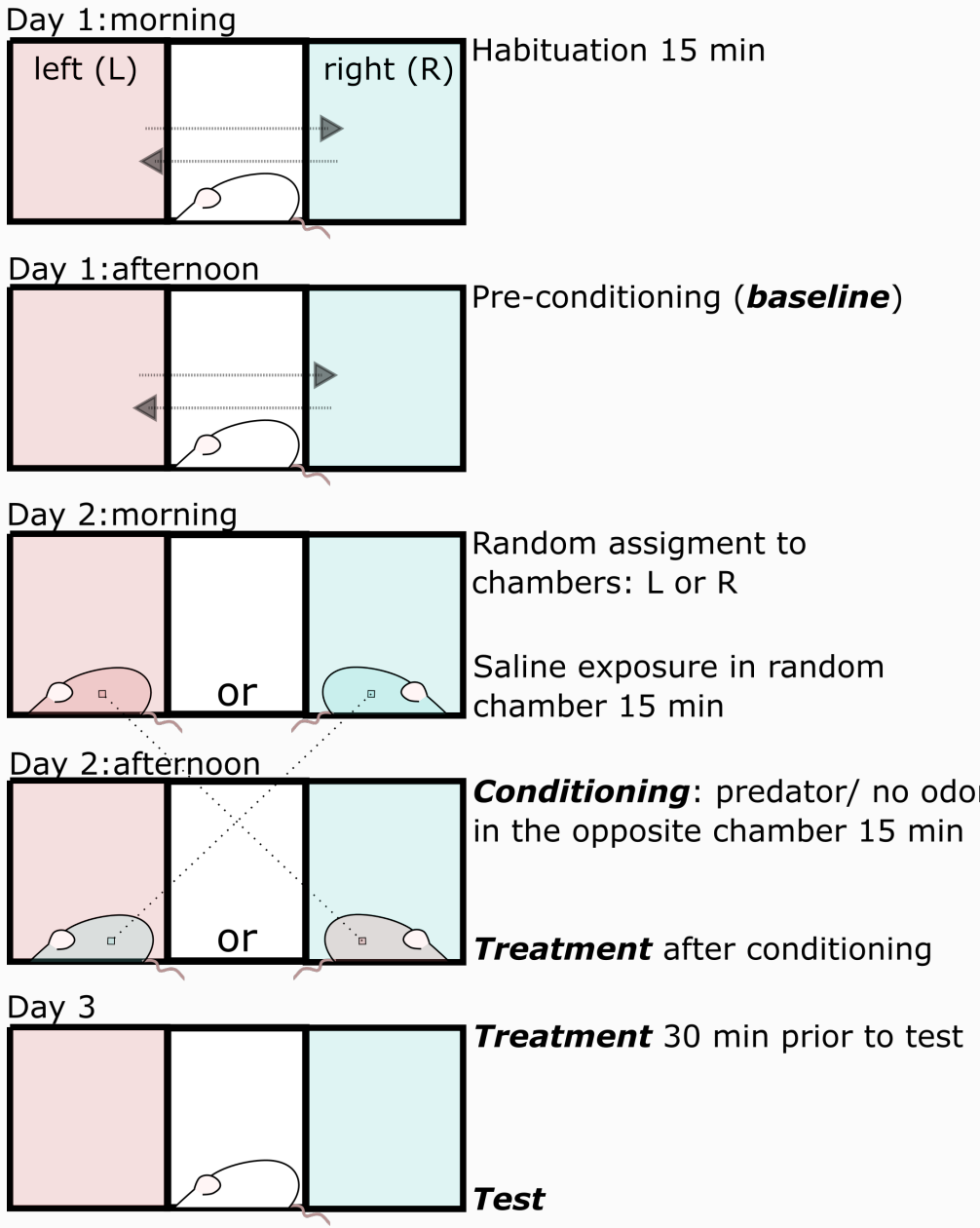


Results

LCGA-17 significantly attenuated predator odor-induced place aversion to a greater degree than doxazosin, a treatment for PTSD.

Data support further development of the LCGA-17 as a potential treatment for PTSD

Conditioned place aversion



*The results are expressed as the mean ± SEM. * p < 0.05 vs. control group. One-way ANOVA with a post hoc Student’s Newman-Keuls Method.*

Safety of LCGA-17: lack of severe side effects associated with newly approved and standard of care treatments

Safety parameters	Current observations	Superior to*
Deaths or severe AEs in animals	None even at a maximum feasible dose	SSRI, BD, KET
Sedation	None even at a maximum feasible dose	BD, KET, APN
Cognitive function (NOR test)	No impairment of cognition at high doses	SSRI, BD, KET, APN
Tolerance and withdrawal syndrome	No indicators found after chronic treatment	BD, KET, APN
Addiction potential (CPP test)	No addiction observed at high doses	BD, KET
Embryotoxicity	No malformations in zebrafish embryos	SSRI, KET
Epilepsy	Do not provoke seizures	N/A

** based on literature data*
AE: adverse events; NOR: novel object recognition; CPP: conditioned place preference;
SSRI: selective serotonin reuptake inhibitors; BD: benzodiazepines; KET: Ketamine; APN: Allopregnanolone

Development plan

Early clinical plan for LCGA-17 de-risks depression and anxiety indications

Preclinical

GLP Tox + CMC

12 months

Phase I

Single / multiple ascending dose

Safety and tolerability
vs Dose

(adverse effects)

Pharmacodynamics by NeuroCart*

(BBB and MoA)

12 months

Phase II

MDD (Major Depressive Disorder)

Fully powered RCT evaluating

efficacy, safety, biomarkers

Phase II**

GAD (Generalized Anxiety Disorder)

Fully powered RCT evaluating

efficacy, safety, biomarkers

** additional study if funding is available

- https://chdr.nl/clinical-studies-development/methods-biomarkers/central-nervous-system/neurocart

18 months

Full program activities

Preclinical LCGA-17

GLP Tox in rats and dogs

CMC

Preclinical LCGM-10

PoP in animal models

DMPK, Tox, CMC

Early development: other targets

Ph I LCGA-17

Phase I in healthy volunteers:

Single Ascending Dose (N=48)

Safety, PK

Multiple Ascending Dose (1 week, N=32)

Safety, PK, Pharmacodynamics (NeuroCart* battery)

Ph II LCGA-17 in MDD

Randomized, double-blind, placebo-controlled, flexibly dosed Phase II trial in MDD pts

Efficacy, safety, biomarkers

N= 220

6 weeks dosing

Series A round being raised	$24 million
Optional raise excluding PhII	$9 million
Commitments in place	$3 million

*MDD - major depressive disorder; PoP – proof of principle; *Groeneveld et al Drug Disc Today Technol 2016, 20, 27-34*

Phase 2 Randomized Controlled Trial of Flexible Dosing LCGA-17 vs Placebo in Major Depressive Disorder (MDD)

Key Inclusion Criteria
- MDD diagnosis, MADRS >25, CG-S > 4

Key Exclusion Criteria
-HDRS score >7 on the anxiety-somatization subscale of the HDRS-17.
-major medical or other serious psychiatric illness
-failed >1 trial of an effective MDD medication in current episode
-ongoing tx for depression or anxiety
-ongoing drug therapy for insomnia except OTC

Study Population
N=220 adults (18-65 yrs)

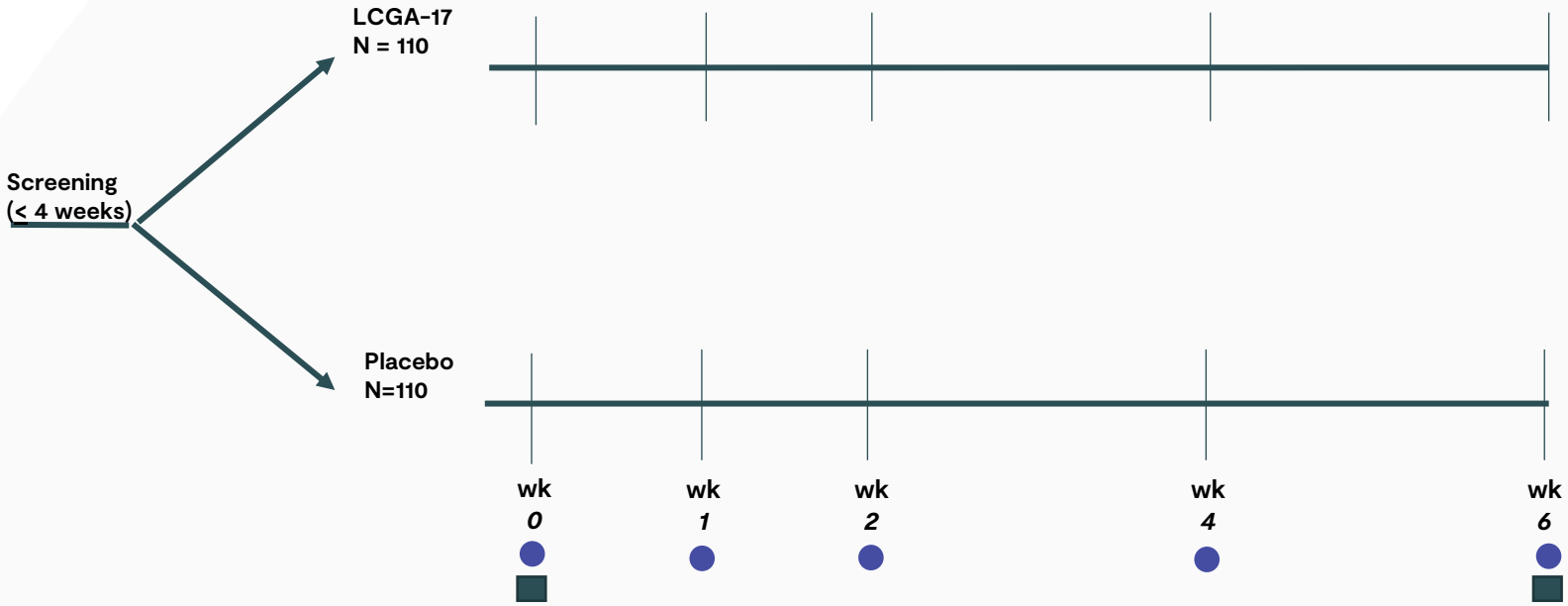
Clinical Measures
1o MADRS
2o SDQ, CGI-I, CGI-S, SDS, CSFQ

Sample size
Power=0.8, alpha=0.05, 2-tailed T test, ES=0.4 (medium)

Duration of Trial
~16 months

Quality Control
Signant CRO

6-week Double-blind RCT (N=220)
1 dose flexibly-dosed of LCGA-17 vs Placebo



Baseline and Final Endpoint

Clinical measures and safety assessments

MADRS=Montgomery-Asberg Depression Rating Scale; SDQ=symptoms of depression questionnaire; CGI-I,S=Clinical Global Impression of Improvement/ severity; SDS=Sheehan Disability Scale; OTC=over the counter; CSFQ=changes in sexual functioning questionnaire

Flexible Dosing: The research physician is allowed to titrate the dose up or down based on the patient's clinical response with respect to efficacy and adverse effects, up to a maximum dose by week 3, after which the dose is fixed.

Team

Management

Askar Kuchumov, Ph.D., CEO

Entrepreneurial biotech executive with 15 years experience in business development and venture capital.

Anton Malyshev, Ph.D., CSO

Co-founder, expert in behavioral neuroscience and peptides drug discovery with 10 years project management experience.

Igor Doronin, Ph.D., CTO

Co-founder, specialist in computer-aided drug discovery with 10 years project management experience.

Andrey Purmal, Ph.D.
Head of preclinical development

Preclinical drug development expert with 30+ years' experience in CMC and toxicology, with multiple INDs and a BLA filing of peptides and protein therapeutics.

Randall D. Marshall, M.D.
CMO Consultant

Serial entrepreneurial and pharmaceutical executive, senior medical scientist and proven leader at the national level, with 30+ years' experience across medicine, industry and academia.

Gennady Babkin, Investor

Co-founder, scientist, entrepreneur with fintech and biotech projects and IPO on NASDAQ experience.

Scientific and clinical advisors

Bernhard Luscher, Ph.D.

Leading expert in mechanisms of antidepressant drug action and role of GABAergic transmission in depression.

Professor of Biology, Pennsylvania State University.

Shane Perrine, Ph.D.

Leading expert in addiction and PTSD.

Associate Professor, Department of Psychiatry and Behavioral Neurosciences Wayne State University School of Medicine

Israel Liberzon, M.D.

Recognized clinician and researcher in PTSD, stress disorders, neuroanatomy and neuroimaging.

Head of Department of Psychiatry, Texas A&M College of Medicine.

Management and SAB experience

BIO PROCESS CAPITAL PARTNERS

BD

Cleveland BioLabs

Alkermes

sunovion

Genome Protection

PennState

A&M

Blue Oak PHARMACEUTICALS

Investment highlights

Company

- Preclinical stage company developing next generation peptide drugs for depression and anxiety disorders.
- Proprietary drug discovery engine.
- Pipeline targeting novel CNS mechanisms affected in mood disorders.
- Brand new IP: one PCT and one provisional filed in March 2020, with more in preparation.
- Experienced management team.

Highly compelling lead product opportunity

- LCGA-17 is a VGCC inhibitor and a GABA-A NAM with both rapid and long-lasting anxiolytic and antidepressant activity currently in IND-enabling studies.
- Short peptide intended for intranasal administration, with excellent blood-brain barrier penetration.
- Completed comprehensive suite of proof-of-concept animal studies.
- Robust activity in both depression and anxiety animal models.
- Lack of safety concerns typical for existing medicines.

Market and Competition

- Tremendous unmet need for novel, superior therapies for depression and anxiety.
- Global revenue for antidepressants: est. $17b in 2020.
- Current treatments are inadequate (both efficacy and safety) and are based on outdated understanding of disease pathology.
- Current experimental pipelines lack innovation.

Financing

- Raising $24M to bring LCGA-17 through proof-of-concept Phase II clinical trials, as well as advance the pipeline.
- Smaller round $9M available for development up to Phase II.
- Current investor commitment: $3M.

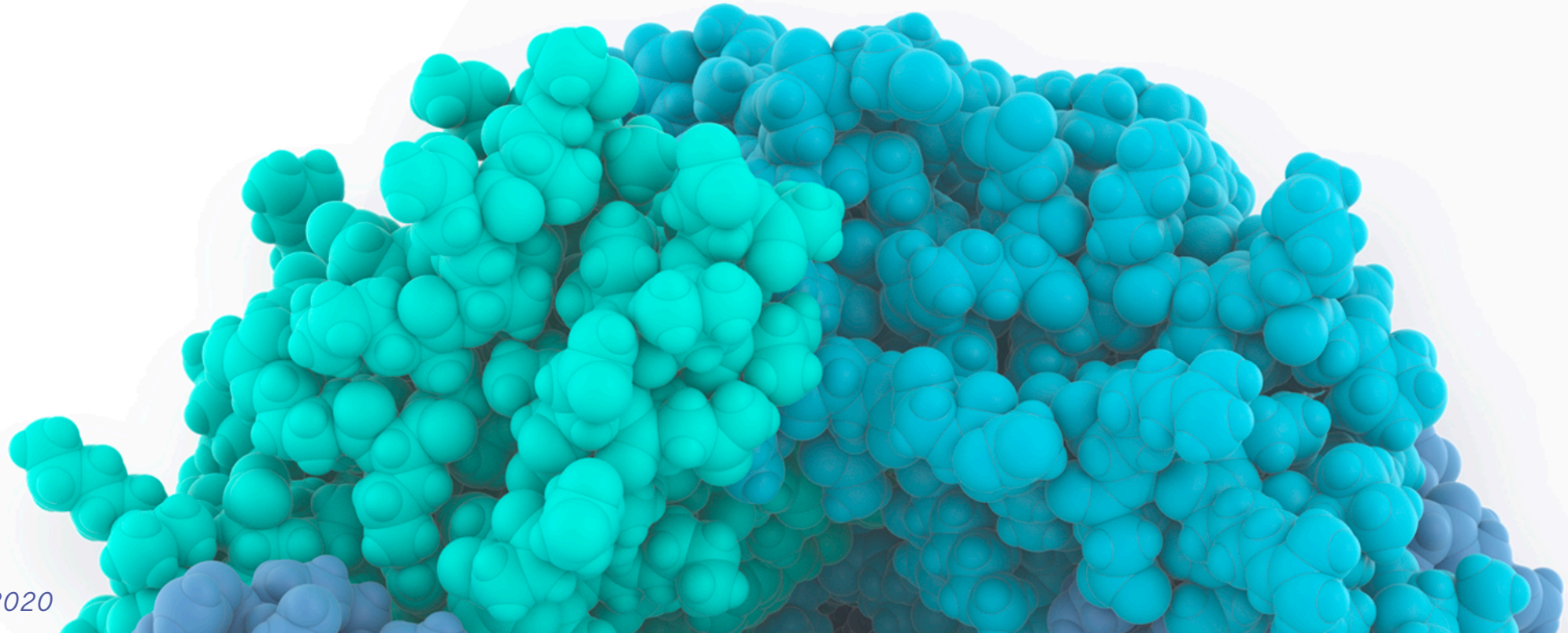
Lactocore

Contact

Askar Kuchumov, Ph.D., CEO

ark@lactocore.com

734-358-8521



September 2020