TETRA PHARM TECHNOLOGIES

TPT0701: CNS-targeted oral treatment for **obesity**

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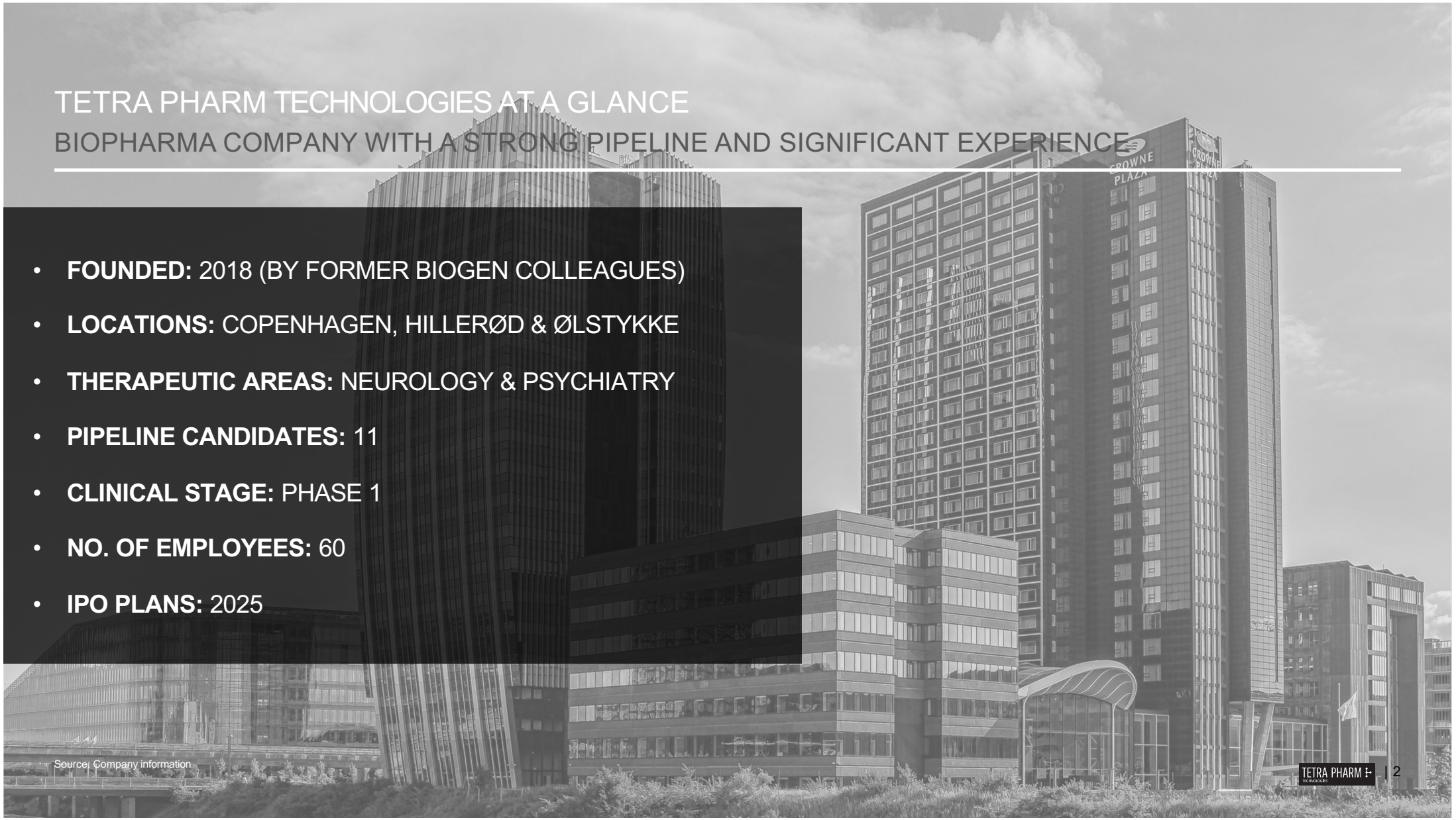
CSO

Investor Konference / Økonomisk Ugebrev
23rd April 2025
Symbion

TETRA PHARM TECHNOLOGIES AT A GLANCE

BIOPHARMA COMPANY WITH A STRONG PIPELINE AND SIGNIFICANT EXPERIENCE



- **FOUNDED:** 2018 (BY FORMER BIOGEN COLLEAGUES)
- **LOCATIONS:** COPENHAGEN, HILLERØD & ØLSTYKKE
- **THERAPEUTIC AREAS:** NEUROLOGY & PSYCHIATRY
- **PIPELINE CANDIDATES:** 11
- **CLINICAL STAGE:** PHASE 1
- **NO. OF EMPLOYEES:** 60
- **IPO PLANS:** 2025

Source: Company information

EXECUTIVE MANAGEMENT TEAM

FOUNDERS REMAIN A CRUCIAL PART OF MANAGEMENT RETAINING CULTURE AND VALUES

Martin Rose
CEO & CO-FOUNDER
MSc
23 Years

Jesper Breum
COO & CO-FOUNDER
MSc
25 Years

Steen Jakobsen
CFO
MSc
27 Years

Morten Allesø
CSO
PhD
18 Years

Jens H. Mikkelsen
CDO
Professor, PhD
37 Years

Kirsten Harting
CMO
Medical Doctor, MBA
34 Years

Martin Caspersen
CCO
BSc
24 Years

Jacob Schlundt
CMO(1)
Intl. Business Com.
28 Years

= Biopharma experience = Finance/Sales/Marketing experience

Source: Company information.
Note: (1) CMO = Chief Marketing Officer.

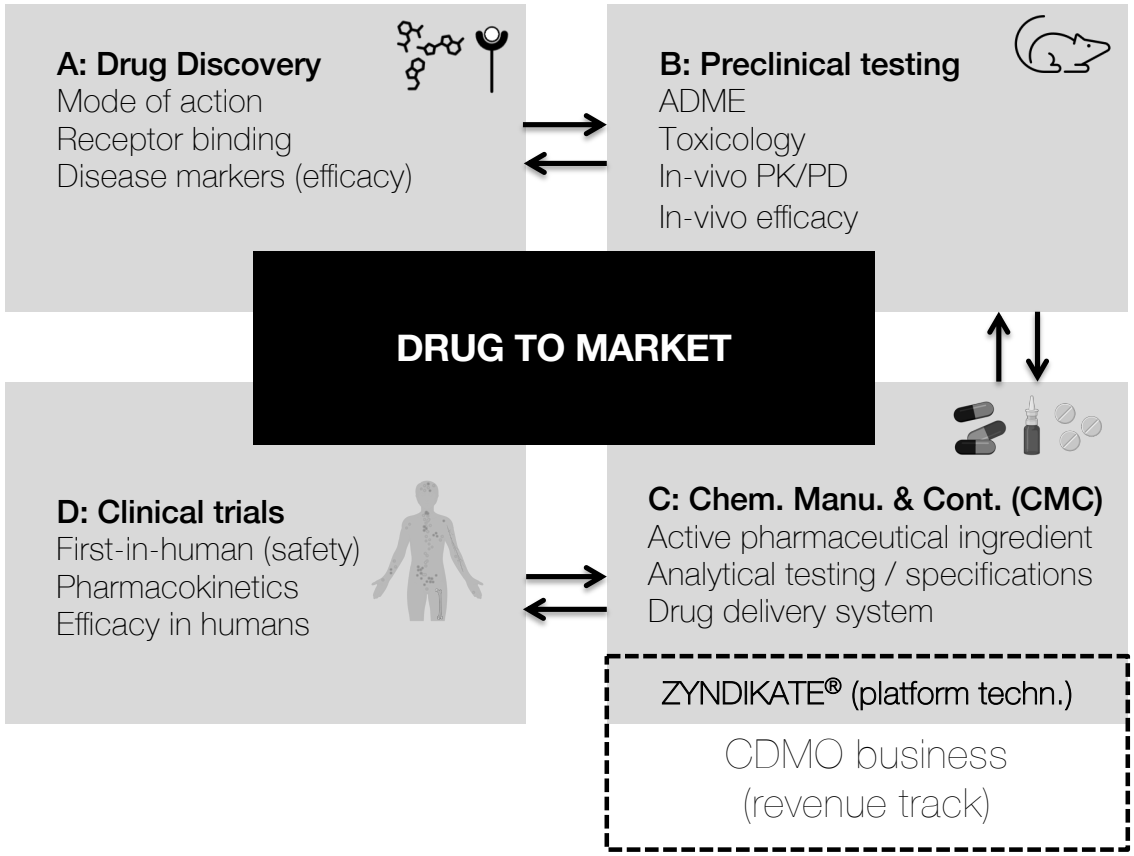
THRIVING PIPELINE WITH PROMISING PRE-CLINICAL RESULTS

PROMISING LEAD ASSET FOR CHRONIC PAIN, OBESITY, AND ALZHEIMER`S DISEASE

Source: Company information.

BUSINESS MODEL

BIOTECH WITH A PARACHUTE

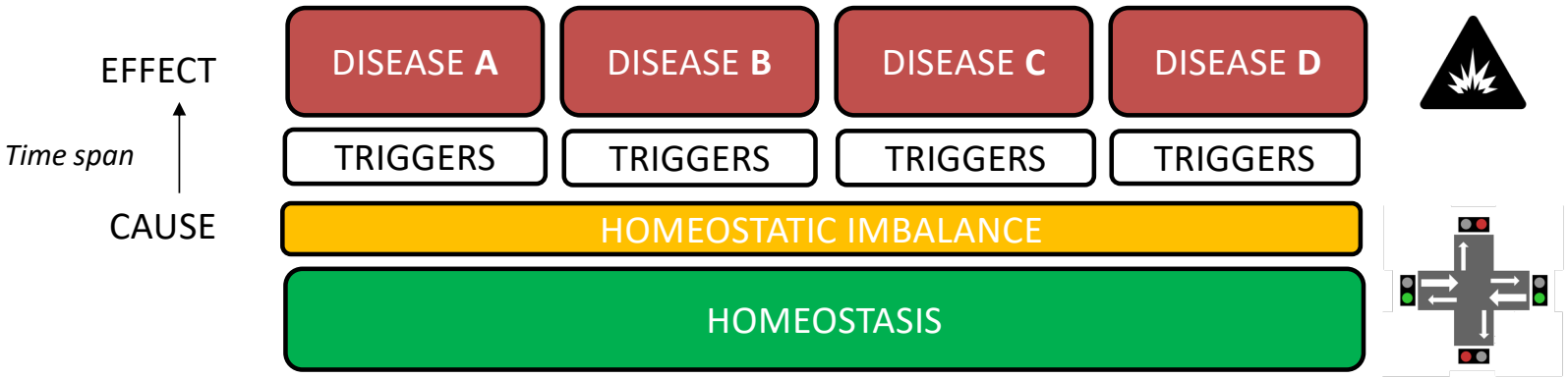


- Contract Research Organizations (CRO) are leveraged to varying extent
- Stage C (CMC) relies heavily on internal resources to ensure **control of drug substance and drug delivery systems** (supply chain) and IP (also) supporting the CDMO track
- TPT's **CDMO business** offers (among other) our proprietary drug delivery technologies for client's own molecules
- **Progression of the TPT pipeline** is synergistically linked to the CDMO business through ZYNDIKATE®

POLYPHARMACOLOGY

TETRA PHARM technologies

HOMEOSTASIS & DISEASE



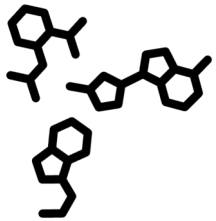
- *For decades, little true innovative progress has happened in the treatment of CNS-related disorders with small molecules.*
- *Existing treatments alleviate symptoms rather than fixing the cause. Patients therefore tend to relapse upon seponation.*
- ***TPT's R&D has identified key mechanistic hallmarks between several CNS-related disorders.***

Source: Company information.

POLYPHARMACOLOGY

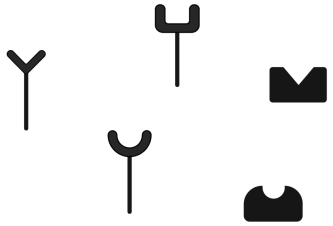
ADDRESSING CAUSE AND EFFECT THROUGH MECHANISM-BASED NOSOLOGY

TPT polypharmacological drug
(from in-house molecular library)



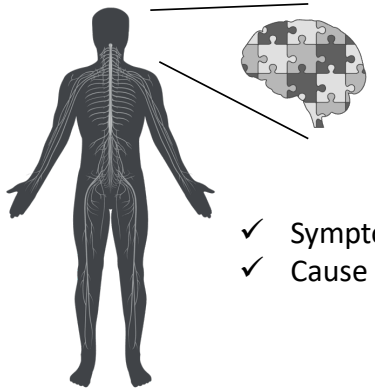
Conceptualize

Multiple targets / (therapies)



Drug delivery

Treatment



- ✓ Symptoms (alleviation)
- ✓ Cause (cure)

One or more active molecules

Receptors, enzymes, transporters

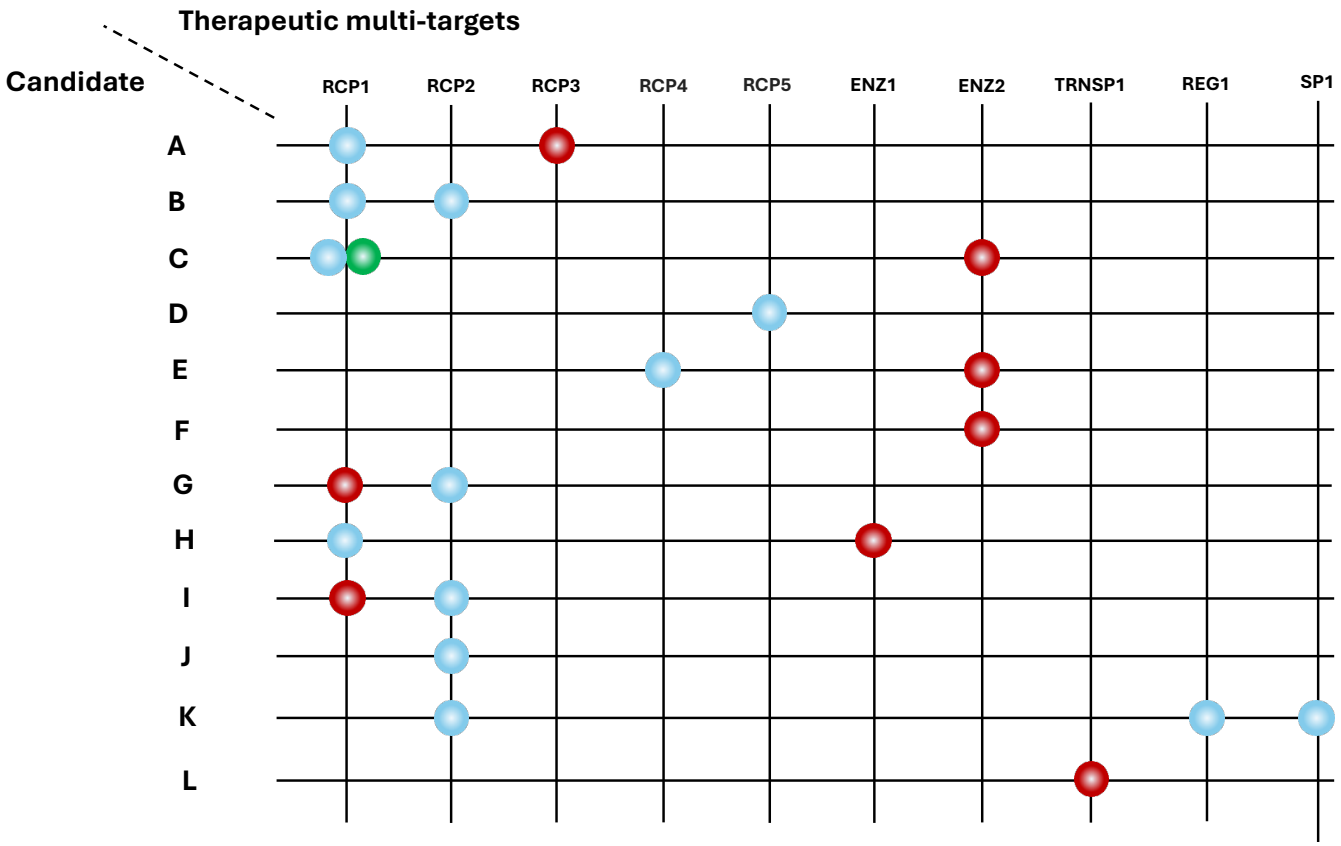
"Combined" efficacy

IP generation

Source: Company information.

TPT PIPELINE

OUR MULTITARGET GAME BOARD



Agonist/inducer

Antagonist/inhibitor

Allosteric modulation

RCP: Receptor

ENZ: Enzyme

TRNSP: Transporter

REG: Regulator protein

SP: Signaling pathway

- ✓ Focus on disease mechanism / nosology rather than designing a single NCE molecule
- ✓ The same drug molecule/ligand covers more than one pipeline candidate
- ✓ Significantly derisks drug development by levering existing data, e.g. ADME/TOX

Source: Company information.

THE zIQube™ PLATFORM

STREAMLINED DRUG DEVELOPMENT

ZEEK™ ("Universal Discovery")

- Database of proprietary and reference molecules
- Targets hallmark and specific disease targets, while avoiding off-targets
- Supports all pipeline candidates through selective receptor mode of action

ZELEKT™ ("Targeted Discovery & Pre-Clinical")

- Prepare drug candidate as a collective-NCE from database (new chemical entity)
- Complete pre-clinical efficacy testing and ADME/TOX

ZYNDIKATE® ("Drug Delivery System")

- Collection of drug delivery systems supporting various routes of administration
- Facilitates effective transport of the poorly soluble CNS-molecules to the target site
- Introduced prior to clinical testing, derisking the drug development process
- Supports the pipeline and CDMO track

ZYNTAKS™ ("First-in-Human ready")

- Fine-tuning of drug delivery system, stability, dossier file for clinical testing etc.

The zIQube™ system

Connecting the dots

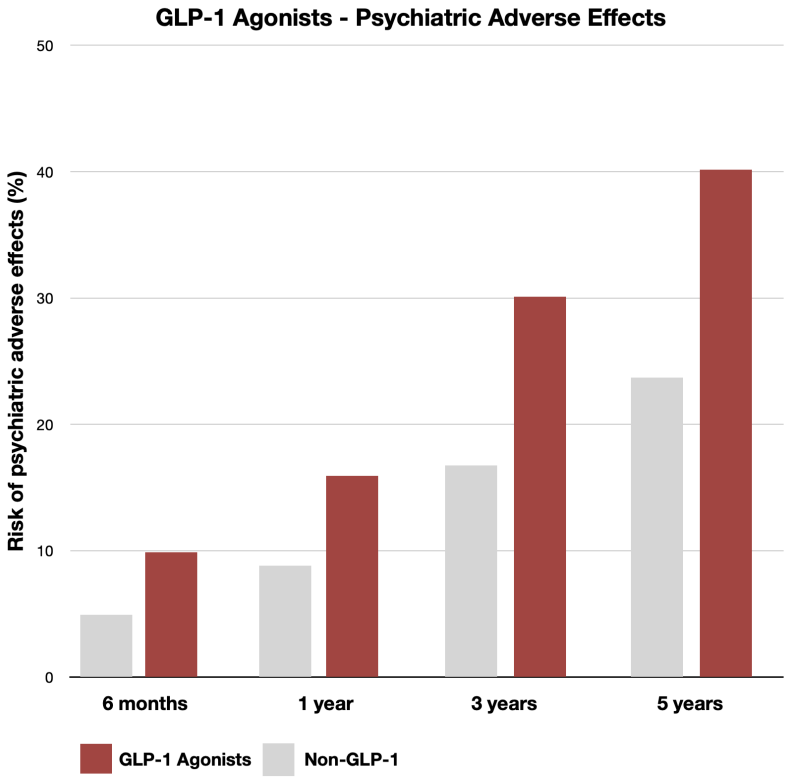
Source: Company information.

“Obesity, in almost all circumstances, is most likely a disorder of the brain”… Dr. Halpern, University of Pennsylvania

TETRA PHARM

GENERAL CHALLENGES WITH ANTI-OBESITY DRUGS CURRENTLY ON THE MARKET

HIGH EFFICACY BUT SIGNIFICANT ADVERSE EFFECTS



Anti-obesity drugs and Psychiatric Adverse Effects

- A large 2024 cohort study[1] investigated the impact of glucagon-like peptide-1 receptor agonists (GLP-1´s), specifically Liraglutide and Semaglutide, on the risk of developing psychiatric conditions such as depression, anxiety, and suicidal behaviours in patients with obesity
- Across all demographic subgroups, GLP-1 users consistently exhibited an elevated risk of psychiatric adverse effects
- The same applies to CB_1R inverse agonists, such as Rimonabant, which also have been associated with psychiatric side effects (in particular anxiety)

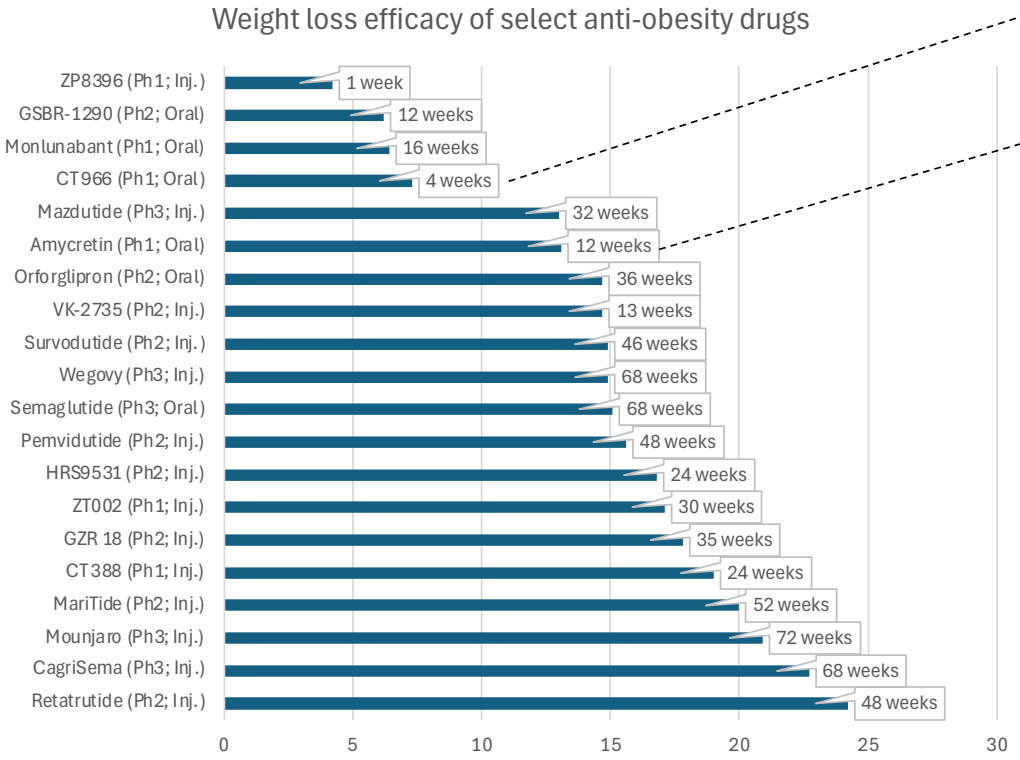
One year following semaglutide withdrawal, patients regain 2/3 of their weight loss, confirming the chronicity of the disease.

*A GLP-1 analogue is **not a cure**, it's a tool!*

1) Kornelius, E., Huang, JY., Lo, SC. *et al.* The risk of depression, anxiety, and suicidal behavior in patients with obesity on glucagon like peptide-1 receptor agonist therapy. *Sci Rep* 14, 24433 (2024). https://doi.org/10.1038/s41598-024-75965-2
2) Wilding, JPH. *et al.* Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. *Diabetes Obes Metab.* 2022 May 19;24(8):1553–1564. doi: 10.1111/dom.14725

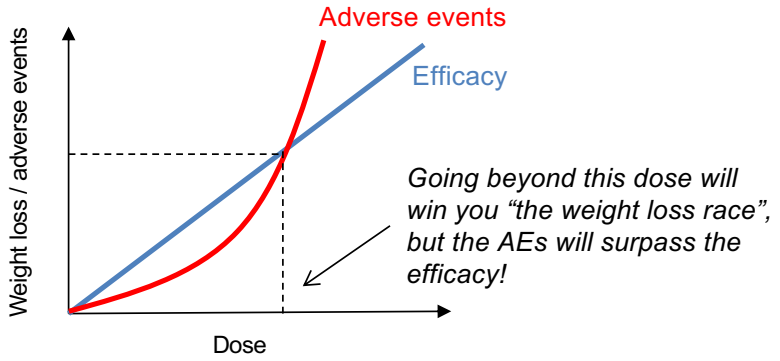
A RACE TO THE TOP…OR THE BOTTOM?

THE BALANCING ACT OF EFFICACY AND ADVERSE EVENTS



CT966 (Roche):
86% (nausea); 50% (constipation/diarrhea); 33% (vomiting)

Amycretin (NN):
75% (nausea)



With such high numbers of AEs being reported (and 10-15% being non-responders to GLP-1 analogues), have we crossed a line where the AE becomes the "therapeutic effect"?...for example an emetic / vomiting inducing drug?

1) https://www.zs.com/insights/obesity-medications-treatment-beyond-weight-loss

ANOTHER SETBACK FOR (ORAL) GLP-1 CANDIDATES

PFIZER ENDS DEVELOPMENT OF DANUGLIPRON

Pfizer Drops Lead Obesity Asset After Liver Safety Concerns, Overall Review

April 14, 2025 | 2 min read | Tristan Manalac

April 14th 2025: Danuglipron discontinued in Phase 3

- Potential drug-induced liver injury detected in a single trial patient (out of 1400)
- *This was the second setback for Danuglipron*

Late 2023: Dosing frequency reduced from twice-daily to once-daily

- Most trial patients dropping out mid-stage due to frequent episodes of nausea and vomiting (among other)

1) https://www.biospace.com/drug-development/pfizer-drops-lead-obesity-asset-after-liver-safety-concerns-overall-review
2) https://www.reuters.com/business/healthcare-pharmaceuticals/pfizer-ends-development-weight-loss-pill-danuglipron-2025-04-14/

TPT0701 – NEXT GENERATION CB_1R ANTAGONISTS FOR OBESITY

WITH FOCUS ON PRIMARY & SECONDARY (OFF-TARGET) RECEPTORS

1st GENERATION	2nd GENERATION	3rd GENERATION
CB_1R Inverse Agonists	CB_1R Inverse Agonists	CB_1R Antagonist/PR-2 Agonist
Designed to target CB_1R in CNS	**Designed to target CB_1R in PNS**	**Designed as multi-target drug for CNS & PNS**
Rejected due to concerns about impact on mental health (e.g. anxiety)	Peripherally restricted compound. Phase 2 study showed similar concerns with anxiety as 1st Gen compounds	Focus on MoA´s for multiple receptors (not only CB_1) to facilitate sustainable weight loss and eliminate known side-effects
SANOFI **Rimonabant**	novo nordisk® **Monlunabant**	TETRA PHARM TECHNOLOGIES **TPT0701**
Pfizer **Otenabant**	CORBUS PHARMACEUTICALS **CRB-913**	
Bristol Myers Squibb™ **Ibipinabant**		
MERCK **Taranabant**		

Tetra Pharm included Rimonabant and never generations in our receptor studies:

- Interaction with critical off-targets were found. These may explain anxiety-related side effects

TPT0701 is a multitarget drug designed to:

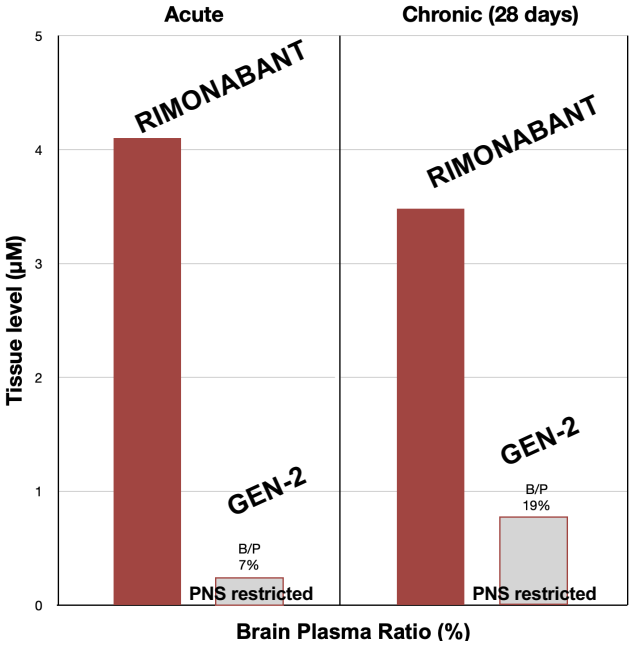
- Dual action to not only reduce appetite but also treat the hormonal imbalances causing obesity: Antagonism on CB_1 receptor (PR1) and agonism on PR2
- Avoid critical off-targets / unfavorable interaction
- Penetrate CNS where CB_1 receptors are abundant

Note: CNS = Central Nervous System; PNS = Peripheral Nervous System; MoA = Mode of Action; PR-2 = Primary Receptor 2 (a made-up name for confidentiality reasons)

CNS PENETRATION – MOLECULAR WEIGHT CUT-OFF VS. PENALTY

PERIPHERALLY RESTRICTED CB1 INVERSE AGONISTS STILL CROSS THE BBB

Peripherally restricted CB_1R inverse agonists still penetrate the BBB



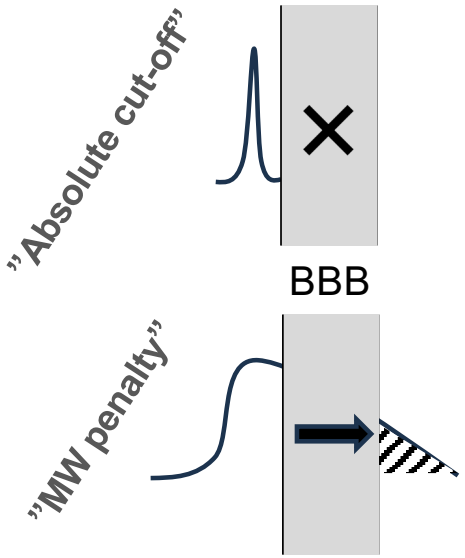
CB_1R inverse agonists still cross the BBB

- **Larger molecules have been seen to cross the BBB** through transcellular diffusion (as opposed to paracellular)
- **It is a MW penalty rather than a cut-off**, i.e. smaller molecules fulfilling Lipinski's rule will have a greater chance of success

Studies on a GEN-2 inverse agonist[2]

- The ligand is highly potent on CB_1 (0.3 nM)
- 7% acutely enters the brain and accumulates to 19% after 28 days (chronic dosing)
- It is likely that accumulation will continue with chronic use
- Unfavorable binding to off-targets is likely

MW > 400-500



(1) Banks, W.A., Greig, N.H. Small Molecules As Central Nervous System Therapeutics: Old challenges, New directions, and a Philosophic Divide. *Future Medicinal Chemistry* **11(6)**, 489-493 (2019). https://doi.org/10.4155/fmc-2018-0436

(2) Liu, Z et al. Functional Selectivity of a Biased Cannabinoid-1 Receptor (CB1R) Antagonist. *ACS Pharmacology & Translational Science.* February 6, 2021. https://doi.org/10.1021/acsptsci.1c00048

Note: BBB = Blood Brain Barrier; PNS = Peripheral Nervous System

TPT0701 – A NEW PERSPECTIVE

FOCUS ON LONG-TERM SUSTAINABLE TREATMENT

THE PROBLEM

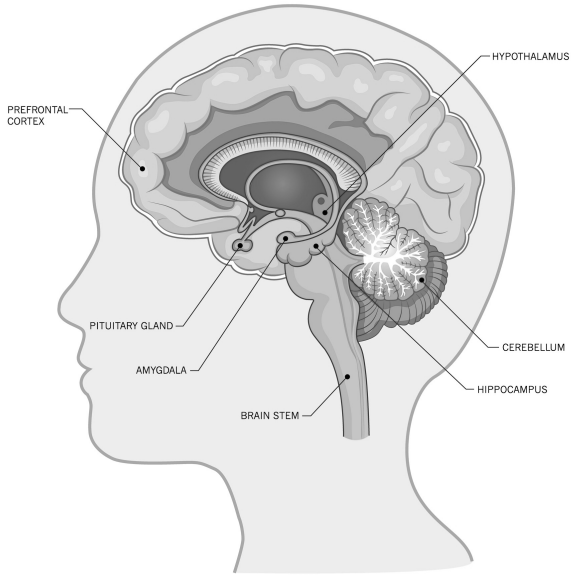
- Emphasis on rapid weight loss
- Weight loss is not sustainable. Patients relapse following seponation of drug
- Long-term adverse events seem to be neglected
- Acute medication is used to treat a chronic disease

OUR SOLUTION

- We acknowledge that obesity is a neurological disorder more than it is metabolic
- Apply polypharmacology to influence the circuit that governs food intake and satiety (effect), as well as help restore homeostasis (cause)
- Designed around critical off-targets to provide an acceptable safety profile
- TPT0701 is designed for a marathon (chronic), not a sprint (acute)

it´s a marathon not a sprint

The next generation of anti-obesity medications must be developed with a focus on long-term administration to avoid any negative impact on mental health



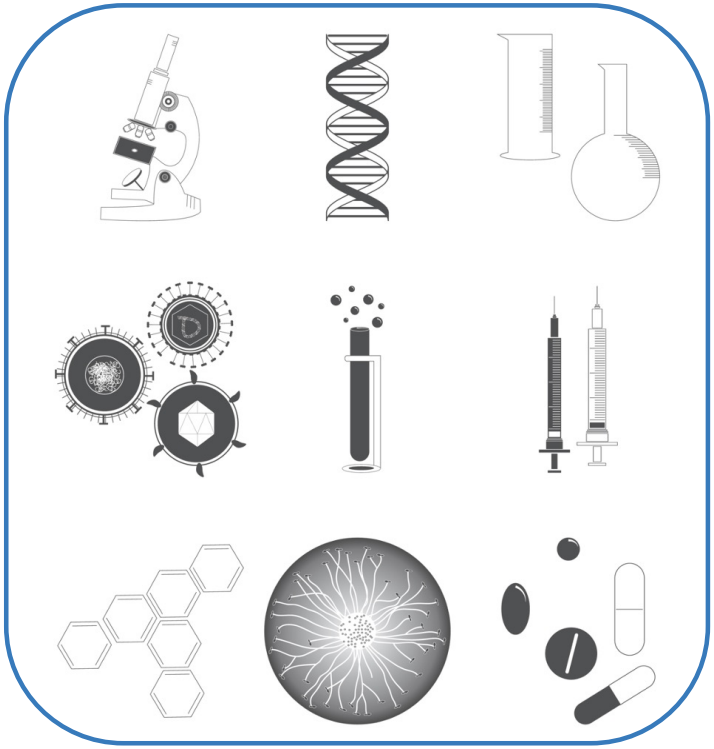
Source: Company information.

TPT0701 – DESIGNED TO BE A SUSTAINABLE DRUG FOR OBESITY

FOCUS ON HEALTHY WEIGHT LOSS AND MENTAL HEALTH

DESIGN CONSIDERATIONS

- **Best-in-class drug formulation** – designed for long-term (chronic) administration
- **Retainment of sustained effect** - with low side-effect profile
- **Protection against adverse effects**– no negative impact on mental health
- **Efficacious as standalone drug** or as enhancement of current anti-obesity drugs (for acute use)
- **Affordable and manufacturable** - low production costs



Source: Company information.

TPT0701 – DESIGN SPECIFICS AND STATUS

COMPLETING THE PUZZLE

Polypharmacology

- Two therapeutic receptor targets and two critical off-targets identified
- Dual function:
  - (1) CB_1R antagonism reduces appetite and increases satiety
  - (2) PR2 agonism restores homeostasis

Drug Design

- The following design templates considered:
  - (A) Reference compounds (safe, but less effective)
  - (B) Rimonabant (unsafe and too potent; to be avoided)
  - (C) Off-target receptors (to be avoided)

- Physicochemical attributes:
  - (1) CNS penetration
  - (2) ZYNDIKATE® (drug delivery) compliant

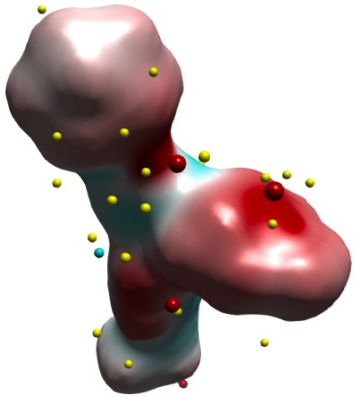
Pre-clinical

- On-going: In-vivo behavioral testing and ADME/TOX

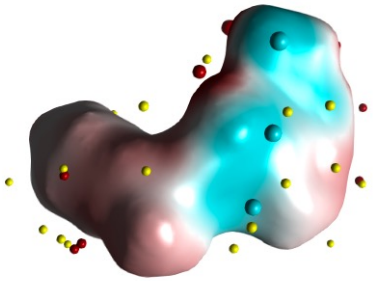
Drug Delivery

- Oral formulation – ZYNDIKATE® nanotechnology

TPT0701 **CB1 antagonist** with electrostatics



TPT0701 **PR2 agonist** with electrostatics



Source: Company information.

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