HMNC Brain Health

HMNC – driven to optimize treatment of depression, anxiety and sleep disorders for a rapidly growing market

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Antidepressant drugs – current situation

- Antidepressants are the **first-line treatment** of major depression
  - ~ 60 % of professionally treated patients **remit after 6-10 weeks**
  - ~ 30 % **need much longer** to respond favorably
  - ~ 10 % **become chronically ill**

- Challenges with current antidepressants:
  - ➢ It takes too long until they work
  - ➢ They work in too few patients
  - ➢ They have too many side effects
  - ➢ Their mechanisms differ not fundamentally from each other

- Challenges with radically new antidepressants:
  - ➢ They failed to demonstrate efficacy in major depression
  - ➢ They work only in subgroups of patients

HMNC has the tools to unlock the high potential of a growing market for antidepressants and anxiolytics

Depression fact:	• Patients meeting criteria for major depression have different causal mechanisms
Antidepressant facts:	• Current drugs have an unspecific mode of action • New drugs are targeting a specific mechanism
The problem:	• Which patient will benefit from a specifically acting drug?
The solution:	• Stratifying patient population with gene tests and biomarkers to match patients with drugs

CRHR1-antagonists: CRH-hypersecretion in patients with depression as causal factor

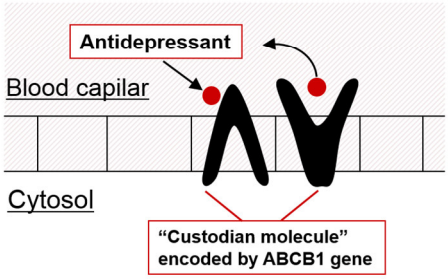
- Corticotropin-releasing hormone (CRH) regulates the adaption to stress
- If CRH hypersecretion endures depression emerges in vulnerable individuals
- CRH is increased **in only about 20% of the patients** with depression
- CRH works via the CRH receptor 1 (**CRHR1**) => Many CRHR1-antagonists were developed to treat depression
- Clinical studies with **CRHR1-antagonists** failed because of lacking stratification according to CRH-status

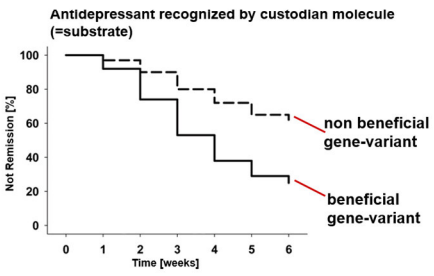
If only about 20% have CRH hypersecretion, CRHR1 will not work in everyone

▶ HMNC developed a lab test that identifies who will benefit from CRHR-antagonists. This test showed already high sensitivity and specificity in a large (n = 500) controlled trial

ABCB1 – determines the entry of drugs into the brain

- The gene product of the ABCB1 gene, the **P-glycoprotein (P-gp)**, is a custodian molecule located at the **blood-brain barrier (BBB)**
- It is responsible for the active efflux of various substances at the BBB, including many antidepressants
- 70% of all current antidepressants are P-gp substrates
- DNA sequence variants in the ABCB1 gene **can predict the individual treatment response** to antidepressants
- These sequence variants can be detected through an **ABCB1 gene test**
- ABCB1 test **informs the physician** about type and dosing of antidepressants
- HMNC has **launched the ABCB1 test to the market in July 2015**





V1B-antagonists: Vasopressin hypersecretion in patients with depression as causal factor

- Next to CRH, **vasopressin** coordinates hormonal and behavioral responses within the stress hormone system
- If **vasopressin hypersecretion** endures depression and anxiety disorders develop in vulnerable individuals
- The **vasopressin receptor (V1B)** mediates vasopressin induced changes
- In animals **blockade of the V1B** showed a decrease in anxiety
- Several pharma companies have started clinical development of **V1B-antagonists**
- Previous phase II b studies **did not test patients according to central vasopressin** activity

▶ HMNC has the tool that identifies which patient has elevated central vasopressin. Only those will benefit from V1B-antagonists

HMNC has an innovative pipeline inspired by basic science

HMNC has a number of additional early stage projects with roots at the Max Planck Institute of Psychiatry

- Lab test that identifies subgroups of patients with posttraumatic stress disorder that require specific treatment (status: patents approved in Europe and US)
- Intranasally administered neuropeptides to treat anxiety disorders and sleep disorders (status: hit to lead)
- Identification of unprecedented targets guiding R&D of innovative antidepressants (status: preclinical validation)

Alliances HMNC is striving for

1. Marketing and distribution of HMNC´s blood-brain barrier test (ABCB1 test) in Europe and the US
2. Marketing and distribution of HMNC´s lab test for diagnosing and guiding treatment of posttraumatic stress disorder in Europe and the US
3. Inlicensing of CRHR1-antagonists that failed in clinical trials aiming at repurposing via lab test-based stratification
4. Co-developing of V1B-antagonists for treatment of depression employing HMNC´s gene-based labtest
5. Co-developing HMNC´s new peptide-based treatment of anxiety and sleep disorders

Benefits of partnering with HMNC

Promising market development

- The demand for personalized therapies and in-vitro diagnostics (IVD) is rising worldwide
- Prescriptions for antidepressants surge but returns stagnate because market is saturated with generics
- Pharma companies tend to join forces with small firms to optimize development and minimize risk

Unique know-how

- HMNC has a team of specialists in psychiatric research and with expertise in realization of complex clinical projects
- HMNC owns IP for gene tests and biomarkers and has shown that repurposing of failed drugs works

Success rate

- Within a few years HMNC achieved its first market launch of a lab test
- HMNC has already shown in several clinical trials that stratifying patient population with lab tests works

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Thank you for your interest!

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