PRIVATE SECTOR THRESHOLDS FOR INVESTMENT IN NEUROSCIENCE CLINICAL TRIALS

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LUNDBECK IN BRIEF

We are a specialized pharmaceutical company engaged in discovering, developing and commercializing new and innovative treatments for psychiatric and neurological disorders

1915	**5,300**	**14.6bn**	**70%**
founded by Hans Lundbeck in Denmark	employees worldwide	DKK in revenue in 2015 (EUR 2.0bn and USD 2.2bn)	owned by the Lundbeck Foundation

THE LUNDBECK FOUNDATION

The Lundbeck Foundation is the largest shareholder of Lundbeck and owns 70% of the company.

The Foundation provides grants for scientific research initiated in Denmark and of the highest international quality in order to make a significant difference to human health and life.

The Foundation annually grants around USD 60-75 million to support research within medical and natural sciences.

A GLOBAL DISEASE BURDEN

350
million people worldwide are living with **depression**

21
million people worldwide are suffering from **schizophrenia**

6
million people worldwide are living with **Parkinson's disease**

48
million people worldwide are living with **Alzheimer's disease** and other dementias




Huge investments neuroscience R&D

Trial/ Phase/ CT identifier	Company	Phase	Principle	Trial
Safety and Efficacy Study Evaluating TRx0237	TauRx	Phase III	Tau aggregation inhibitor	NCT01689246
Masitinib	AB Science	Phase III	C-Kit tyrosin kinase inhibitor	NCT01872598
Solanezumab EXPRDITION3	Eli Lilly	Phase III	A-beta antibody	NCT01900665
Aducanumab PRIME (BIIB037)	Biogen	Phase 1b	A-beta antibody	NCT01677572
Safety and Efficacy Study Evaluating TRx0237	TauRx	Phase III	Tau aggregation inhibitor	NCT01689233
Merck MK8931, EPOCH	Merck	Phase II/III	BACE1 inhibitor	NCT01739348
E2609	EiSAI	Phase II	BACE1 inhibitor	NCT02322021
Gantenerumab	ROCHE	Phase III	A-beta antibody	NCT02051608
Azeliragon (TTP488), STEADFAST	TransTech Pharma	Phase III	RAGE inhibitor	NCT02080364
Axon Neuroscience AADvac1, ADAMANT	Axon Neuroscience	Phase II	Tau active vaccine	NCT02579252
ALZT-OP1	AZTherapies	Phase III	Cromlyn + Ibuprophen combination trial	NCT02547818
Merck MK8931, APECS	Metck	Phase III	BACE1 inhibitor	NCT01953601
Astra AZD3293, AMARANTH	Astra, Eli Lilly	Phase II/III	BACE1 inhibitor	NCT02245737
Astra AZD3293, DAYBREAK-ALZ	Astra, Eli Lilly	Phase III	BACE1 inhibitor	NCT02783573
Pioglitazone (sustained release), TOMORROW	Takeda	PhaseIII	P-PAR-g agonist	NCT01931566
Solanezumab, A4	Eli Lilly	Phase III	A-beta antibody	NCT02008357
Biogen Aducanumab (BIIB037), ENGAGE	Biogen	Phase III	A-beta antibody	NCT02477800
Biogen Aducanumab (BIIB037), EMERGE	Biogen	Phase III	A-beta antibody	NCT02484547
Crenezumab	Roche	Phase III	A-beta antibody	NCT02670083
Gantenerumab	Roche	Phase III	A-beta antibody	NCT01224106
Solanezumab, EXPEDITION-PRO	Eli Lilly	Phase III	A-beta antibody	NCT02760602
CAD106, Generation/ API APOE4 trial	Novartis	Phase II/III	A-beta active vaccine	NCT02565511
JNJ-54861911	J&J	Phase II/III	BACE1 inhibitor	NCT02569398

Key Scientific Achievements Essential for Preclinical Innovation

- **iPSCs**
  - Basic research tool within biology, safety and toxicology
  - Potential to study disease heterogeneity
  - Key translational tool

- **Non-human disease models with strong translational focus**
  - Methods for induction of relevant phenotypes:
    - Optogenetics, CRISPR etc
  - Behavior studies - still a part of the picture
  - Automation and advanced data analysis

- **-omics**
  - Functional genetics
  - Epigenetics
  - Single cell sequencing methods
  - Bioinformatics

- **Delivery of antibodies and other drug substances into the brain in high(er) concentrations**

Key Scientific Achievements
Essential for translational innovation

- **Translatable endophenotypes**
  - Rhythmic activity (oscillations) assessed by EEG/MEG
  - Event related electrophysiological responses (P50, P300, mismatch, etc), assessed by EEG
  - Glutamate, glutamine, GABA levels (or other) assessed by H-MRS
  - Connectivity (resting state or event related) assessed by MR, eg cortico – amygdala dysfunction in response to fearful experiences

- **Non-interventional methods in Humans (EEG, PET, MRI etc)**
  - Target engagement in the human brain
  - PoM for new mechanisms
  - Characterizing disease state and subsegments
  - Studying disease pathologies in the brain

Key Scientific Achievements – Essential for understanding of diseases

- **Clinical scales:**
  - Scales linking to functional outcome
  - Independent living scales
  - Global assessment of functioning
  - Subjective scales (or caretaker responding scales), in contrast to investigator or clinician rated scales.

- **New tools (devices) for studying disease progression and stage**
  - Language (pitch as well as semantics/syntax) via phones
  - Social interaction, social cognition monitored remotely with handheld or wrist/ankle devices
  - Wearable (and constant monitoring) EEG devices
  - Remote assessment of cognitive function or activities of daily living

- **Redefining disease entities:**
  - Linking a specific disease biology to specific patient population (genetics, symptomatology, pathology)
  - Markers for disease progression/disease stage in specific patient population

Many (new) disease hypotheses…..

Alzheimer's disease:
- Abeta
- Tau
- Misfolded protein clearance mechanisms
- Inflammation

Parkinson's disease
- Alpha-synuclein
- LRRK2
- Misfolded protein clearance mechanisms
- Inflammation

Schizophrenia
- Interneuron hypothesis
- Cholinergic hypothesis
- Mesolimbic pathway
- Neurodevelopmental disease
- Origin and impact of genetic risk factors

Depression
- NMDA hypothesis for action of ketamine
- HPA/stress axis
- Neuro inflammation
- Dysfunctional neuro circuitry

Build for even more private sector investment

- Continued investment in basic neuroscience
  - Develop our understanding of underlying pathology
  - Develop new technologies to visualize biological processes
  - Develop research talents

- Strengthen research with focus on human population studies

- Strengthen research in translational sciences with basis in disease biology hypotheses
  - Allow for cross-talk and validation between pre-clinical and exploratory clinical research
  - Decrease cycle-time for hypotheses to be validated in patients