D-Pharm Ltd.
The Targeted Neuroscience Company
Company Overview, November 2014
Disclaimer

• The information detailed in this presentation concerning the Company’s deployment regarding the expected timelines for the development of the Company’s products, sales potential of the lead products, the potential of Company’s products for additional indications and the size of the target markets for these treatments, constitute “forward-looking statements” as defined under Israeli securities law and is based on D-Pharm’s work plans and on information presently available to D-Pharm.

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Targeted Neuroscience
The Company

*Developing targeted drugs in billion dollar markets*

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<td>• Three Phase 2 clinical-stage products: in safe thrombolysis, epilepsy and pancreatitis</td>
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<td>• More effective therapies with no/fewer adverse effects</td>
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<td>Expertise</td>
<td>• Discovery and development of innovative targeted drugs</td>
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<td>• Multinational advanced clinical studies under the FDA, EMA and under 18 other national regulators</td>
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<td>D-Pharm Ltd.</td>
<td>• IPO in 2009 on Tel-Aviv stock exchange (TASE). Symbol DPRM</td>
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*Targeted Neuroscience*
Name & Face

Experienced management team and Board of directors

Dr. Aharon Schwartz, Chairman of D-Pharm’s Board of Directors, formerly VP of Strategic Business Planning and New Ventures at Teva Pharmaceutical Industries; prior that Dr. Schwartz served at Teva as a Head of Global Products Division; Copaxone® Division; Business Development/Export Division; and Pharmaceutical Division.

Dr. Alex Kozak, the Founder and Chief Executive Officer, has been responsible for creating and implementing of company’s vision and corporate strategy. Dr. Kozak managed D-Pharm’s private and public financing rounds. The inventor of D-Pharm’s technologies, he holds a Ph.D. in Neurobiology from the Weizmann Institute of Science.

Dr. Gilad Rosenberg, Vice President, Research & Development, formerly the medical director of Merck, Sharp and Dohme’s Israeli subsidiary. He received post-graduate training in neurology at the Hadassah Medical Center, Jerusalem, holds an M.D. from the Israel Institute of Technology and an M.Sc. in Neuroscience from Oxford University.

Ofra Yamin, Vice President, Finance & HR, has been managing D-Pharm’s financial policy, planning and record-keeping, as well as financial reporting to the stock market, holds an MBA from Tel Aviv University and B.A. in Economics and Accounting from the Hebrew University in Jerusalem. She qualified as a Certified Public Accountant (CPA).

Targeted Neuroscience
## The pipeline

### Three Phase 2 clinical-stage products

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<th>Product</th>
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<td>Phase 2 clinical study. Patient enrolment completed</td>
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<td>&quot;Safe tPA&quot;</td>
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<td>Co-development, Jiangsu Nhwa Co*</td>
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<td>3 Pancreatitis</td>
<td>DP-b99</td>
<td>1 2 3</td>
<td>Ongoing Phase 2 clinical study</td>
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(*) Jiangsu Nhwa Pharmaceutical Co. Ltd. licensed DP-VPA for China and funding the Epilepsy program
D-Pharm has three large-market, patented CNS drugs in Phase 2 clinical trials

- **“Safe tPA” (THR18).** Alteplase (tPA) the only clot-busting drug FDA approved for treatment of acute ischemic stroke, is significantly underused primarily due to the risk of brain bleeding. D-Pharm’s “Safe tPA” (THR18) has shown in initial trials to be the first drug to materially decrease the occurrence of brain hemorrhage and edema in acute ischemic stroke patients treated with tPA. tPA has about $1 Billion in annual sales.

- **DP-VPA** incorporates the well-known anti-epileptic drug valproic acid (VPA) in a form which elegantly targets and affects only the brain neurons which over-actively fire to cause the epilepsy. DP-VPA significantly increases efficacy and decreases side effects of the incorporated VPA. D-Pharm has shown efficacy of DP-VPA in phase 2a clinical trials in Europe. DP-VPA is licensed to Jiangsu NHWA ("NHWA"), the leader in CNS in China. NHWA is entering into a large, phase 2b clinical trial in China, according to Western standards. D-Pharm maintains rights to DP-VPA for the rest of the world.

- **DP-b99** is the only known therapy for pancreatitis where the pancreas, a vital organ, destroys itself and, in severe cases, causes damage to other organs such as the kidney and lungs. DP-b99 was shown to be safe and D-Pharm is taking DP-b99 into a Phase 2a trial which should be completed in 2015.
Intellectual Property

- D-Pharm products, THR18, DP-VPA and DP-b99, are new chemical entities (NCE) protected by composition and use patents worldwide.

- Statistics:
  - Total 109 patents granted
    - 14 granted in the USA
    - 58 granted in European countries
  - 10 pending applications
  - 4 US provisional applications
THR18 to make clot-busting with tPA safe

**Goal:** Triple the number of patients treated with tPA

**Technology:** antagonizing neurotoxic effect of tPA

**Drug:** New chemical entity (NCE); Small synthetic peptide derived from natural inhibitor of tPA, PAI-1

**Effect:**
- No effect on the clot-busting
- Prevents brain swelling and bleeding
- Decrease disability following AIS

**Status:** Top-line results
The majority of strokes are caused by a clot cutting off vital blood flow to the brain

*The estimated annual cost of stroke in the U.S. is $73.7 B*

- Ischemic strokes in the Western Hemisphere are approximately 87% of total strokes
- Stroke is a leading cause of death and disability in the U.S. and Europe
  - There are an est. 7,000,000 stroke survivors in the U.S.
- 1.6 mil strokes will occur this year in the U.S. and Europe

* by National Stroke Association

tPA is only drug approved for treatment of acute ischemic stroke (AIS)

- tPA (Alteplase) is the drug of choice for treatment of major thrombotic diseases:
  - Acute ischemic stroke (AIS)
  - Myocardial infarction (MI)
  - Pulmonary embolism (PE)
- tPA (Alteplase) worldwide sales estimated at ~ $1 B*

*A Source: EvaluatePharma
http://www.evaluatepharma.com/Universal/View.aspx?type=Entity&entityType=Product&lType=modData&id=333&componentID=1003
Treatment with tPA is coupled with the risks of life-threatening adverse effects

*Doctors are reluctant to use tPA fearing brain bleeding*

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**Targeted Neuroscience**
Phase IIa Study of THR18 in Acute Ischemic Stroke (AIS) Patients Treated with tPA

• **Study Design:**
  – Double-blind, placebo-controlled, escalating single-dose, phase IIa study of THR18 co-administered with tPA to subjects with AIS. N=30

• **Pre-specified endpoints:**
  – Safety profile, Maximal Tolerated Dose, Pharmacokinetics (PK)
  – Clinical outcome: mRS score at day 30 and NIHSS scores at admission, at days 1, 2, 3, and 30

• **Treatment groups:**
  1. THR18 (0.18 mg /kg) n=6; 2 and 3) THR18 (0.56 mg /kg) n=12 (6X2) with the interim analysis in-between; 4) Placebo n=12

• **Status:** top-line results
THR18 significantly decreases the occurrence of brain edema & hemorrhage

THR18 decreases brain edema in patients treated with tPA

 THR18 prevents intracranial hemorrhage (ICH) in patients treated with tPA

- top-line data, n=30; no symptomatic hemorrhage occurred
- assessment in patients with big infarctions (acute hypodensities on CT)

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THR18 significantly, in a dose-dependent manner, enhances post-stroke recovery.

<table>
<thead>
<tr>
<th>Time (days following stroke)</th>
<th>NIHSS</th>
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<tr>
<td>Placebo</td>
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<tr>
<td>THR18 0.18mg/kg</td>
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<tr>
<td>THR18 0.54mg/kg</td>
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** P = 0.01

Less disability in patients treated with THR18

THR18 enhanced recovery following ischemic stroke

* - interim report, n=21

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Market research forecasts over billion dollar sales of THR18

- Stroke experts and payers were interviewed in the US, UK, Germany, France, Spain, Italy
- Responders estimated that:
  - About 90% of patients receiving tPA would also receive THR18
  - THR18 is expected to double or triple the current $0.8 B market of tPA*
  - The responders were comfortable with THR18 priced at 80-100% of tPA

*Source: www.evaluategroup.com
DP-VPA at glance

A breakthrough in epilepsy targeted neuroscience
Superior pro-drug of VPA: potency and safety

Status: Phase II; 246 subjects exposed to date

Drug: New Chemical Entity (NCE); Prodrug of VPA

Technology: Drug activation “on demand”, in over-firing neurons

Risk sharing: Epilepsy program is funded by Nhwa Pharm. Co.

Benefits: DP-VPA surpasses VPA in potency & safety
  • Potentially Once-a-Day-Drug
  • Inherits key advantages of VPA

Epilepsy: the disease of abnormally-firing neurons. Affecting 0.1% of population.
DP-VPA selectively activated by over-firing neurons involved in epileptic activity

Targeting diseased cells offers added safety and potency

Normal neurons have little or no enzymatic activity sufficient to activate DP-VPA

Abnormal enzymes in over-firing neurons selectively activate DP-VPA within “diseased” cells

Targeted Neuroscience
In Phase 2 D-Pharm’s DP-VPA showed superior efficacy & safety

**DP-VPA significantly reduced number of epileptic seizures**

- **Patient population, n=60:**
  - Refractory partial onset epilepsy
  - 30 patients per arm
  - Add-on therapy
- **Safety:**
  - Superior to historical Divalproex
- **Efficacy:**
  - DP-VPA significantly reduced number of seizures, *p*=0.02 (Period 1, DP-VPA-naive patients)
Co-development with Jiangsu Nhwa

**Leverage for D-Pharm’s development program**

**Jiangsu Nhwa Pharmaceutical Co., Ltd (China)**

- Nhwa is one of the largest CNS companies in China
- In-licensed rights to develop and market DP-VPA in China
- NHWA is developing DP-VPA in compliance with ICH/FDA guidelines
- DP-VPA is granted Fast Track Status by the CFDA

**D-Pharm Ltd.**

- D-Pharm keeps all rights for markets outside of China
- D-Pharm has worldwide rights to data generated by Nhwa
- D-Pharm has exclusive rights to purchasing of DP-VPA for ROW
- Economic terms include payments for development and sales milestones as well as royalty payments
DP-b99 in high-risk acute pancreatitis

*First-in-class disease-modifying drug*

Acute pancreatitis

- 20% at high risk
- 80% recover
- ~30% mortality
- Survivors frequently disabled

Hospitalization cost in USA is > $2 B annually*. No disease-modifying drug is available.

* source: Fagenholz et al., 2007
Acute High Risk Pancreatitis: mechanisms of cell damage and opportunities

Cell Ca\(^{2+}\) and inflammation play central role in cell damage

DP-b99 may become 1\(^{\text{st}}\) disease-modifying drug in acute pancreatitis

Targeted Neuroscience
Phase 2 study of DP-b99 in the treatment of acute high risk pancreatitis

*First proof-of-concept clinical study*

- Design: Intervventional, Randomized, Parallel, Double Blind, Placebo Controlled, Phase 2. N=30, 1:1 ratio drug or placebo
- Aims: Efficacy & Safety
- Primary Outcome Measures: Markers of systemic inflammation (e.g., CRP) and clinical outcome
- **Status:** Phase 2 study is ongoing
Short-term catalysts, 2015/16

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<td>Financing</td>
<td>Major Financing</td>
<td>FDA meeting re: DP-b99</td>
<td>1st patient Phase 2b THR18</td>
<td>Enrolment and interim reports in Phase 2b: THR18 and DP-VPA</td>
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<td>End of Phase 2 THR18</td>
<td>Last patient in Phase 2 DP-b99</td>
<td>IND Phase 2b THR18</td>
<td>1st patient Phase 2b DP-VPA</td>
<td>IND and 1st patient in Phase 2b DP-b99</td>
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 THR18 Phase 2a completed
 DP-b99 Phase 2 completed
 Two INDs
 Two Phase 2b started
 Three Phase 2b on-going
Long-term clinical catalysts towards value inflection point, final reports 2017

**Phase 2b “Safe tPA” / THR18**

**Phase 2b Pancreatitis / DP-b99**

**Phase 2b Epilepsy / DP-VPA**

**Development in misfolded protein diseases, e.g. Alzheimer’s**
D-Pharm at glance

Positioned to breakthrough in 2015 – 2017

• Three advanced clinical-stage products
• Developing drugs in billion dollar markets
• Shared risk: one of the three development programs (Epilepsy) is funded by co-development partner in China
• Experienced management team and Board of directors
  – Proven record of CNS drug development under FDA and EMA
  – Well trained, experienced and highly motivated team