# **Medical Therapies Limited**

## Midkine Portfolio Acquisition 9 May 2008



## **Forward looking statements**

This presentation contains forward-looking statements. These statements are not guarantees of Medical Therapies Limited's future performance and involve a number of risks and uncertainties that may cause actual results to differ materially from the results discussed in these statements.

Factors that might cause the Company's results to differ materially from those expressed or implied by such forward-looking statements include, but are not limited to, development and commercialisation of the Company's product portfolio, development or acquisition of additional products and other risks and uncertainties.



# Midkine portfolio acquisition

- Rationale for the acquisition of the midkine portfolio
- What is midkine?
- O Details of the IP Agreement
- Midkine therapeutics portfolio
- Midkine diagnostics portfolio
- MTY post acquisition
- o Timetable of key events



## Rationale for midkine (MK) acquisition

| MTY acquisition criteria  | Midkine portfolio  |  |
|---|--|--|
| Sound scientific principles<br>underlying the technology with clear<br>regulatory path and strong<br>commercial potential | <ul> <li>Known composition and mechanism of action</li> <li>Extensive in vitro and preclinical data (strong regulatory position) with a range of commercialisation opportunities</li> <li>Interest in MK from major pharma/biotech companies</li> <li>\$10M spent on midkine since 2001</li> </ul> |  |
| Therapeutic areas of cancer and inflammation  | <ul> <li>MK for heart tissue damage</li> <li>MK inhibitors for cancer, RA and auto-immune disease</li> </ul>   |  |
| Late stage technology or technology platform with development potential   | <ul> <li>Rich technology platform</li> <li>Potential for delivering early revenue via diagnostics</li> <li>High value therapeutic product development programs</li> </ul>  |  |
| Mostly share based acquisition  | © 20 million shares<br>© \$1.5M cash   |  |
| PLUS +  | <ul> <li>Outstanding scientists, including discoverer of midkine</li> <li>Strong IP position with clear FTO in key areas of interest</li> <li>Diagnostic platform with early revenue potential</li> <li>Therapeutic collaboration potential in a number of indications</li> </ul>                  |  |

## Midkine



- Discovered in 1988 by professors Muramatsu and Kadomatsu at Nagoya University
- Low molecular weight growth factor like protein (13kD) with two domains
- Highly expressed in oncogenesis, autoimmune and inflammatory diseases
- Midkine has a role in anti-apoptosis, cell migration, angiogenesis and cell growth

#### **MIDKINE MEDIATES:**

Cancer progression Onset of inflammatory diseases Preservation and repair of injured tissue

Midkine is strong therapeutic and diagnostic target

# Intellectual Property Agreement

#### MTY will acquire from Cell Signals (CS)

- Therapeutic applications for midkine the protein
- 120+ anti-midkine antibodies with their therapeutic applications and antimidkine nucleotides (cancer and autoimmune diseases such as MS)
- Diagnostic applications of midkine and anti-midkine antibodies owned by CS

#### o Consideration

- \$1.5M cash
- 20 million MTY shares

#### O Conditions

- Due diligence on the midkine intellectual property portfolio
- Approval of the transaction by a general meeting of MTY shareholders
- Private placement of shares to the value of \$2M

# Midkine portfolio



# **Intellectual Property Portfolio**

- O 28 patents covering use and manufacture of midkine, anti-midkine antibodies and anti-midkine nucleotides for diagnostic and therapeutic applications:
  - 120+ anti-midkine antibodies and all reagents
  - ELISA tests for
    - Early detection of cancer
    - Diagnosis of rheumatoid arthritis
    - Diagnosis of Alzheimer's disease
    - Diagnosis of Sjogren's Syndrome
  - Therapeutics
    - Preclinical data supporting use of midkine for the prevention and treatment of heart damage during myocardial infarct
    - Anti-midkine antibodies for the treatment of inflammatory conditions and autoimmune diseases
    - Anti-midkine antibodies and nucleotides for the treatment of cancer

## **Therapeutics Portfolio: Midkine**

#### Using midkine and its protective function



## Treatment for heart tissue damage

Addition of midkine reduces heart tissue injury in animal models by reducing apoptosis and increasing angiogenesis

#### **Pig model**



Control

#### Midkine treated

Mortality rate after 24h:

•Control: 4/12 (33.3%)

• MK-treated: 1/9 (11.1%)

#### **Mouse model**









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## **Therapeutics portfolio: Midkine inhibitors**

#### Inhibition of midkine using anti-midkine antibodies and nucleotides



## Inhibition of midkine is potential treatment

Solid Tumours Rheumatoid arthritis Multiple sclerosis Endometriosis

Midkine is expressed during oncogenesis, inflammation and tissue repair

## **Treatment for rectal carcinoma**

 Anti-midkine antisense DNA directed to suppress growth of mouse rectal carcinoma cells (CMT-93) (Takei et al, 2001)



## Treatment for multiple sclerosis

 MS symptoms are reduced when MOG35-55 is administered to mice with no midkine genes (Wang et al, 2008)



## Treatment for rheumatoid arthritis



| increase | alev | eis | ΟΙ | IV |
|----------|------|-----|----|----|
| patients | with | RA  |    |    |

|         | No. of mice<br>arthritis |   | Incidence (%) |  |
|---------|--------------------------|---|---------------|--|
|         | +                        | - |               |  |
| WT      | 6                        | 1 | 86            |  |
| КО-МК   | 1                        | 9 | 10            |  |
| MK pump | 9                        | 3 | 75            |  |



• 6/7 (86%) WT mice show symptoms from antibody-induced arthritis

• 1/10 of MK-KO (10%) mice show symptoms

# Global markets for key indications

| INDICATION               | GLOBAL<br>PREVALENCE                 | TREATMENT  | GLOBAL MARKET<br>(US\$)   |
|--------------------------|--------------------------------------|--|---|
| Acute myocardial infarct | ~ 32 million heart<br>attacks / year | <ul> <li>Surgery</li> <li>ACE inhibitors</li> <li>Beta blockers</li> <li>Fibrinolysis</li> </ul> | • Cardiovascular drugs<br>worth ~ \$82.4 billion in<br>2007   |
| Cancer                   | ~ 25 million                         | Chemotherapy<br>Radiotherapy<br>Targeted therapies   | <ul> <li>\$4 billion in 2007 for<br/>Herceptin alone</li> <li>Estimated \$45 billion<br/>in 2012 for global<br/>cancer drug market</li> </ul> |
| Multiple sclerosis       | ~ 3 million                          | Disease-modifying agents   | \$4.9 billion in 2006   |
| Rheumatoid arthritis     | ~ 5 million                          | NSAIDs<br>Corticosteroids<br>Biologicals   | \$16 billion in 2006  |
| Endometriosis            | ~ 89 million                         | NSAIDs<br>Surgery<br>Hormonal therapy  | \$2.2 billion by 2014 for pharmaceutical treatments alone   |

# **Therapeutic portfolio**



## **Diagnostic Products**

Detection of midkine using Enzyme-linked Immunoassay (ELISA)





# Incidence and cost of cancer

#### Almost 11 million new cases of cancer diagnosed each year globally





## **Breast cancer diagnostic**

| Breast cancer | Other Biomarkers** |         | Midkine* |          |  |
|---------------|--------------------|---------|----------|----------|--|
| Stage         | CA15-3             | BCA225  | CEA      | Miakine" |  |
| 0             | 0%                 | 0%      | 0%       | 45.5%    |  |
| I             | 4%                 | 8%      | 6%       | 27.9%    |  |
| IIA           | 0.04               | 22% 11% | 44.9/    | 50.0%    |  |
| IIB           | 8%                 |         | 11%      |          |  |
| IIIA          | 10%                | 20%     | 100/     | 22.2%    |  |
| IIIB          | 19%                | 39%     | 18%      | 33.3%    |  |
| IV            | 38%                | 100%    | 56%      | 100%     |  |

Source:\*Cell Signals, \*\*The Journal of The Japan Medical Association 2004

#### • Midkine detected in 45.5% of stage 0 breast cancers

## **Neuroblastoma Diagnostic**

# Correlation of elevated level of blood midkine with poor prognostic factor of human neuroblastomas (Ikematsu et al, 2003)



# **Diagnostic Portfolio**



# **MTY – Post Acquisition**

## **Capital structure**

| Shares                     | 74,085,624  |  |  |
|----------------------------|-------------|--|--|
| New Shares (NS Capital Co) | 23,500,000  |  |  |
| New Shares (Cell Signals)  | 20,000,000  |  |  |
| Total shares on issue      | 117,585,624 |  |  |
| Options (Employee)         | 7,505,000   |  |  |
| Convertible notes          | 9,381,096   |  |  |

## **Operations**

- Sydney will remain the pre-clinical/clinical and administrative centre
- Therapeutic R&D will be conducted in Tokyo and in Australia under collaborative arrangements
- Diagnostic portfolio will be clinically validated via collaborations

## Proposed timetable of key events\*

EGM Notice Shareholder briefings EGM Issuing of shares under the IP Agreement Settlement of IP Agreement 15 May 2008 16 May – 10 June 2008 16 June 2008 18 June 2008 19 June 2008

\*This timetable is subject to change

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