Targeting Adenosine Receptors & Nucleotide Metabolism in Cancer
Executive Summary

Strong Cancer Immunotherapy Pipeline

- Comprehensive portfolio of adenosine receptor antagonists
- Differentiated programs vs. competition (best-in-class / first-in-class)
- Large market potential

Partnered with $100bn + Company

- Exclusive worldwide rights acquired from the TATA Group, a $100bn + company with deep R&D expertise

Strong Management Team

- Senior Management each have 20+ years of R&D, healthcare investment, capital markets, and pharma deal-making experience
- Supported by a Board of preeminent industry leaders

Multiple Inflection Points

- Major Value Inflection Points Near & Mid Term
  - Filing of IND for 3 drugs within 6-8 months
  - Clinical data in multiple cancer indications within 18 months

Low Development Risk

- Validated pathway in multiple diseases
  - Strong efficacy and extensive safety data generated for IND filing
  - Mode of action and clinical efficacy successfully evidenced for adenosine receptor antagonism

High Valuation for Comparators

- Comparator companies valued between $100m - $1bn+
  - Tarus positioned favorably against competition with differentiated assets

Partnering Opportunity for Non Cancer Indications

- Upside potential from out-licensing non-cancer applications
  - Tarus has generated extensive data in Parkinson’s, Lung Fibrosis, Sickle Cell Disease and IBD (Ulcerative Colitis)
## Leadership

### Mark S. Cohen
Chairman of the Board

- Founder of international law firm, Pearl Cohen Zedek Latzer Baratz, LLP
- Senior Partner, and Chair of Life Sciences Practice Group
- Internationally recognized life-sciences patent attorney
- Former Board Member, Masthercell Global, a subsidiary of Organesis, Inc
- Former Vice-Chair of Board, and Chair of Governance Committee of Akari Therapeutics

### David Epstein
Independent Director

- 25+ years of global pharma leadership, drug development and deal-making
- Ex-CEO of Novartis Pharmaceuticals
- Led commercialization of 30 new molecular entities
- Executive Partner, Flagship Pioneering
- Chairman of Axcella Health, Rubius Therapeutics, Evelo Biosciences

### C. David Nicholson, PhD
Independent Director

- 40 years experience of global pharma R&D
- Previously Chief R&D Officer at Allergan
- CTO and EVP, R&D Bayer CropScience
- Leadership roles in R&D at Schering-Plough, Merck, Organon
- Board Director, Actinium Pharmaceuticals, Science Exchange

### Sushant Kumar, PhD
Co-Founder, Chief Executive Officer

- 20+ years as BioPharma investor and strategic advisor
- Led multi-billion cross border healthcare transactions
- Partner, Mehta Partners & MP Asset Management
- Managing Partner, Ardana Capital
- ACS Post Doc Fellow, Harvard Medical School
- PhD Molecular Biology, Rutgers Medical School

### Peter Molloy
Co-Founder, Executive Director

- 25 years as global healthcare investor and advisor
- Founder and prior CEO of Edison Group
- Successful track record as entrepreneur
- Expert in financial markets in US and EU
- Alumni, London Business School, Exeter University

### Kasim Mookhtar, PhD
Chief Scientific Officer

- 25+ years experience of drug discovery
- Founder and CEO of Advinus Therapeutics (TATA)
- Senior positions at Bristol-Myers Squib, Ranbaxy Labs
- PhD Molecular Biophysics, Florida State University
- Post Doc Fellow, Yale University School of Medicine
Adenosine is a key suppressor of immune cells in the tumor microenvironment (TME)

Extracellular adenosine elicits a major immuno-suppressive signal through adenosine A2A and A2B receptors, thwarting anti-tumor immunity

Adenosine’s role in immune suppression is corroborated by observations that the TME has significantly elevated concentrations (100-500 fold) of extracellular adenosine

A critical mechanism of cancer immune evasion is the generation of high levels of immunosuppressive adenosine via the purinergic pathway within the tumor microenvironment

Extracellular adenosine has a marked dampering effect on the immune response, suppressing effector cell function and stabilizing immunosuppressive regulatory cells

Upon engagement of the A2A or A2B receptors, adenosine triggers increased adenylyl cyclase activity with concomitant increases in intracellular cAMP resulting in profound dampening of the immune response – a fundamental mechanism of cancer immune evasion

Accordingly, it is a high priority target for immunotherapeutic intervention

Targeting Adenosine Receptors

A Breakthrough Approach for Cancer Immunotherapy

• Selective inhibition of adenosine receptors can markedly enhance anti-tumor immunity

Adenosine A2A and A2B receptors mediate profound tumor resistance

• Over-expression of A2AR and A2BR leads to poor prognosis in multiple cancers

• Genetic ablation of A2AR and A2BR leads to spontaneous regression of established tumors
## Competitive Landscape

### Tarus Strongly Positioned with the Most Comprehensive Portfolio of Adenosine Receptor Antagonists in the Industry

<table>
<thead>
<tr>
<th>Company</th>
<th>Lead programs</th>
<th>Target</th>
<th>Status</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tarus</td>
<td>TT-10, TT-4, TT-3, TT-53</td>
<td>A2AR, A2BR, A2BR-Gut, Dual</td>
<td>IND-enabling</td>
<td></td>
</tr>
<tr>
<td>Arcus</td>
<td>AB928</td>
<td>Dual</td>
<td>Phase Ib</td>
<td>NASDAQ listed (RCUS)</td>
</tr>
<tr>
<td>Corvus</td>
<td>CPI-444</td>
<td>A2AR</td>
<td>Phase II</td>
<td>NASDAQ listed (CRVS)</td>
</tr>
<tr>
<td>iTeos</td>
<td>EOS100850</td>
<td>A2AR</td>
<td>Phase I</td>
<td>$125M Series B (April '20)</td>
</tr>
<tr>
<td>AdoRx</td>
<td>A2AR Antagonist</td>
<td>A2AR</td>
<td>Discovery</td>
<td>$10M Series A (June'18)</td>
</tr>
<tr>
<td>AZN/Heptares</td>
<td>AZD4635</td>
<td>A2AR</td>
<td>Phase Ib</td>
<td>$500M+ deal value</td>
</tr>
<tr>
<td>Merck/Domain</td>
<td>AR Inhibitors</td>
<td>AR</td>
<td>Discovery</td>
<td>$290M+ deal value</td>
</tr>
<tr>
<td>Novartis/Palobiofarma</td>
<td>PBF-509</td>
<td>A2AR</td>
<td>Phase II</td>
<td>$15M upfront plus milestones &amp; royalties</td>
</tr>
</tbody>
</table>
### Oncology Programs

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>IND-enabling</th>
<th>Phase 1a/b</th>
<th>Phases 2/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT-10 A2AR Inhibitor</td>
<td>Solid tumors</td>
<td>IND-filing 4Q'20</td>
<td>1Q'21</td>
<td></td>
</tr>
<tr>
<td>TT-4 A2BR Inhibitor</td>
<td>Solid tumors</td>
<td>IND-filing 4Q'20</td>
<td>1Q'21</td>
<td></td>
</tr>
<tr>
<td>TT-3 Gut-restricted A2BR Inhibitor</td>
<td>Colorectal, GI tumors</td>
<td>IND-filing 4Q'20</td>
<td>1Q'21</td>
<td></td>
</tr>
<tr>
<td>TT-53 A2AR/A2BR Dual Inhibitor</td>
<td>Solid tumors</td>
<td>IND-filing 1Q'21</td>
<td>2Q'21</td>
<td></td>
</tr>
</tbody>
</table>

### Non-oncology Programs

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>IND-enabling</th>
<th>Phase 1a/b</th>
<th>Phases 2/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2AR Inhibitors</td>
<td>Parkinson's</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A2BR Inhibitors</td>
<td>Sickle Cell Disease, Lung Fibrosis, Asthma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gut-restricted A2BR Inhibitors</td>
<td>Ulcerative Colitis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Best-in-Class & First-in-Class Adenosine Receptor Antagonists**

<table>
<thead>
<tr>
<th><strong>TT-10</strong></th>
<th><strong>TT-4, TT-3</strong></th>
<th><strong>TT-53</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A2AR Inhibitor</strong></td>
<td><strong>A2BR Inhibitor</strong></td>
<td><strong>Dual Inhibitor A2AR &amp; A2BR</strong></td>
</tr>
<tr>
<td>Highly Potent and Selective Oral Inhibitor of A2AR</td>
<td>Highly Potent and Selective Oral Inhibitor of A2BR</td>
<td>TT-53 is an equipotent lead compound with low nanomolar/picomolar activity against both A2AR and A2BR</td>
</tr>
<tr>
<td>Significant Therapeutic Potential as Single Agent and Combination Therapy</td>
<td>Significant Therapeutic Potential as Single Agent and Combination Therapy</td>
<td></td>
</tr>
</tbody>
</table>

**Best-In-Class**

**First-In-Class**

**Best-In-Class**
TT-10

AZAR

INHIBITOR

Best-In-Class
<table>
<thead>
<tr>
<th><strong>TT-10</strong></th>
<th><strong>A2AR INHIBITOR</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>☀</td>
<td>Most potent (sub nanomolar) and highly selective oral A2AR inhibitor</td>
</tr>
<tr>
<td>☀</td>
<td>Efficacy and safety established in preclinical PoC studies in syngeneic breast and colon cancer models</td>
</tr>
<tr>
<td>⚠️</td>
<td>Long receptor occupancy even at high extracellular adenosine concentrations; QD dosing</td>
</tr>
<tr>
<td>⚠️</td>
<td>No safety issues in mouse, rat and dog toxicity studies</td>
</tr>
<tr>
<td>🌍</td>
<td>Patents issued in US, Europe, Japan</td>
</tr>
<tr>
<td>🛍️</td>
<td>IND filing Q4 2020</td>
</tr>
</tbody>
</table>
TT-10 Inhibits A2AR with Picomolar Potency and High Selectivity over other receptor subtypes

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Ki (nm)</th>
<th>Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2A</td>
<td>0.065</td>
<td>1</td>
</tr>
<tr>
<td>A1</td>
<td>10,000</td>
<td>&gt;10,000</td>
</tr>
<tr>
<td>A2B</td>
<td>100</td>
<td>&gt;1,400</td>
</tr>
<tr>
<td>A3</td>
<td>10,000</td>
<td>&gt;10,000</td>
</tr>
</tbody>
</table>

Picomolar potency is critical for inhibition of the high-affinity A2AR receptor

TT-10 potency is a key differentiating factor vs. competition – given high concentrations of adenosine in the TME

Superior selectivity against other adenosine receptors predicts better safety profile vs. other agents

Functional antagonism (change in intracellular cAMP induced by agonist) IC50 0.40nM
TT-10 Profile is Highly Differentiated vs. Competition

<table>
<thead>
<tr>
<th>Company</th>
<th>Drug</th>
<th>Affinity (Ki nm)</th>
<th>Selectivity against A2AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>TARUS</td>
<td>TT-10</td>
<td>0.68</td>
<td>700 2000 10,000</td>
</tr>
<tr>
<td>Corvus</td>
<td>CPI-444</td>
<td>3.52</td>
<td>54 531 693</td>
</tr>
<tr>
<td>AZN/Heptares</td>
<td>AZD4635</td>
<td>1.58</td>
<td>0.1 na na</td>
</tr>
<tr>
<td>Juno/Redox Tx</td>
<td>Vipadenant</td>
<td>1.3</td>
<td>48 52 773</td>
</tr>
<tr>
<td>Kyowa Hakko</td>
<td>Istradefylline</td>
<td>36</td>
<td>79 50 83</td>
</tr>
</tbody>
</table>

**TT-10** binds A2A receptor with very high affinity and selectivity.
Prolonged Receptor Occupancy

- Slow off rate

**TT-10**

- Prolonged pharmacodynamic (PD) effect of 10+ hours
- Critical differentiator in the presence of high ligand concentration in TME
- Predicts once/day (QD) dosing

**Extended Resident Time vs. Other A2AR Antagonists**

- Time of Incubation, hr
- [3H]-ZM-241385 Binding (100 - % Specific Binding)

- TT-10 (6nM)
- Preladenant (60nM)
- DMSO
- Tozadenant (200nM)
- MRS-1191 (300nM) (negative control)
Efficacy of TT-10 and TT-4 as Monotherapy was Evaluated in Established Immunotherapy Resistant Murine Models

4T1 Syngeneic Breast Cancer Model

Hi‌ly malignant and poorly immunogenic model which resembles advanced breast cancer in humans
Refractive to most immune-stimulation therapies
Highly Metastatic

CT-26 Syngeneic Colon Cancer Model

Immunotherapy resistant mouse model
CD73 positive

Efficacy of TT-10 & TT-4 was directly compared with anti-PD-1 antibody
TT-10
Effect on Tumor Volume

Breast Cancer (TNBC)

4T1 Syngeneic Mouse Model

48% Reduction in tumor growth vs. control (p<0.05)
29% Reduction vs. anti-PD-1 antibody (p<0.05)

12 mice/group (female BALB/c)
TT-10: 1mg/kg PO, BID; Anti-PD-1 MAb: 200ug/mouse IP (day 8, 11, 14, 18)
Effect of TT-10 statistically significant vs. control
Effect of TT-10 statistically significant vs. anti-PD-1
TT-10 Significantly Reduces Lung Metastasis

4T1 Syngeneic Breast Cancer Mouse Model

65% Reduction in lung metastasis vs. control  
*p<0.05*

40% Reduction vs. anti-PD-1 antibody  
*p<0.05*
Colon Cancer

CT-26 Syngeneic Colon Cancer Mouse Model

Effect on Tumor Volume

Reduction in tumor growth vs. control (p<0.05)
54%
Reduction vs. anti-PD-1 antibody
27%

12 mice/group (female BALB/c)
TT-10: 1mg/kg PO, BID; Anti-PD-1 MAb: 200ug/mouse IP (day 8, 11, 14, 18)
Effect of TT-10 statistically significant vs. control
TT-4

A2BR

INHIBITOR
<table>
<thead>
<tr>
<th><strong>TT-4</strong></th>
<th><strong>A2BR INHIBITOR</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Icon" /></td>
<td>Novel, First-in-Class, highly potent &amp; selective oral A2BR inhibitor</td>
</tr>
<tr>
<td><img src="image" alt="Icon" /></td>
<td>Hypoxia-inducible, promotes metastasis in breast, bladder, colon and other solid tumors</td>
</tr>
<tr>
<td><img src="image" alt="Icon" /></td>
<td>Efficacy and safety established in preclinical PoC studies in syngeneic breast and colon cancer models</td>
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TT-4 Inhibits A2BR with High Potency and Selectivity

Functional antagonism of receptor

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Ki (nm)</th>
<th>Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2B</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>A1</td>
<td>300</td>
<td>23</td>
</tr>
<tr>
<td>A2A</td>
<td>1800</td>
<td>138</td>
</tr>
<tr>
<td>A3</td>
<td>60,000</td>
<td>&gt;4000</td>
</tr>
</tbody>
</table>

Binding affinity

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Ki (nm)</th>
<th>Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2B</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>A1</td>
<td>&gt;30,000</td>
<td>&gt;400</td>
</tr>
<tr>
<td>A2A</td>
<td>&gt;10,000</td>
<td>&gt;150</td>
</tr>
<tr>
<td>A3</td>
<td>&gt;30,000</td>
<td>&gt;400</td>
</tr>
</tbody>
</table>

High selectivity against other adenosine receptors predicts wide safety window
TT-4
Effect on Tumor Volume

Breast Cancer
4T1 Syngeneic Mouse Model

- 46% Reduction in tumor growth vs. control (p<0.05)
- 26% Reduction vs. anti-PD-1 antibody (p<0.05)

Effect of TT-4 statistically significant vs. control
Effect of TT-4 statistically significant vs. anti-PD-1

12 mice/group (female BALB/c)
GN-4: 3mg/kg PO, BID; Anti-PD-1 MAb: 200ug/mouse IP (day 8, 11, 14, 18)
TT-4

Significantly Reduces Lung Metastasis

4T1 Syngeneic Breast Cancer Mouse Model

80% Reduction in lung metastasis vs. control
\[ p<0.05 \]

64% Reduction vs. anti-PD-1 antibody
\[ p<0.05 \]
TT-3
GUT RETENTIVE
A2BR INHIBITOR
TT-3
First in Class
Novel Target Agent for Gastro-Intestinal Cancers

Gut-restricted distribution of TT-3 offers a unique opportunity to attain superior therapeutic window in GI cancers

- Adenosine 2B receptors are consistently upregulated in colorectal cancer (2/3rd of adenocarcinomas)
- Hypoxia induces A2B expression
- A2BR antagonists inhibit colon cancer cell proliferation

IND READY
No safety issues in animal studies
Patents granted in US, Europe and Japan
A2BR Inhibition Impedes Colon Cancer Growth

Over Expression Promotes Colon Carcinoma Growth

A2BR is induced by hypoxia

A2BR is over-expressed in colon adenocarcinoma

Cell proliferation (A570 - 650 nm)

A2BR Inhibition Impedes Colon Cancer Growth
TT-53
A2AR & A2BR
DUAL INHIBITOR
TT-53

Dual Inhibitor:
Targeting Both A2AR and A2B
With A Single Molecule

A2AR and A2BR promote tumor resistance via independent mechanisms

A2AR inhibition potentiates anti-tumor effects by enhancing effector functions of cytotoxic lymphocytes and preventing the recruitment of immunosuppressive cells in the TME

By contrast, A2BR antagonism affects tumor-intrinsic and host mediated pathways – such as myeloid cells / tumor-associated macrophages (TAMs)
TT-53 Shows Synergistic Inhibition of Adenosine Mediated Immunosuppression

Highly potent dual A2AR / A2BR antagonists with low nanomolar/ picomolar activity identified

Lead compound TT-53 is equipotent against both receptor subtypes

Suitable ADME and pharmacokinetic profiles

No liability for hERG, CYP inhibition, or hepatocyte instability

Preclinical PoC studies in animals to be initiated

TT-53 shows synergistic inhibition of cAMP signaling - the main pathway for adenosine-mediated immunosuppression

Compound series covered by two issued patents
Clinical Indications

**TT-10 (A2AR)**
- Renal
- Lung
- Prostate

**TT-3 (A2BR Gut)**
- Colorectal
- Gastric

**TT-4 (A2BR)**
- TNBC
- Bladder

**TT-53 (Dual)**
- Renal, Lung, TNBC, Bladder, Ovarian, Prostate

*Single agent and in combination with ICP’s and Chemo*
**Value Proposition**

Robust platform of differentiated immuno-oncology assets with high therapeutic value

- **TT-10**: Best-In-Class A2AR Inhibitor
- **TT-4**: First-In-Class A2BR Inhibitor
- **TT-3**: Unique gut-restricted A2BR inhibitor for GI cancers
- **TT-53**: Dual Inhibitor with Highest Potency and Selectivity
- Single Agent Activity Against Immunotherapy Resistant Cancers
- Higher Efficacy vs. anti-PD-1 MAb

*Together, the company’s assets represent a high value proposition for addressing unmet need with a large market potential*
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