Next generation immuno-oncology targeting hot and cold tumors

March 2017
“This presentation has been prepared by iTeos and is furnished to you by iTeos on a confidential basis and solely for your information.

This presentation contains forward-looking statements, including (without limitation) statements concerning the progress and expectations of our (pre-)clinical pipeline and the financials of the company. When used in this presentation, the words “anticipate,” “believe,” “can,” “could,” “estimate,” “expect,” “intend,” “is designed to,” “may,” “might,” “will,” “plan,” “potential,” “possible,” “predict,” “objective,” “should,” and similar expressions are intended to identify forward-looking statements. Forward-looking statements involve known and unknown risks, uncertainties and other factors which might cause the actual results, financial condition, performance or achievements of iTeos, or industry results, to be materially different from any future results, financial conditions, performance or achievements expressed or implied by such forward-looking statements.

All statements contained herein speak only as of the release date of this document. iTeos expressly disclaims any obligation to update any statement in this document to reflect any change or future development with respect thereto, any future results, or any change in events, conditions and/or circumstances on which any such statement is based, unless specifically required by law or regulation.

Neither iTeos nor any of its officers, employees, advisers, or agents makes any representation or warranty, express or implied, as to any matter or as to the truth, accuracy, or completeness of any statement made in this presentation, made in conjunction therewith or in any accompanying materials or made at any time, orally or otherwise, in connection with the matters referred to herein and all liability in respect of any such matter or statements is expressly excluded.”
# Rapidly-Emerging Clinical-Stage IO Company

**Targeting the Tumor Microenvironment for next generation immunotherapies**

---

**HOT (inflamed) tumor**

**COLD (non-inflamed) tumor**

---

<table>
<thead>
<tr>
<th>Phase</th>
<th>HOT (inflamed) tumor</th>
<th>COLD (non-inflamed) tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Activate Immunity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Phase I</strong></td>
<td>IDO1 Inhibitor</td>
<td></td>
</tr>
<tr>
<td><strong>Preclinical development</strong></td>
<td>A\textsubscript{2A} Antagonist TIGIT Antibody</td>
<td></td>
</tr>
<tr>
<td><strong>Lead Identification</strong></td>
<td>Galectin-3 Antibody</td>
<td>STING Agonist (Targeted delivery)</td>
</tr>
<tr>
<td><strong>iTeos Technology</strong></td>
<td>Phenotyping Screening assay mimicking tumor microenvironment for target discovery &amp; rational combo</td>
<td></td>
</tr>
</tbody>
</table>

---

[iTeos Therapeutics](#)
Strong Momentum For Value Creation In 2017

2018
- Phase I A2A & TIGIT

2017
- Planned Series B €40M incl. €15-20M from existing investors
- Nanoparticles platform access
- IDO1 Phase I start

2016
- mAb Platform access

2014
- IDO1 & TDO2 deal (€24M upfront) + Series A €1.4M + €3M grants

2012
- Seed €3M + €6M grants
IDO1 inhibitor
Strong Differentiation Profile
Phase I
IDO1 Inhibitor Program In Phase 1

• Program started from HTS in 2013

• iTeos EOS200271 becomes Pfizer’s PF-06840003 in Dec

• PF-06840003 is a highly selective IDO-1 inhibitor with favorable predicted human PK properties
  o Favorable projected human half-life
  o CNS penetration for potential impact on brain metastases

• Increased anti-tumor efficacy in combination with PD-(L)1 antibodies and other ICI in preclinical models

• Phase 1 ongoing since Sept 2016
A<sub>2A</sub> Receptor Antagonist

Best-in-Class Program

FIH 1H2018
iTeos A$_{2A}$ Receptor Antagonist program

*Custom-Designed To Work In Tumor Microenvironment*

Adenosine inhibits immune response through A$_{2A}$ receptors

A$_{2A}$ receptor **competitive** antagonists developed for Parkinson’s Disease

- Corvus
- Heptares / AZ
- Palobiofarma / Novartis
- Redox / Juno
- Domain / Merck Kg

Arcus : non brain penetrant, preclinical

\[ \text{[Adenosine]}_{\text{Tumor}} \gg \text{[Adenosine]}_{\text{brain}} \]

Adapted from Bastid et al, Oncogene 2012
Ohta et al., *Frontiers in Immunology* 2016
iTeos A$_{2A}$ Antagonist Designed for efficacy & safety

Low adenosine environment

![Graph showing percentage of inhibition vs. log M](image)

Tumor-like environment*

![Graph showing percentage of inhibition vs. log M](image)

iTeos A$_{2A}$ Antagonist: EOS100550

- Potent in high intratumoral adenosine concentration (5μM)
- Limited CNS penetrance
- A$_{2A}$ antagonists repurposed from Parkinson’s programs penetrate the CNS and may cause dose-limiting neurological AEs at doses required for immuno-oncology

*2% human albumin, 5μM adenosine
Clinical Development, Enhanced by Biodata-Mining

**Acceleration with FIH in Healthy Volunteers**

**1Q 2018**
- IMPD
- GLP toxicology
- Combination Testing

**2Q 2018**
- FIH – SAD/MAD
- Healthy volunteers N=60

**3Q 2018**
- Phase Ib – Systemic therapy
- Decision point
- Adaptive design: RCC, SCCHN, CLL, Pancreas and all comers oncology N = 75
- Confirmatory efficacy expansion in 1 selected indication – Monotherapy N = 15 (→ 40 → 120)
- Confirmatory efficacy expansion in 1 selected indication – anti PD-1 Mab Combination N = 15 (→ 40)

**Q3 2019**

**Q2 2020**

**Big Data:** Mining biomarkers, image analysis, and population trends

**IMPD:** Investigational Medicinal Product Dossier; **RCC:** Renal Cell Carcinoma; **SCCHN:** Squamous Cell Carcinoma Head & Neck; **CLL:** Chronic Lymphocytic Leukemia; **FIH:** First-in-human; **SAD/MAD:** Single/multiple ascending dose; ** Decision point
TIGIT antibody
TIGIT Antibody: a new generation ICI
Blocking Co-Inhibitory TIGIT To Enhance CD8+ T & NK

TIGIT inhibits T cells by

- Direct inhibitory signaling
- Competition with CD226 co-stimulatory receptor for ligand (PVR) binding
- Depletion of TIGIT+ highly suppressive Treg

TIGIT competitive landscape
Genentech MTIG7192A/RG6058 - Phase 1
BMS- Phase 1
Oncomed/Celgene: IND filed
Cascadian, Arcus - Discovery
Genentech, Merck, Oncomed, BMS – patent applications

Johnston RJ et al. Cancer Cell, 2014
**Lead mAbs Selected for Initiation of CMC**

**Achievements**
- Lead mAb and one back-up selected for initiation of mammalian cell production.
  - $K_D = 0.2\text{nM}$
  - $EC_{50} = 0.6\text{nM}$ (IFN$_\gamma$ production by human CD8)
  - Cross-reactivity to Cyno and Mouse TIGIT
  - Suitable early developmentability profile
  - Parent series demonstrate in vivo efficacy
- Wuxi Biologics selected as CDMO

**Next Steps**
- *Ex vivo* and *in vivo* PK/DRF for isotype selection
- Filing, epitope mapping, non-GLP tissue cross-reactivity and immunogenicity evaluation in progress
Galectin-3 Inhibitory Antibody

First-in-Class Program
Lead Identification in H1 2017
Galectin-3 Antibody Program

*Designed To Inhibit Galectin-3 Binding on TILs*

- Galectin-3 lattice on cell surface inactivates tumor-reactive lymphocytes\(^1\)
- Inhibition of Galectin 3 binding to TILs increases IFN\(\gamma\) secretion and cytotoxicity\(^1\)
- Neutralizing anti-Galectin-3 Ab associated with longer DFS in GVAX and Sipuleucel–T trials \(^2, 3\)

\(^1\)Demotte et al., *Cancer Res* 2010 70:7476-88
\(^3\)GuhaThakurta et al., *Clin Cancer Res.* 2015 21(16):3619-30

---

**Galectin-3 competitive landscape**

- Galecto Biotech: Phase I for IPF (with BMS)
- Galectin Therapeutics: PhII in NASH stopped
- Glycomantra: discovery
iTeos anti-Galectin-3 mAb ADI-25909 stimulates TIL cytotoxicity

Nathalie Demotte
Pierre van der Bruggen, LICR
STING Agonist

Proprietary STING Agonists
Proof of Concept for Targeted Delivery Q4 2017
STING Agonist Program To Target Cold Tumors

STING Agonist To Reboot Anti-Tumor Immunity In Non-Inflamed Tumors

- STING required for immune rejection of tumors
  - Stimulates IFN\(\gamma\) and pro-inflammatory cytokine production

- STING agonists: systemic efficacy but narrow therapeutic index
  - Aduro / Novartis ADU-S100 PhI – intratumoral\(^1\)

\(^1\)Corrales et al., Cell Rep. 2015
STING Agonists Require Tumor-Specific Delivery
Nanoparticle Delivery Partnership With Cristal Therapeutics

Rational design and High Throughput Screening

<table>
<thead>
<tr>
<th></th>
<th>Intratumoral</th>
<th>Nanoparticles</th>
<th>Targeted nanoparticles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
<td>Limited</td>
<td>Wide</td>
<td>Specific</td>
</tr>
<tr>
<td>Competition</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Therapeutic index vs. systemic</td>
<td>High</td>
<td>Improved</td>
<td>High</td>
</tr>
<tr>
<td>Complexity</td>
<td>Low</td>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td>Partner</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

mPEG-Polyacrylamide-Lactate
- 30-100nM size
- Tuneable release rate
- Doxetacel CriPec Phase 1
iTeos TME Technology

Reproduces Tumor Micro-Environment (TME) to Identify Rational Combinations & Novel Targets
High Content Screening Platform
Reproduce Tumor Immunosuppression to Identify Novel Targets or combination

**Target cell plating**
- 96-well spotted compound plates

**Effector cell plating**
- Chemogenomics library
- E:T A549:CD3stim 1:1

**Stop co-culture**
- Plate imaging
- T cell proliferation
- Collect SN
  - IFNγ alphaLISA
  - Cytotoxicity assay

**T cell activity**
1. T-cell proliferation imaging
2. Cytokine secretion

**Immunosuppressive cell killing**
3. Nuclear counting
4. Caspase quantification
Corporate & Financials
# iTeos Management

**Proven Track Record In Drug Discovery And Development**

<table>
<thead>
<tr>
<th>Team</th>
<th>Role</th>
<th>Experience</th>
</tr>
</thead>
</table>
| Michel Detheux *(Eng, PhD)* | Co-founder & Chief Executive Officer       | • 20yrs in biotech R&D, BD, entrepreneurship  
• Euroscreen, LICR              |
| Yves Mertens *(Eng, PhD)*     | Chief Financial Officer                    | • 25yrs in finance and general management  
• CFO Etex Group; Aliaxis  
• CEO Aliaxis (2009 to 2015) |
| Christophe Quéva *(PhD)*     | Chief Scientific Officer                   | • 20yrs oncology drug discovery, SME & mAbs  
• AstraZeneca, Amgen, Gilead |
| Alain Thibault *(MD)*        | Chief Medical Officer                      | • 20yrs oncology development; 3 marketed products (Xeloda®, Yondelis®, Zaltrap®)  
• NCI, Roche, J&J, Regeneron, arGEN-X |
| Al Gray *(PhD)*              | Business Development                       | • 35yrs Research and BD  
• Abbott, Recombinant Capital, Euroscreen |
| Stefano Crosignani *(PhD)*   | Director, Medicinal Chemistry              | • 10yrs medicinal chemistry  
• Merck Serono                      |
| Bruno Gomes *(DVM, PhD)*      | Director, Tumor immunology                 | • 10yrs oncology drug discovery  
• Sanofi, Pierre Fabre                  |

## Scientific Committee

Benoît Van den Eynde  
Jean-Yves Bonnefoy  
Vincenzo Bronte  
Vincenzo Cerundulo  
Pierre Coulie  
Doug Fearon  
Tom Gajewski  
Jedd Wolchock
# Key Milestones Anticipated for 2017 - 2018

<table>
<thead>
<tr>
<th>Program</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>A$_{2A}$</td>
<td>LO</td>
<td>Preclinical</td>
<td>Phase I-Ib</td>
</tr>
<tr>
<td>TIGIT</td>
<td>LO</td>
<td>Preclinical</td>
<td>Phase I</td>
</tr>
<tr>
<td>STING</td>
<td>LI</td>
<td>LO</td>
<td>Preclinical</td>
</tr>
<tr>
<td>IDO1</td>
<td>Phase I</td>
<td>Phases Ib/II</td>
<td></td>
</tr>
<tr>
<td>Galectin-3</td>
<td>LO</td>
<td>Partnership</td>
<td></td>
</tr>
</tbody>
</table>

### 2017 inflection points
- A$_{2A}$ GLP Toxicology
- TIGIT Development Candidate identified
- Proprietary STING agonist identified, nanoparticle technology validated

### 2018 inflection points
- A$_{2A}$ Phase I
- TIGIT Phase I
- STING agonist development candidate
- IDO1 in Phase II: milestone
Next generation immuno-oncology targeting hot and cold tumors