ACTIVATING THE PATIENT’S IMMUNE SYSTEM TO FIGHT CANCER

Company presentation

OSE: TRVX

January 2022
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ONCOS-102: Leading immune activator with clinical efficacy in several solid tumors in monotherapy and in combination with anti-PD1 and chemotherapy

MoA confirmed in multiple indications: Broad local and systemic immune activation associated with clinical outcome

Preparing a platform trial based on class-leading responses: 35% ORR in PD1 refractory melanoma and 25.0 months mOS in mesothelioma

Market Exclusivity: ONCOS-102 is protected by composition of matter and method of use patents until 2037, 3 orphan and 2 fast track FDA designations

Innovative pipeline: Expanding ONCOS platform to deliver highly targeted novel circular RNA concepts; mutRAS immunotherapy program
HIGH AND GROWING MEDICAL NEED FOR IMMUNE ACTIVATORS

CPIs are revolutionizing cancer therapy...  ...but most patients do not respond...  ...leading to a high medical need for immune activators

$25bn
Global CPI market

44%
Patients eligible for CPI²:

60 - 90%
Non-responders

1 Immune Checkpoint Inhibitors Markets Report, 2020 March, ResearchAndMarkets.com
2 Estimation of the Percentage of U.S. Patients With Cancer Who Are Eligible for and Respond to Checkpoint Inhibitor Immunotherapy Drugs, JAMA Netw Open. 2019 May; 2(5), Haslam A., Prasad V.
THE SOLUTION: ONCOS-102 IMMUNE ACTIVATION

Unblinds the tumor to the immune system

Activates the body’s own T-cells against the cancer

Reverses immuno-suppressive defence mechanisms in the tumor
## CLINICAL AND PRECLINICAL PIPELINE

<table>
<thead>
<tr>
<th>Product candidate</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Next expected event</th>
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</thead>
<tbody>
<tr>
<td>ONCOS-102</td>
<td>PD1 Refractory Melanoma</td>
<td>Platform IO combination trial</td>
<td></td>
<td></td>
<td>2022 First patient</td>
</tr>
<tr>
<td></td>
<td>Mesothelioma</td>
<td>Combination w/pemetrexed/cisplatin</td>
<td></td>
<td></td>
<td>2H 2021 Survival update</td>
</tr>
<tr>
<td></td>
<td>Metastatic Colorectal cancer</td>
<td></td>
<td></td>
<td></td>
<td>1H 2022 Clinical data</td>
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<tr>
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<tr>
<td>NextGen ONCOS vectors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Preclinical data and selection of candidates</td>
</tr>
<tr>
<td>mutRAS immunotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Preclinical data and initiate clinical study</td>
</tr>
</tbody>
</table>
1. PD1 Refractory Melanoma
2. Mesothelioma
3. Metastatic Colorectal cancer
4. NextGen ONCOS vectors
5. mutRAS immunotherapy
6. Corporate strategy and finance
## PD1 Refractory Melanoma Market Opportunity

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>~100,000 new stage III/IV cases of malignant melanoma per year in the major markets</td>
</tr>
<tr>
<td><strong>Unresectable</strong></td>
<td>~50% recur and become unresectable</td>
</tr>
<tr>
<td></td>
<td>Total ~50,000 patients per year</td>
</tr>
<tr>
<td><strong>PD1 resistance</strong></td>
<td>~50% of cases become PD resistant</td>
</tr>
<tr>
<td></td>
<td>Total ~25,000 patients per year</td>
</tr>
<tr>
<td><strong>Addressable</strong></td>
<td>Estimated 10,000 - 20,000 patients per year addressable with intra-tumoral therapies</td>
</tr>
<tr>
<td><strong>Other PD1 resistance</strong></td>
<td>&gt;100,000 patients per year lung cancer</td>
</tr>
<tr>
<td></td>
<td>&gt;50,000 patients per year head and neck</td>
</tr>
</tbody>
</table>

*Source: GlobalData, Targovax analysis*
## ONCOS-102 Has Demonstrated Class-Leading Efficacy in PD1-Refractory Melanoma

<table>
<thead>
<tr>
<th>Antigen/Therapy</th>
<th>CR (5/pts)</th>
<th>PR (20/pts)</th>
<th>ORR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONCOS-102</td>
<td>5%</td>
<td>30%</td>
<td>35%</td>
</tr>
<tr>
<td>BNT111</td>
<td>0%</td>
<td>35%</td>
<td>35%</td>
</tr>
<tr>
<td>RP1</td>
<td>6%</td>
<td>25%</td>
<td>31%</td>
</tr>
<tr>
<td>TAVO</td>
<td>8%</td>
<td>20%</td>
<td>28%</td>
</tr>
<tr>
<td>CMP-001</td>
<td>7%</td>
<td>16%</td>
<td>23%</td>
</tr>
<tr>
<td>Sotigalimab</td>
<td>15%</td>
<td>15%</td>
<td>28%</td>
</tr>
<tr>
<td>Tilsotolimod</td>
<td>9%</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Lifileucel</td>
<td>3%</td>
<td>33%</td>
<td>36%</td>
</tr>
</tbody>
</table>

**Comment:**
- Adenovirus expressing GM-CSF
- Four melanoma antigens, mRNA
- Herpes virus expressing GM-CSF and GALV
- IL-12 DNA plasmid with electroporation
- TLR-9 agonist
- Data from high-dose cohort
- CD40 agonist, systemic
- TLR-9 agonist
- Same ORR in CTLA4-only control arm
- Autologous TIL therapy with IL-2
- Complex and costly treatment and manufacturing
MULTIPLE EXAMPLES OF SYSTEMIC (ABSCOPAL) EFFECT
TWO PATIENTS WHERE A NON-INJECTED LesION COMPLETELY DISAPPEARED

No universally agreed definition of abscopal effect:
- 12 of 36 (33%) non-injected target lesions reduced in size
- 8 of 15 patients with reduction in non-injected target lesions

Conservative definition of abscopal effect per lesion\(^1\):
- ≥30% tumor reduction from baseline
- ≥5mm absolute reduction

4 of 15 patients (27%) with non-injected target lesions had abscopal effect according to conservative definition
- 1 patient in Part 1
- 3 patients in Part 2, where two patients had complete regression (100%) in one lesion

1 Similar to RECIST 1.1 criteria for response
CASE EXAMPLE: PATIENT WITH COMPLETE RESPONSE

Tumor response, 1 of 1 injected lesion

<table>
<thead>
<tr>
<th>Tumor response</th>
<th>Baseline</th>
<th>Week 3</th>
<th>Week 9</th>
<th>Week 18</th>
<th>Week 27 (EoS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression on pembrolizumab</td>
<td>3x ONCOS-102 only (no pembrolizumab)</td>
<td>3x ONCOS-102 &amp; 2x pembrolizumab</td>
<td>3x ONCOS-102 &amp; 5x pembrolizumab</td>
<td>3x ONCOS-102 &amp; 8x pembrolizumab</td>
<td></td>
</tr>
</tbody>
</table>

Patient characteristics

<table>
<thead>
<tr>
<th>Tumor stage at enrolment:</th>
<th>IIIb</th>
<th>Prior therapies:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T4a, N2b, M0</td>
<td>Surgery (x3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ipilimumab</td>
</tr>
<tr>
<td>RECIST 1.1:</td>
<td>CR, week 9-27</td>
<td>Dabrafenib + Trametinib</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pembrolizumab</td>
</tr>
</tbody>
</table>
CASE EXAMPLE: PATIENT WITH COMPLETE RESPONSE TUMOR T-CELL INFILTRATION

**T-cell infiltrate**, 1 of 1 injected lesion

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 3</th>
<th>Week 9</th>
<th>Total level of T-cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD8+ T-cells</td>
<td>Low CD8+ level at baseline</td>
<td>15x increase from baseline</td>
<td>CR, mainly necrotic tissue; some T-cells still present</td>
</tr>
<tr>
<td>CD4+ T-cells*</td>
<td>Low CD4+ level at baseline</td>
<td>12x increase from baseline</td>
<td></td>
</tr>
</tbody>
</table>

Progression on pembrolizumab 3x ONCOS-102 only 3x ONCOS-102 & 2x pembrolizumab

* FOXP3+ cells (T_{reg}) only present at very low level
HIGHEST INCREASE IN TUMOR T-CELL INFILTRATES OBSERVED IN MELANOMA RESPONDERS

T-cell infiltrate (TIL) for individual patients; tumor mIHC, relative level

Average T-cell level per group

---

Patient with pseudo-progression

1: One CR patient only
RNAseq gene expression provides further insights:

- **Pro-inflammatory “hot” tumor remodeling** through multiple pathways and molecular mechanisms

- **“Hot” tumor remodeling persists** at least until Day 64, following 6 ONCOS-102 IT administrations and 3 weeks post previous ONCOS-102 injection

- Increased expression of chemokines and cytokines explain higher immune cell infiltrate

- **Strong upregulation of cytotoxic machinery** explains tumor shrinkage

- Upregulation of immunomodulatory molecules present **targets for novel combinations beyond anti-PD1**
NEXT STEP: MELANOMA PHASE 2 PLATFORM TRIAL TO EXPLORE MULTIPLE ONCOS-102 COMBINATIONS

Part 1 – run-in

1. ONCOS-102 monotherapy
   - Randomize

2. ONCOS-102 + PD1 combination
   - Assess contribution of components

Part 2 – multi-cohort extension

3. ONCOS-102 + CTLA4
   - Additional cohorts to explore novel combinations

4. ONCOS-102 + PD1 + CTLA4
   - Aim to further boost response rates beyond 35% ORR

5. ONCOS-102 + co-stim
   - Collaboration with partners – dialogues ongoing

Several opportunities:
- vaccine, bi-specifics, T-cell engagers, etc...

The cohorts can independently form the basis for subsequent registrational trial(s)
Mesothelioma

3. NextGen ONCOS vectors
4. Novel mutRAS concepts
5. Corporate strategy and finance
THERE IS A HIGH UNMET MEDICAL NEED IN MALIGNANT PLEURAL MESOTHELIOMA

Surgery
- Only 10% of patients suitable for resection
- Often diagnosed too late for surgery
- Technically challenging

Radiotherapy
- Rarely effective due to tumor shape
- Hard to focus radiation
- Mainly palliative care

Chemotherapy
- Standard of care (SoC) with limited efficacy
- Pemetrexed/cisplatin only approved option until 2020
  - 12-16 mo. mOS in 1L

Immunotherapy
- Opdivo/Yervoy combination recently approved
- Replacing chemotherapy as preferred first-line treatment option in USA, EU and Japan
  - 18 mo. mOS in 1L, high toxicity
ONCOS-102 HAS SHOWN 25.0 MONTHS mOS IN 1L MESOTHELIOMA, WHICH IS THE BEST SURVIVAL DATA REPORTED IN THIS POPULATION

mOS: median Overall Survival. mPFS: median Progression Free Survival

1. Tsao 2019 (JCO) compared cediranib + pem/cis vs pem/cis; data from pem/cis arm presented on plot
2. Vogelzang 2003 was the basis for FDA approval of pemetrexed.
3. Ceresoli 2006, Pemetrexed plus carboplatin
4. Scagliotti 2019 (Lancet) compared nintedanib + pem/cis vs pem/cis; data from pem/cis arm presented on plot
5. Zalcman 2016 (Lancet) compared bevacizumab + pem/cis vs pem/cis; data from pem/cis arm presented on plot.
6. Baas 2021 (The Lancet) CheckMate 743. Nivolumab + ipilimumab for two years vs pem/cis (or carboplatin). Ipi/nivo was approved in first line by FDA on October 2, 2020.
7. Nowak 2020 (Lancet Oncology) Pem / cis (6 cycles) + durvalumab (12 months)
8. 1L randomized patients mOS not final: Experimental group, 8 patients (3 censored). Control group, 6 patients (0 censored)
IMPROVED SURVIVAL OUTCOME IS ASSOCIATED WITH POWERFUL ONCOS-102 INDUCED IMMUNE ACTIVATION

Immuno-modulation in tumor tissue; Mesothelioma, Day 36 vs. baseline

- ONCOS-102 treated: Alive 18mo. (n=6)
- ONCOS-102 treated: Deceased 18mo. (n=9)
- Control: Alive 18mo. (n=2)
- Control: Deceased 18mo. (n=3)
Immune-modulation in tumor tissue; Mesothelioma, Day 36 vs. baseline

Co-stims:
Help T-cells expand, survive and kill

Anti-PD1:
Block the tumor’s “don’t kill me” defense signal

Anti-CTLA4:
Further reduce T_{reg} ratio to favor cytotoxic activity

T-cell engagers:
Exploit T-cell cytotoxic machinery to kill the tumor more effectively

Vaccines and Anti-CTLA4:
Enhance tumor antigen priming by stimulation of APCs
## STRENGTH AND BREADTH OF ONCOS-102 CLINICAL DATA PACKAGE OPENS BROAD OPPORTUNITIES

<table>
<thead>
<tr>
<th>Class-leading efficacy</th>
<th>ONCOS-102 drives meaningful clinical benefit, competitive with leading drug candidates</th>
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</thead>
<tbody>
<tr>
<td>Highly consistent</td>
<td>ONCOS-102 data package is highly consistent across tumor types, survival, clinical response, immune cell infiltration and gene expression</td>
</tr>
<tr>
<td>Novel combinations</td>
<td>Mechanistic data provides strong biological rationale for combinations beyond anti-PD1 blockade to further boost efficacy</td>
</tr>
<tr>
<td>Biomarker selection</td>
<td>Potential genetic biomarkers for patient selection identified in tumor biopsy NGS data set</td>
</tr>
</tbody>
</table>
3

NextGen ONCOS vectors

4. Novel mutRAS concepts
5. Corporate strategy and finance
NOVEL RNA DELIVERY FORMATS:
RNA EXISTS NATURALLY IN CIRCULAR FORM
TWO RECENT LAUNCHES OF CIRCULAR RNA BIOTECHS HAVE ATTRACTED MEGA SERIES A ROUNDS

As RNA remains hot, Flagship’s Laronde raises $440m for a new class of medicines

By Anissa Gardizy Globe Staff. Updated August 30, 2021, 6:30 a.m.

Orna Therapeutics debuts with $100M, engineered circular RNA treatments to rival cell therapies

nature biotechnology

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nature > nature biotechnology > news > article

News | Published: 02 September 2021
Startups set off new wave of mRNA therapeutics
Elie Dolgin

After the vaccine triumphs of Pfizer/BioNTech and Moderna, a raft of startups is developing mRNA, circular RNA and self-amplifying RNA therapeutics.
ONCOS PROVIDES AN IDEAL, CLINICALLY VALIDATED PLATFORM FOR CIRCULAR RNA

Novel ONCOS circular RNA vectors

- Express transgenes
- Encode tumor antigens
- Immunological activation
- Onco-microRNA sponge

Highly versatile delivery system
Novel mutRAS concepts

5. Corporate strategy and finance
BUILDING MUTANT RAS IMMUNOTHERAPY PROGRAM THROUGH STRATEGIC PARTNERSHIPS

Targovax mutRAS immunotherapy strategy

- **Enhanced mutRAS vaccination**
  - Clinical stage
  - Enhanced versions of TG vaccines and novel combination strategies
  - NOK 9.8m grant from Norwegian Research Council (NFR)

Next generation mutRAS concepts

- Pre-clinical discovery
  - Innovative, first-in-class mutRAS IO concepts
  - Leverage ONCOS platform
  - Strategic R&D partnerships

Next generation mutant RAS pipeline

- **Boost TG vaccine immunogenicity**
  - Next gen. adjuvants

- **Option to license TG01/02 vaccines** for Greater China and Singapore

- **Oncolytic virus w/ mutRAS vaccine coating** - Coat ONCOS-102 with mutant RAS neoantigen PeptiCRAd peptides

- **Oncolytic virus w/ mutRAS antibody payload** - Express AbiProt mutant RAS targeting antibodies from ONCOS backbone
5 Corporate strategy and finance
Let the science guide us:
Make smart, scientifically based decisions based on data and insights generated in the phase 1/2 program

Advance ONCOS-102 in aPD1 refractory melanoma:
Boost response rates beyond the current 35% ORR by identifying the best combination approach in phase 2 platform trial

Establish ONCOS as a versatile delivery platform:
Engineer novel RNA concepts into ONCOS for enhanced delivery of highly targeted, immune stimulatory genetic payloads
R&D STRATEGY: VALIDATING ONCOS AS A VERSATILE DELIVERY TOOL AND IDENTIFY BEST COMBINATION APPROACH

Two-pillar R&D strategy

Clinical
ONCOS-102
platform trial

- Lead clinical-stage product candidate
- Phase 2 multi-cohort trial in melanoma
- Assess multiple combinations in parallel to identify best partner and schedule

Expand and enhance the platform

Pre-clinical
Build NextGen
ONCOS vectors

- Novel payload inserts based on deep mining of clinical phase 1/2 data
- Circular RNA delivery
- Novel regulatory functionality

Clinical validation of the platform
## 3Q FINANCIAL SNAPSHOT

### Key figures

<table>
<thead>
<tr>
<th>Description</th>
<th>NOK million</th>
<th>USD million</th>
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<tbody>
<tr>
<td>Net cash flow in 3Q</td>
<td>-17</td>
<td>-2.0</td>
</tr>
<tr>
<td>Cash at end of 3Q</td>
<td>54</td>
<td>6.4</td>
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<tr>
<td>Market cap</td>
<td>374</td>
<td>42</td>
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### Shareholder base

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<tr>
<th>Shareholder</th>
<th>Shares million</th>
<th>Ownership</th>
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<tr>
<td>Avanza Bank AB (nom.)</td>
<td>19.9</td>
<td>10.6 %</td>
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<tr>
<td>HealthCap</td>
<td>12.4</td>
<td>6.6 %</td>
</tr>
<tr>
<td>AP4</td>
<td>8.7</td>
<td>4.6 %</td>
</tr>
<tr>
<td>Nordnet Bank AB (nom.)</td>
<td>6.6</td>
<td>3.5 %</td>
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<tr>
<td>ABN AMRO Global (nom.)</td>
<td>5.8</td>
<td>3.1 %</td>
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<td>Goldman Sachs Int. (nom.)</td>
<td>5.2</td>
<td>2.8 %</td>
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<td>Nordea</td>
<td>4.5</td>
<td>2.4 %</td>
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<tr>
<td>RadForsk</td>
<td>4.4</td>
<td>2.4 %</td>
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<tr>
<td>Bækkelaget Holding</td>
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<td>Nordnet Livsforsikring</td>
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<td>1.4 %</td>
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**10 largest shareholders**

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<tr>
<th>Shares million</th>
<th>Ownership</th>
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<tr>
<td>74.4</td>
<td>39.5 %</td>
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**Other shareholders (5 002)**

<table>
<thead>
<tr>
<th>Shares million</th>
<th>Ownership</th>
</tr>
</thead>
<tbody>
<tr>
<td>113.9</td>
<td>60.5 %</td>
</tr>
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</table>

**Total shareholders**

<table>
<thead>
<tr>
<th>Shares million</th>
<th>Ownership</th>
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<tbody>
<tr>
<td>188.3</td>
<td>100.0 %</td>
</tr>
</tbody>
</table>

1 As per 3 January 2022

*Rights Issue executed December 2021/4Q*