Development of next generation DC-based cancer vaccines (DCVAC)

Jiří Heřmánek, CEO Russia
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„Connecting patients and science“
1. Company Introduction
SOTIO is an international biotechnology company headquartered in Prague, Czech Republic, developing new therapies based on autologous in vitro activated dendritic cells (DCVAC), focusing on the treatment of cancer and autoimmune diseases. Sotio is a fully integrated R&D company with proprietary research, clinical development and GMP manufacturing. Sotio is a part of PPF Group, one of the largest investment groups in CEE.
International presence of SOTIO

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<thead>
<tr>
<th>EU</th>
<th>USA</th>
<th>China</th>
<th>Russia</th>
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<tr>
<td><img src="image" alt="EU flag" /></td>
<td><img src="image" alt="USA flag" /></td>
<td><img src="image" alt="China flag" /></td>
<td><img src="image" alt="Russia flag" /></td>
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<tr>
<td>- 4 Phase II clinical trials in prostate cancer currently underway in Czech Republic (&gt;200 patients enrolled by November 2013)</td>
<td>- SOTIO, LLC with office in Boston, MA serves as a service company for SOTIO’s activities in the U.S.</td>
<td>- SOTIO Medical Research Beijing Co., Ltd. in Beijing</td>
<td>- SOTIO Russia LLC with office in Moscow serves as a service company for SOTIO’s activities in Russia</td>
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<td>- ~ 750 patients with prostate cancer from 15 European countries will be enrolled into a Phase III VIABLE global registration clinical trial</td>
<td>- ~ 300 patients with prostate cancer to be enrolled into a Phase III VIABLE global registration clinical trial</td>
<td>- Construction of own GMP-compliant clean laboratories in Huilongsen International Business Incubator biotechnology park in South Beijing will be completed in 2013</td>
<td>- SOTIO Russia joined cell therapy industry association Actremed in 2012</td>
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<td>- 3 Phase II clinical trials in ovarian cancer (210 patients) starting in October 2013 in Czech Republic, Germany and Poland</td>
<td>- Manufacturing contracted with Progenitor Cell Therapy (PCT) in Allendale, New Jersey</td>
<td>- Manufacturing contracted with Progenitor Cell Therapy (PCT) in Allendale, New Jersey</td>
<td>- ~ 150 patients with prostate cancer to be enrolled into a Phase III VIABLE global clinical trial</td>
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2. Technology and product
About cancer immunotherapy

Cancer immunotherapy aims to stimulate immune response of body’s own immune system against tumor cells

• Dendritic Cells (DCs) play a central role in initiating human body’s immune response. In order to induce immune response, DCs need to be activated.

• After being exposed to killed tumor cells, immature DCs develop into activated mature DCs. Activated DCs are able to induce a broad CD4 and CD8 T-cell mediated immune response.

• According to both expert theoretical assumptions and experimental data, cancer immunotherapy solely on its own has the greatest chance of success if applied to patients at the early stages of the disease.

• In advanced stages, cancer immunotherapy needs to be combined with standard treatment modalities, such as chemotherapy.

Source: Sotio
Use of SOTIO’s proprietary ACI-MAP\textsuperscript{1} technology
Following this proprietary method, the patient's own dendritic cells are activated by a broad range of tumor antigens that induce a complex immune response.

Concept of combination therapy
While immunotherapy alone is best suited for early stage patients, we believe that advanced cancer requires multiple treatments to be orchestrated in a synergistic way to control disease progression.

Long-term boosting of the immune response
The results of previous clinical trials confirm that antitumor immune responses are short lived and repeated boosting is necessary to maintain high frequencies of tumor specific T cells.

The combination of the above-mentioned principles is expected to result in more effective Active Cellular Immunotherapy for those patients who have limited treatment options.

\textsuperscript{1} Active Cellular Immunotherapy Multiple Antigen Presentation
Science behind our products

SOTIO products represent the cutting edge of modern immunotherapy

Preparation of SOTIO’s active cellular immunotherapy product

Monocytes are separated from the rest of the white blood cells.

Monocytes are cultivated into immature dendritic cells. Tumor cells are subjected to immunogenic cell death.

Tumor cells prepared in this way are able to activate dendritic cells and to stimulate a stronger immune system response.

A mature dendritic cell starts to express tumor antigens from killed cancer cells on its surface within several hours.

The prepared mature dendritic cells represent the actual cancer immunotherapy treatment.

Action of SOTIO’s active cellular immunotherapy product in patient’s body

After application, dendritic cells migrate into lymph nodes. There they meet and activate naive T-lymphocytes and allow them to recognize tumor antigens.

The naive lymphocytes become effector lymphocytes which rapidly proliferate.

Anti-tumor specific T cells migrate with blood through the entire body, searching for and destroying tumor cells.
DCVAC/PCa

1. Leukapheresis
2. Monocytes
3. Immature DCs
4. Tumor cells LN CaP cell line
5. Mature DCs
6. 
7. 

Sotio
3. Product pipeline and clinical trials
## Overview of Sotio product pipeline

SOTIO is developing immunotherapy products for multiple indications

<table>
<thead>
<tr>
<th>Product Treatment</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase I/II</th>
<th>Phase II</th>
<th>Phase III</th>
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<tr>
<td><strong>Prostate cancer treatment</strong> (DCVAC/PCa)</td>
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<td><strong>Ovarian cancer treatment</strong> (DCVAC/OvCa)</td>
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<td><strong>Lung cancer treatment</strong> (DCVAC/LuCa)</td>
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1 SOTIO’s prostate cancer treatment is currently being tested in four Phase II clinical trials and will enter Phase III VIABLE clinical trial in 2013.
   - SP001 – Phase II – Patients with castrate-resistant prostate cancer (CRPC)
   - SP002 – Phase II – Patients with metastatic prostate cancer
   - SP003 – Phase II – Patients with localized prostate cancer after primary radical prostatectomy
   - SP004 – Phase II – Patients with localized high-risk prostate cancer after primary radiotherapy
   - SP005 – Phase III – Patients with metastatic CRPC indicated for chemotherapy

2 SOTIO’s ovarian cancer treatment is being tested in three Phase I clinical trials.
   - SOV001 – Phase II – Patients with epithelial ovarian cancer
   - SOV002 – Phase II – Patients with relapsed platinum-sensitive epithelial ovarian cancer
   - SOV003 – Phase II – Patients with relapsed platinum-resistant epithelial ovarian cancer

✔️ - in progress, ✔️ - planned for 2014
**Indication of Significant Survival Advantage**

- Phase I/II trial for DCVAC/PCa showed promising clinical efficacy.
- Therapy demonstrated a median overall survival of 23 months for 20 mCRPC patients.
- This exceeded the predicted overall survival of 13 months for these patients using the Halabi nomogram.

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1 Results preliminary, not finalized as the trial is still ongoing
Source: SOTIO
DCVAC/PCa – Prostate cancer clinical trials

PSA level development in time

Phase I/II clinical trial in patients with the biochemical relapse of the prostate cancer (20 patients)

- A study of patients with rising levels of prostate specific antigen (PSA) after primary prostatectomy or salvage radiation therapy for biochemical relapse measured the patient’s PSA doubling time.

  -Patients experienced a significantly prolonged PSA doubling time of 44.7 months after treatment compared to the pre-treatment period, which was only 7 months.

1 Results preliminary, not finalized as the trial is still ongoing
Source: SOTIO
Overview of the trial

- The Phase III trial for DCVAC/PCa, entitled “VIABLE”\(^1\), is a large (n=1,170) global multicenter double-blind placebo-controlled trial that will enroll mCRPC\(^2\) patients who are eligible for chemotherapy.

- The study intends to evaluate DCVAC/PCa in combination with standard of care docetaxel therapy against the standard of care alone. The study will thus rigorously test the efficacy of DCVAC/PCa.

- Key opinion leaders in prostate cancer from the United States and European Union reviewed the study protocol and contributed to the final design. SOTIO works closely with the leading clinicians in the field of immunotherapy and genitourinary cancer care.

Study endpoints

- The primary outcome for the trial is overall survival. Secondary outcomes for the trial are time to tumor progression, time to PSA progression, progression free survival, incidence of skeletal related events, and safety.

- Investigators will also monitor patients’ quality of life using standard questionnaires and the number of patients who require further treatment, as well as time to that treatment.

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1 The acronym VIABLE is derived from the description of the trial: active ImmunotherApy using dendritic cell-Based treatment forLate stage prostate cancer
2 Metastatic castration-resistant prostate cancer
4. Future of Cancer Immunotherapy?
Cancer Immunotherapy = Promising approach

PRO’s:

• Critical role of immune system in the control of cancer growth has been established → immune evasion concept

• Fully **personalized approach** in the case of autologous cell immunotherapy → should be by its nature a **relatively safe treatment** (no toxicity, relatively low potential for adverse effects)

• Not easy / possible to copy (cells are not chemicals) + high entry costs (super-clean manufacturing facilities) → no / low danger of generic competition

CON’s:

• Relatively “soft” treatment modality vs. “hard” ones (surgery, chemotherapy, radiotherapy) → not “killing it all”, just “controlling” → relatively higher clinical efficacy could be expected in early stages of cancer

• However key regulators (EMA, FDA) require hard **overall survival data for granting registration** → forcing clinical development into advanced / terminal stages → limited chance for success → many **promising results in Ph II** clinical trails vs. **multiple failures in Ph III** registration clinical trials (up to now only single cell immunotherapy product approved by FDA and EMA = sipuleucel)

• Relatively complex manufacturing & logistics → high manufacturing & developmental costs → expensive treatment

Source: Sotio
For more information about SOTIO please visit

www.sotio.com

or contact us at

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