Immunicum is a biopharmaceutical company based in Gothenburg, Sweden, developing cancer immunotherapies to increase QoL and OS

Founded in 2002 by three researchers working in the field of transplantation immunology. Lead platform, COMBIG, for the development of cancer immune primers is based on the realization that allogeneic dendritic cells (from healthy blood donors) function as great cancer immune primers in combination with patients’ own mutated (neo) antigens.

- Three platform technologies: COMBIG, CD70, and Ad5PTDf35-vector
- Strong patent portfolio with several approved patents and pending applications in seven patent families.
- Strategy to out license products after late stage clinical trials
- Research collaborations with:
  - NCI: Ad5PTDf35 in the CRISPR/Cas9 field
  - Rutgers Cancer Institute: Cancer stem cell research.
  - Uppsala University: CD70, Ad5PTDf35 and SUBCUVAX development

**Financial Snapshot**
- Ticker: IMMU: Nasdaq OMX Nordic
- Share price – 26,9 SEK*
- Market cap – SEK 690 million*
- Total of SEK 273 million invested/raised to date
  - SEK 5m of grants received

*as of September 15, 2016
Project pipeline

- In collaboration with prof. Essand at Uppsala University
- Exclusive back-license to VirEX AB
- Under MTA with NCI
- Under MTA with Rutgers Cancer Institute

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IMMUNICUM
ALLOGENEIC DC-BASED IMMUNOTHERAPIES
INTUVAX
- Positioning as the preferred cancer immune primer of choice to be combined with multiple different therapies that dampen immunosuppression

TARGETING CANCER CELLS
"Priming T cells"
"Putting the foot on the gas"

CANCER VACCINES

CAR T CELLS

TARGETING IMMUNOSUPPRESSION
"Allowing T cells to better function"
"Releasing the breaks"

CHECKPOINT INHIBITORS
TYROSINE KINASE INHIBITORS
CHEMOTHERAPY
ETC

COMPETING PRODUCTS
• No convincing clinical data, likely due to
  • use of suboptimal adjuvants
  • use of poor antigens

COMPETING PRODUCTS
• No convincing clinical data in solid tumors as expanded CAR T cells are too exhausted to survive in the immunosuppressive tumor microenvironment in solid tumors

INTUVAX
Position as preferred cancer immune primer of choice
• Allogeneic DCs function as natural adjuvants and INTUVAX is designed to create a tailored and optimal immune activation
• Intratumoral injection, using patients’ own mutated (neo) antigens for optimal anti-tumor immune response

POTENTIAL COMBINATIONS
• Immune checkpoint inhibitors such as PD1/PDL1-inhibitors only work in the subset of cancer patients where there are already sufficient amounts of T cells in the tumors
  • Strong rationale for combination with INTUVAX (T cell primer)

• TKIs and chemotherapy dampen immunosuppression by killing T regs and myeloid suppressor cells
  • Majority of INTUVAX-treated mRC patients show massive/strong intratumoral infiltration of CD8+ T cells with clear signs of synergistic effect in combination with TKIs and chemotherapy

STRONG ANTI-TUMOR EFFECT!
INTUVAX® – Lead cancer immune primer
INTUVAX® highlights – Immunicum’s lead cancer immune primer

Off-the-shelf product

• Large scale production process in place. Allogeneic cells for therapeutic vaccination derived from leukapheresis products from healthy blood donors (> 50 vaccine doses from each donor) can be produced cost effectively and stored in frozen state over long periods of time using the Immunicum patented protocol. Two production sites in place.

Personalized treatment – but not patient dependent

• Aimed to target the full set of each patient’s unique and tumor-specific mutated (neo-)antigens

Intratumoral administration

• Applicable to all injectable solid tumors

Status

• Phase I/II mRCC finalized
• Phase II mRCC ongoing
• Phase I/II-trial HCC ongoing
• Phase I/II GIST ongoing
Phase I/II-study in 12 patients with newly diagnosed renal cell carcinoma - No treatment related SAEs reported

- **Patients** diagnosed with RCC, with at least one metastasis, scheduled for nephrectomy, and preserved major organ functions, were included

- **The dose** levels of the INTUVAX-DC-vaccine were 5 (patient 1-4), 10 (patient 5-9) and 20 (patient 10-12) x $10^6$ viable and MHC class II expressing cells

- **The treatment regimen**: INTUVAX was injected (CT-guided) two times with 14+3 days interval into the renal tumor (viable part of the tumor) during the period while the patient was awaiting nephrectomy

First INTUVAX-treatment in February 2012
Histopathological evidence of tumor specific and systemic immune response

Fig. 1: Untreated tumor

Fig. 2: Treated tumor

Fig 3: Metastasis

Fig 4: Normal kidney tissue surrounding treated tumor
A, B, C: Non-vaccinated RCC controls

1-12: CD8+ T-cell infiltration in patients treated with INTUVAX
Figures A, B, and C show the CD8+ T-cell infiltration in three untreated RCC-tumors that were stained for as a comparison to figures 1-12, showing intratumoral infiltration of CD8+ T-cells in patients treated with INTUVAX. The insignificant amount of tumor infiltrating T-cells in A, B, and C is representative of the amount of tumor infiltrating T-cells found by others in published studies on 105 untreated RCC-patients.

Figures on tumor tissue slides stained for CD8+ T cells in central tumor cell areas from patient 2, 4, 8, 11, and 12 show a massive intratumoral infiltration of CD8+ T-cells. Patients 6 and 9 also show a substantial intratumoral infiltration, assessed as strong, of CD8+ T cells.
mRCC clinical phase I/II survival data looks very promising (September 2016) compared to historical data

- Strong/massive intratumoral infiltration of CD8+ T cells in 7 of 12 primary tumors
- 5 of 11* patients are still alive
- Ongoing mOS for entire patient population more than doubled (40 months Vs 15.2 months)
- Ongoing mOS for poor prognosis group is tripled (32 months Vs 9 months)
- Ongoing mOS for intermediate group is 45 months Vs 26 months
- One patient with incomplete metastasectomy showed complete response without add-on therapy with TKI
- Exciting response data for patients who receive add-on treatment with TKIs
  - Complete response of 4 brain metastases
  - Objective response in poor prognosis patient with extensive sarcomatoid tumor development

* One patient excluded from efficacy evaluation due to wrong diagnosis
Case report – patient treated with INTUVAX followed by sunitinib showing complete remission of 4 brain metastases

- High risk group according to MSKCC-criteria.
- Strong infiltration of CD8+ T-cells in the resected kidney tumor.
- Development of 4 new brain metastases, one new lung metastase and 5 large (up to 5 cm largest diameter) liver metastases at follow up 3 months after nephrectomy.
- Received standard sunitinib treatment due to progression, Follow up 3, 6 and 9 months after initiation of sunitinib treatment reveals a continuous tumor regression at all metastatic sites (including complete remission of all 4 brain metastases). Still alive 27 months from INTUVAX-treatment.

Patient with brain metastases before sunitinib treatment

Showing complete response of 2 of the brain metastases six months after start of sunitinib treatment
Hepatocellular cancer phase I/II (April 2016)

- Second-line setting for patients that previously have failed on standard treatment. No combination of INTUVAX and standard treatment (Sorafenib or TACE)

- Eleven (11) patients treated with primary hepatocellular carcinoma

- Nine (9) patients have been fully treated with three (3) INTUVAX-doses

- Five (5) patients have passed their expected median overall survival based on historical data

- Two (2) of the three (3) fully treated patients still alive had not yet passed the expected median overall survival

- Bile duct cancer: received INTUVAX + gemcitabin and cisplatin (G/C). Alive after 26 months Vs expected 11.7 months.

- Approval to treat an additional six patients in the first-line setting in combination with Sorafenib (for potential synergistic antitumor effect). First patient treated in this setting
Positive immunological HCC-data that correlates with prolonged survival

Assays were performed that compared the frequency of interferon-producing CD8 + T cells in the blood, indicating that the T cells have a killing function, by stimulation with two different tumor-associated antigens (antigens that can be expressed in primary liver tumors) before first INTUVAX-dose and one week after the third and final dose.

- Six (6) of the nine (9) fully-treated patients showed an increased frequency of these interferon-producing CD8 + T cells in the blood, reactive against at least one of the two tumor-associated antigens for liver cancer, after treatment with INTUVAX. For five of these six patients, an increase in the frequency of CD8+ T cells reactive against at least one of the two tumor-associated antigens for liver cancer remained at renewed analysis six weeks after the third and final INTUVAX-dose.

- Four (4) of the six (6) patients that showed an increased frequency of these tumor-specific CD8 + T cells have surpassed their expected median overall survival and the other two (2) patients are still alive and have not yet surpassed the expected median overall survival.

- Two (2) of three (3) fully-treated patients who did not exhibit an increased frequency of tumor-specific T cells in the blood after full INTUVAX treatment passed away before they could pass their expected median overall survival.

- One patient with bile duct cancer was also treated with three doses of INTUVAX and showed an increased frequency of CD8 + T cells in the blood, reactive against the two different tumor associated antigens (which may also be expressed in bile duct cancer) after full INTUVAX-treatment.
INTUVAX® – Next steps
Phase II INTUVAX/sunitinib combo mRCC design

- IND application has been submitted to the FDA and is under review. Clearance expected within the next couple of weeks.
Adaptation of production process completed, resulting in a direct injectable product, which enables more clinics to use INTUVAX and broadens the future market

12 enrolled patients

No adverse vaccine-related events

Preliminary immunological data regarding the infiltration of CD8+ T cells in primary tumors and in healthy tissue, as well as a comparison between INTUVAX-treated patients and patients in the control group, indicate a tumor-specific activation of the immune system in INTUVAX-treated patients

Efficacy data is still too early to evaluate
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