Cancer Specific Therapeutic Vaccines Targeting Oncogenic RAS Mutations
Gunnar Gårdemyr, CEO
Disclaimer

This report contains certain forward-looking statements based on uncertainty, since they relate to events and depend on circumstances that will occur in future and which, by their nature, will have an impact on the results of operations and the financial condition of Targovax. Such forward-looking statements reflect the current views of Targovax and are based on the information currently available to the company. Targovax cannot give any assurance as to the correctness of such statements.

There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in these forward-looking statements. These factors include, among other things, risks or uncertainties associated with the success of future clinical trials; risks relating to personal injury or death in connection with clinical trials or following commercialization of the company’s products, and liability in connection therewith; risks relating to the company’s freedom to operate (competitors patents) in respect of the products it develops; risks of non-approval of patents not yet granted and the company’s ability to adequately protect its intellectual property and know-how; risks relating to obtaining regulatory approval and other regulatory risks relating to the development and future commercialization of the company’s products; risks that research and development will not yield new products that achieve commercial success; risks relating to the company’s ability to successfully commercialize and gain market acceptance for Targovax’s products; risks relating to the future development of the pricing environment and/or regulations for pharmaceutical products; risks relating to the company’s ability to secure additional financing in the future, which may not be available on favorable terms or at all; risks relating to currency fluctuations; risks associated with technological development, growth management, general economic and business conditions; risks relating to the company’s ability to retain key personnel; and risks relating to the impact of competition.
Agenda

1. Introduction to Targovax
2. Ras Mutations and Market
3. Targovax Therapeutic Cancer Vaccines are positioned to succeed
4. Clinical update
5. Financial Highlights
6. Organisation
7. Priorities going forward
8. Key Take-Aways
Targovax, a Norwegian biotech company founded by world pioneers in cancer immunotherapy

- The technology was initially developed and documented by Norsk Hydro/Pronova (1990-2000) in collaboration with The Norwegian Radium Hospital
- Founders of Targovax are co-inventors of technology: Professor Gustav Gaudernack and Jon Amund Eriksen, COO Targovax
- Established 2010
- Product portfolio with a substantial market potential with a high unmet medical need
- Orphan Drug Designation (US/EU) for TG01
- Solid patent position
- Experienced Team with more than 150 years of Drug Development Experience and track record of bringing products to the market
Targovax highlights

Attractive pipeline with products in Phase I and Phase II clinical trials

Uniquely positioned with promising clinical data in operable pancreatic cancer, an orphan drug indication

Large unmet medical need for cancer with RAS* mutations – Immunotherapy targeting RAS mutations

Phase I study with TG01 in operated pancreatic cancer finished – TG01 is safe and induces persistent immune responses

Phase II study with TG01 in operated pancreatic cancer ongoing at internationally renowned clinical centres – recruitment completed and primary end point achieved

*RAS is a molecule inside the cells regulating cell division. Mutations cause sustained division, and is a driver in cancer development. RAS mutation is an early cancer marker, present in approximately 20% of all cancers.
Strong track record 2011-2014

Significant progress made so far

2011
- Orphan Drug status granted in EU and US for TG01
- GMP production established for TG01
- Public grant OFU program MNOK 9

2012
- GMP production for adjuvant GM-CSF from a reliable source
- European Medicines Agency advice supporting the clinical development plan for TG01
- Clinical trial initiated December – Phase I/II in operable pancreatic cancer

2013
- First patient treated
- Public grant BIA MNOK 12.3
- Expanding study to two sites in UK
- Patent application supporting expanded pipeline

2014
- Phase I successfully completed with RAS specific immune response in 6/6
- Phase II initiated
- First patient treated UK
- OTC listing
- Start production and pre-clinical development of TG02
- Pancreatic Cancer Advisory Board
- Completed enrollment of 18 patients in TG01 phase II trial in resected pancreatic cancer
- The Board selects Mr Gunnar Gårdenmyr as new CEO
Agenda

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2. Ras Mutations and Market
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5. Financial Highlights
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Targovax products covers a substantial market potential with a high unmet medical need

Incidence of RAS mutations in cancer

percent

Cancer incidence

percent

(xx) = No. of cancer patients
Globocan 2012
Cancer Re, No 15, 2012

Targovax products cover a substantial market potential with a high unmet medical need.
RAS is a driver in cancer development

Cancer is a broad group of diseases involving unregulated cell growth. RAS is a molecule inside the cells regulating cell division. Mutations cause sustained division, and is a driver in cancer development. RAS mutation is an early cancer marker, present in approximately 20% of all cancers*.

No effective treatments exist for cancer with RAS mutations

* Prior et al, 2012

RAS mutations:
- ~ 90 % Pancreatic cancer
- ~ 40 % Colorectal cancer
- ~ 12 % Lung cancer
- ~ 20 % Malignant melanoma
TG01 – Specific Peptide Based Therapeutic Cancer Vaccine

Targets the most common oncogenic RAS mutations

1. The TG01 peptides are injected into the skin together with Molgramostim

2. The TG01 peptides are taken up by activated dendritic cells that migrate to lymph nodes where they present the peptides to T cells
   - Presented by HLA class II; DR, DQ and DP
   - No need of tissue typing

3. Subsets of T cells learn to recognize the RAS mutations and enter the circulation of the body
   - CD4+ T helper cells directly
   - CD8+ Cytotoxic T cells by cross presentation

4. When encountering cancer cells with RAS mutations, the T cells are re-activated to proliferate and trigger immunological killing of the cancer cells
Agenda

1. Introduction to Targovax
2. Ras Mutations and Market
3. **Targovax Therapeutic Cancer Vaccines are positioned to succeed**
4. Clinical update
5. Financial Highlights
6. Organisation
7. Priorities going forward
8. Key Take-Aways
Targovax Therapeutic Cancer Vaccines are positioned to succeed

Potential reasons for failure of other e.g. pancreatic cancer vaccines

- Target poorly defined – Not cancer specific

- Wrong vaccine or vaccine design – Dependent on tissue type and induce cytotoxic T cells without necessary T helper cell support. Complex logistics for cell based vaccines.

- Choice of adjuvant – Depot effect attracts induced T cells back to the vaccination site rather than to the tumour

- Sub-optimal patient selection – Late stage disease and patients too sick to benefit

- “Cutting corners”– Moving into large randomized clinical studies based on limited phase II results and information
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Targovax strategy

- Target well defined - cancer specific mutations in the RAS protein
- RAS mutation is a driver in cancer development
- Large unmet medical need for cancers with RAS mutations
Targovax Therapeutic Cancer Vaccines are positioned to succeed

Potential reasons for failure of other e.g. pancreatic cancer vaccines

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Targovax strategy

- Induction of RAS mutation specific T helper cells and T cytotoxic cells

- Reactivation of the RAS mutation specific T helper cells at the tumour site will support and enhance cancer cell killing, and will be strengthened by cross presentation and broadening of the anti cancer immune-response

- RAS peptides are not dependent on tissue type

- Easy and scalable production and logistics, stable product, no per-patient adjustment
Targovax Therapeutic Cancer Vaccines are positioned to succeed

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Targovax strategy

- Use the well proven immune modulator GM-CSF (molgramostim) which gives:
  - No depot effect and trapping of induced T cells
  - Rapid and persistent T cell response
Targovax Therapeutic Cancer Vaccines are positioned to succeed

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Targovax strategy

- Careful selection of eligible patient groups - Inclusion and exclusion criteria securing patient populations most likely to respond to treatment

- Treat patients with limited tumour burden, including adjuvant treatment after resection of primary tumour in the first instance
Targovax Therapeutic Cancer Vaccines are positioned to succeed

Potential reasons for failure of other e.g. pancreatic cancer vaccines

- Target poorly defined – Not cancer specific
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Targovax strategy

- Conduct exploratory phase II studies to ensure optimal design of POC studies
- Extensive use of clinical advisory boards with key opinion leaders
- Active communication with regulatory authorities (EMA, Country-specific, FDA)
Agenda

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3. Targovax Therapeutic Cancer Vaccines are positioned to succeed
4. **Clinical update**
5. Financial Highlights
6. Organisation
7. Priorities going forward
8. Key Take-Aways
Strong pipeline leveraging on product history and lead product TG01

Current pipeline

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Disc. &amp; lead dev.</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
</tr>
</thead>
</table>
| TG01 (7 peptides) + Molgramostim | Pancreas Cancer  
Adjuvant treatment after resection  
Prevent/delay recurrence of disease | Pre-clinical   | Phase I      |         |          |           |
| TG02 (8 peptides) + Molgramostim | Colorectal cancer  
Lung cancer  
Therapeutic vaccination | Pre-clinical   | Phase I      |         |          |           |
| TG03 (6 peptides) + Molgramostim | Malignant melanoma  
Colorectal cancer | Pre-clinical   | Phase I      |         |          |           |
CT TG01-01

“A Phase I/II Trial of TG01 and Gemcitabine as Adjuvant Therapy for Treating Patients with Resected Adenocarcinoma of the Pancreas”
Assess the safety of TG01/Molgramostim vaccination and adjuvant chemotherapy

Assess the immune response to TG01 and the effect of adjuvant chemotherapy in patients receiving TG01 and Molgramostim
- **Target:** Immune response detected in 9 of 18 treated patients

Secondary objectives: Efficacy at 2 years
- Disease free survival
- Overall survival

Exploratory objectives
- Assess the relationship of KRAS status to recurrence of disease
- Monitor CA19-9 levels

Trial Centres
- The Norwegian Radium Hospital, Norway
- Clatterbridge Cancer Centre NHS Foundation Trust in Liverpool, UK
- Christie NHS Foundation Trust in Manchester, UK
CT TG01-01 Phase I/II Clinical Trial

Phase I part completed - Phase II ongoing

Phase I

- Immune response (DTH *) in 6 of 6 patients
- No DLTs ** in phase I part of the study (by study week 11)

![DTH response chart](chart)

Phase II

- Recruitment completed for phase II part
- Target for immune response achieved

*Delayed Type Hypersensitivity
**Dose Limiting Toxicity
Production and logistics advantages

Defined combination of synthesized peptides

Production
- Well controlled and proven production process of vaccine peptides
- Production processes and methods for all peptides established and validated for Phase II clinical trials
- Long term stability data for drug product – Documented 3 years shelf life
- Exclusive agreement with world class supplier
- Immune modulator Molgramostim (GM-CSF): secure and controlled supply chain for Phase II clinical trials

Logistics
- Standard shipping - easy and simple
- Standard on-site preparations (reconstitution in water)
- No per-patient adjustments
Agenda

1. Introduction to Targovax
2. Ras Mutations and Market
3. Targovax Therapeutic Cancer Vaccines are positioned to succeed
4. Clinical update
5. **Financial Highlights**
6. Organisation
7. Priorities going forward
8. Key Take-Aways
Key Financials 2014

NOK 1000

Profit & Loss

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<thead>
<tr>
<th></th>
<th>2014</th>
<th>2013</th>
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<tbody>
<tr>
<td>OPERATING REVENUES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grants</td>
<td>4 801</td>
<td>4 337</td>
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<tr>
<td>Other revenues</td>
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<td>364</td>
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<tr>
<td>TOTAL OPERATING REVENUES</td>
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<td>4 701</td>
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<td>OPERATING EXPENSES</td>
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<tr>
<td>Payroll expenses</td>
<td>-6 600</td>
<td>-4 721</td>
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<tr>
<td>Other operating expenses</td>
<td>-15 689</td>
<td>-7 110</td>
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<tr>
<td>TOTAL OPERATING EXPENSES</td>
<td>-22 289</td>
<td>-11 831</td>
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<tr>
<td>OPERATING PROFIT/LOSS</td>
<td>-17 415</td>
<td>-7 130</td>
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<tr>
<td>NET FINANCIAL ITEMS</td>
<td>-2</td>
<td>-15</td>
</tr>
<tr>
<td>PROFIT/LOSS FOR THE PERIOD</td>
<td>-17 417</td>
<td>-7 144</td>
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Balance sheet

<table>
<thead>
<tr>
<th></th>
<th>31 Dec 2014</th>
<th>31 Dec 2013</th>
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</thead>
<tbody>
<tr>
<td>ASSETS</td>
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<tr>
<td>Fixed assets</td>
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<td>-</td>
</tr>
<tr>
<td>Receivables</td>
<td>4 660</td>
<td>5 826</td>
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<tr>
<td>Bank deposits</td>
<td>62 549</td>
<td>8 370</td>
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<tr>
<td>TOTAL ASSETS</td>
<td>67 359</td>
<td>14 197</td>
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<tr>
<td>TOTAL EQUITY</td>
<td>60 681</td>
<td>201</td>
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<tr>
<td>Accounts payable</td>
<td>2 564</td>
<td>2 657</td>
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<tr>
<td>Public duties payable</td>
<td>768</td>
<td>454</td>
</tr>
<tr>
<td>Other current liabilities</td>
<td>3 346</td>
<td>10 884</td>
</tr>
<tr>
<td>TOTAL LIABILITIES</td>
<td>6 678</td>
<td>13 996</td>
</tr>
<tr>
<td>TOTAL EQUITY AND LIABILITIES</td>
<td>67 359</td>
<td>14 197</td>
</tr>
</tbody>
</table>

Activities in 2014 developed according to plan. Net loss amounted to 17,4 MNOK.

The financial position at the end of 2014 is satisfactory. Total cash at year end amounted to 62,5 MNOK.
Burn Rate

Cash Burn 2013 and 2014 (mill. NOK)

Key Burn Rate Drivers

- Timing and scope of clinical trials
- R&D activities
- Personnel
- Infrastructure
Prepare Targovax financially for the future

**Implemented in 2014**
- Proper capital base to boost the development of the company
- Significant increase in amount of investors: 88 at year-end
- Quarterly reporting to the market
- Active use of NOTC message system and other relevant media channels in Norway and Internationally to communicate company news
- Elected new external auditor: EY
- Relevant, expandable and effective financial reporting structure

**To be developed in 2015**
- Revise strategic and financial plan
- IFRS from Q1 2015
- Policy for remuneration of key persons
- Principles for corporate governance
- Communication platform
10 largest shareholders, 31 December 2014

<table>
<thead>
<tr>
<th>Shares</th>
<th>Owner share</th>
</tr>
</thead>
<tbody>
<tr>
<td>RADIUMHOSPITALETΣ FORSKNINGSSSTIFTELSE</td>
<td>3 410 589</td>
</tr>
<tr>
<td>DATUM INVEST AS</td>
<td>1 162 000</td>
</tr>
<tr>
<td>TIMMUNO AS *</td>
<td>724 650</td>
</tr>
<tr>
<td>PRIETA AS **</td>
<td>720 000</td>
</tr>
<tr>
<td>BIRK VENTURE AS</td>
<td>438 657</td>
</tr>
<tr>
<td>ALGOT INVEST AS</td>
<td>392 465</td>
</tr>
<tr>
<td>PORTIA AS</td>
<td>300 000</td>
</tr>
<tr>
<td>TRYGVE SCHIØRBECKS EETF AS</td>
<td>286 449</td>
</tr>
<tr>
<td>ARCTIC FUNDS PLC  BNY MELLON SA/NV</td>
<td>182 000</td>
</tr>
<tr>
<td>OP-EUROPE EQUITY FUN C/O CITIBANK NA</td>
<td>157 869</td>
</tr>
<tr>
<td><strong>Total, 10 largest shareholders</strong></td>
<td><strong>7 774 679</strong></td>
</tr>
<tr>
<td>78 other shareholders, each representing an ownership of less than 1.7%</td>
<td>1 654 724</td>
</tr>
<tr>
<td><strong>Total, 88 Shareholders</strong></td>
<td><strong>9 429 403</strong></td>
</tr>
</tbody>
</table>

* Jon Amund Eriksen, ** Gustav Gaudernack
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5. Financial Highlights
6. **Organisation**
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### The Targovax Team – focused on delivery

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Experience Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gunnar Gårdemyr, CEO</td>
<td>More than 30 years of international experience from the pharmaceutical and biotech industry.</td>
<td></td>
</tr>
<tr>
<td>Jon Amund Eriksen, COO</td>
<td>Co-founder and inventor of Targovax technology.</td>
<td></td>
</tr>
<tr>
<td>Gunnar Aarnes, CFO *</td>
<td>Financial executive with more than 20 years experience and several senior financial positions in listed companies</td>
<td></td>
</tr>
<tr>
<td>Robert Miller, Chief Medical Officer</td>
<td>Extensive experience from international development projects involving regulatory processes, medical responsibility for clinical trials and development strategy.</td>
<td></td>
</tr>
<tr>
<td>Anne Kirsti Aksnes, VP Clinical Development</td>
<td>20 years of experience within clinical research and development in pharma and biotech industry and 10 years of experience with clinical physiology.</td>
<td></td>
</tr>
<tr>
<td>Berit Iversen, VP Technical Development</td>
<td>25 years of experience within product R&amp;D and operations in the pharma and biotech industry.</td>
<td></td>
</tr>
<tr>
<td>Tina Madsen, VP Quality Assurance</td>
<td>More than 20 years of experience within R&amp;D and commercial manufacturing in pharma and biotech industry.</td>
<td></td>
</tr>
<tr>
<td>Tone Otterhaug, VP Non-clinical Development</td>
<td>Broad experience from pharma and biotech within R&amp;D and clinical development of cancer drugs.</td>
<td></td>
</tr>
<tr>
<td>Gustav Gaudernack, Professor, Chief Scientific Adviser</td>
<td>Co-founder and inventor of Targovax technology.</td>
<td></td>
</tr>
</tbody>
</table>

*Øystein Soug starts as new CFO June 1, 2015*
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Priorities going forward

- Decide on clinical strategy to reach Proof of Concept
- Optimise organisation and team
- Deepen and broaden partner contacts
- Improve visibility, communication and messaging
- Align the financial plan with the up-dated clinical strategy
Paving the way for future success

Anticipated milestones 2015-2016

2015

- Targovax appoints Mr. Øystein Soug as new CFO
- Interim analysis disease free survival TG01 phase II (12m)
- Established protocol Phase II randomized TG01
- Complete pre-clinical package TG02
- Initiate TG02 phase I in colorectal and/or lung cancer
- Start production and pre-clinical development TG03
- Strengthening organization
- Updated product development plan

2016

- Complete TG01 phase II operable pancreatic cancer (24m)
- GM-CSF source for Phase III/commercial use concluded
- Complete TG02 phase I in colorectal and/or lung cancer
- Complete pre-clinical package TG03 for phase I
- IPO (1H)
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Key Take-Aways

1. Targovax continues to deliver as planned

2. Targovax is well positioned with promising clinical data and a pipeline of follow-on peptide vaccines

3. Targovax is with Specific Peptide Based Therapeutic Cancer Vaccine targeting niche oncology indications with an unmet medical need

4. Realistic and ambitious product development plan

5. Experienced Team with more than 150 years of Drug Development Experience and track record of bringing products to the market
Supporting materials

THERAPEUTIC CANCER VACCINES
# Targovax Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Drug Substance</th>
<th>Function</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG01</td>
<td>7 Peptides</td>
<td>Cancer specific antigens</td>
<td>Pancreatic cancer</td>
</tr>
<tr>
<td>TG02</td>
<td>8 Peptides</td>
<td>Cancer specific antigens</td>
<td>Colorectal cancer Lung cancer</td>
</tr>
<tr>
<td>TG03</td>
<td>6 Peptides</td>
<td>Cancer specific antigens</td>
<td>Malignant melanoma</td>
</tr>
<tr>
<td>“GM-CSF”</td>
<td>Molgramostim</td>
<td>Regulation of various cellular processes (cytokine)</td>
<td>Immune modulator for vaccination and general immune stimulation</td>
</tr>
</tbody>
</table>
Established, validated technology and lead product protected by Orphan Drug Designation

First product in Phase II

- Lead product TG01 – treatment of operated pancreatic cancer
  - Complete preclinical documentation
  - Phase I completed in combination with chemotherapy – safe and well tolerated by the patients
  - Phase II ongoing
  - Clinical development plan validated by European Medicines Agency

- Immunological Proof of Concept in cancer patients from historical data*
  - RAS mutation specific immune responses (T cells) are induced
  - Immune response indicates a survival benefit for patients

- Production established at phase II level

First indication protected by Orphan Drug Status

- TG01 protected by Orphan Drug Designation in US & EU
  - 7 and 10 years market exclusivity for product in indication from date of market approval (see appendix for details)

- Patents covering peptide based immunotherapy targeting RAS:
  - USA: US 5 964 978, (exp. May 2016)
  - Norway: NO309798B1 (exp. Apr 2019)

- Patent application, priority Dec 9th 2013, covering products TG02, TG03 and other products **

- The company works continuously with establishing new patents and patent extensions where applicable

- Freedom to operate for TG01, TG02 and TG03 based on analysis from 2014.

* (Gjertsen et al, 2001, Weden et al, 2011)

** The patent application is in early stage of the application process and has not yet been subject to an examination by the EPO. An assessment with respect to patentability will be part of the EPO examination. Patent office: Marks & Clerck, UK
Definitions and glossary of terms

- **Cancer Immunotherapy**: treatment that uses the body’s own immune system to help fight cancer.

- **Peptides** are small proteins. They can be produced chemically in quantities of many kilograms. The RAS peptides are very stable and can be stored for several years.

- **T cells** are the cells of the immune system that defend the host against intracellular changes and infections (virus). By using peptides mimicking special intracellular changes, like RAS mutations, subset of T cells can be induced that recognize cells with such mutations and that will trigger immunological eradication of these cells. T cells also provide immunological memory and are rapidly retriggered upon reappearance of cells with the specific intracellular changes.

- **Dendritic cells (DC)** are specialized immune cells that are present in the skin. When activated DC engulf foreign material and present protein fragments (peptides) to T cells in the lymph nodes where specific T cells are induced.

- **Immune response**: is how the body recognizes and kills virus, bacteria, and substances that appear foreign and harmful.

- **DTH**: a way of measuring an immune response towards a specific antigen. When the immune system has learnt to recognize e.g. the RAS peptides as foreign, the immune response can be measured by using DTH (delayed type hypersensitivity reaction). It is similar to the Pirquet – skin test used to measure effect of tuberculosis vaccination, by applying the foreign material to scratches on the skin and observing the size of swelling / redness.

- **Adjuvant** is used to activate the dendritic cells at the injection site to take up the peptides. Targovax is using GM-CSF (granulocyte macrophage – colony stimulating factor) as adjuvant.

- **Molgramostim - GM-CSF** (the adjuvant) is a protein that activates DC by interacting with their GM-CSF receptor. GM-CSF is commercially available (currently for use in phase II).