Exquisitely Personalized Immunotherapy for Cancer: GT-EPIC™

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CEO & President, Co-Founder

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The drugs and devices contemplated by this Corporate Summary are investigational in nature and have not received marketing approval by the FDA or other regulatory authority. The safety or effectiveness of these investigational products has not been established.
CONVENTIONAL VIEW ON DISEASE & TREATMENT

- Population treatments - one size fits all
- Focus on common targets
- If heterogeneity is addressed, it is by biomarker guided patient selection
THERE ARE MULTIPLE TREATMENT OPTIONS FOR CANCER....

No two tumors are alike. The differences are propagated at the genetic level (Somatic variants)

BUT THEY RARELY TAKE INTO ACCOUNT ITS INDIVIDUALITY
GENEOS’ FOCUS IS ON CANCER TREATMENTS THAT ARE:

• PATIENT CENTERED &
• PATIENT TUMOR DRIVEN

………..BECAUSE EACH PERSON’S CANCER IS DIFFERENT!
Cancer treatment innovation:

Personalized/Individualized

Immunotherapy (T cells as effectors)

Target differences in cancer versus normal cells
(e.g. Somatic variants in tumors; Cancer neoantigens)

With its GT-EPIC™ platform,
Geneos is developing cancer neoantigen - targeted, personalized immunotherapies

- Geneos established as a venture capital backed Immuno-Oncology startup
- GT-EPIC™ Platform: Optimized, DNA plasmid based, antigen-specific, T cell inducer
  - Demonstrated cancer antigen specific CD8+ T cells, and TILs
  - CPI combinations in the clinic in different IO settings
CHECKPOINT INHIBITOR IMMUNOTHERAPY (CPI): MIRACULOUS FOR SOME, PROVIDE NO-BENEFIT FOR MANY

Figure 1. Percentage of US Patients With Cancer Who May Benefit From and Respond to Checkpoint Inhibitor Immunology Drugs (2011-2018)

Less than half of oncology patients are eligible for checkpoint inhibitor therapy & only about 1 in 3 (0.28) of eligible patients respond to therapy  

GENEOS IMPACT OPPORTUNITY

Modified from: Haslam & Prasad JAMA Oncology, 2019
Mutations and other somatic changes in the tumor (cancer neoantigens) are recognized by the immune system as “foreign” to mount an immune response against the neoantigens.

Colorectal Cancer provides the most striking example of mutations driving T Cell responses which lead to clinical responses with CPIs.

Evidence continues to build that a robust CD8+ T-cell response is necessary to generate a response to checkpoint inhibitors.

- Mutations and other somatic changes in the tumor (cancer neoantigens) are recognized by the immune system as “foreign” to mount an immune response against the neoantigens.
- Colorectal Cancer provides the most striking example of mutations driving T Cell responses which lead to clinical responses with CPIs.


Note: ORR for studies of anti–PD-1 or anti–PD-L1 monotherapy that enrolled at least 10 patients who were not selected for PD-L1 tumor expression.

GENEOS ADDRESSES THE THREE KEY CHALLENGES OF CURRENT PERSONALIZED NEOANTIGEN VACCINES

Current challenges

Lack of CD8 T Cell Responses
• Mostly CD4 T cells

Neoantigen Payload Limitations
• Typically 10-20 neoantigens/patient

Long Turnaround Times
• > 12 - 16 weeks

GT-EPIC™ Personalized Products

CD8 + CD4 responses

>50 neoantigens/patient

Turnaround time: 6-8 weeks

Geneos’ value proposition: (i) Clinical Efficacy; (ii) Cost Effective; (iii) Time Efficient
OPTIMIZED DNA NEOANTIGENS + pIL12 + CELLECTRA® ELECTROPORATION (EP)

- Personalized product has three components –
  - Optimized DNA plasmid encoding neoantigens
  - IL-12 (pIL12): Cytokine immune-modulator; Boosts T cells
  - CELLECTRA® delivery device (in vivo electroporation; EP): Efficient plasmid uptake for optimal antigen production
- Combination activates robust functional antigen specific CD4+ & CD8+ killer T cells*
- Optimized DNA + EP delivery-based treatment has favorable safety profile*: 2,000+ subjects and 6,000+ immunizations
- Comprehensive licensed technology IP, and Geneos-filed IP around the GT-EPIC™ neoantigen targeting approach, design of inserts and their combinations

* DNA Platform safety and immunogenicity data courtesy Inovio Pharmaceuticals; CELLECTRA® EP Device, pIL12 licensed from Inovio Pharmaceuticals
OPTIMIZED (DESIGN + DELIVERY) = IMPROVED EXPRESSION & IMPROVED IMMUNE RESPONSES

Rabbits

Display of GFP gene expression after electroporation (EP) delivery into rabbit muscle

Highly efficient delivery of DNA plasmids by in vivo electroporation has led to >1000 fold enhancement in intra-cellular antigen expression

Ref: Sardesai & Weiner, 2011

T Cell Responses By ELISpot Assay

Dosed 3x with 15ug pNP antigen; Responses @2 wk post 3rd Imm

Mice

Sequence optimization & EP delivery has led to >100+ fold increase in immune responses from antigens encoded by DNA plasmids

Ref: Sardesai & Weiner, 2011
Stronger CD8 & CD4 T-cell Responses by DNA + EP vs Ad5

SIV vaccine model
UPenn/Merck/Inovio

OPTIMIZED DNA VACCINES + CELLECTRA® EP: NHP

pIL12 and EP delivery boost T cell responses

Boosting of HIV Env + gag ELISpot responses with each vaccination

Ref: Hirao, Sardesai, Weiner et al. Molecular Therapy, August 2010

Ref: Hirao, Weiner et al. Vaccine 2008
Phase 1 study of MEDI0457
22 HPV+ HNSCC Patients

- Robust antigen-specific CD8+ killer T cell responses observed in 20/22 (90.9%) patients (both tumor tissue and peripheral blood)
- Of 22 pts in Phase I, 18 showed no progression to data cut off date (01/19)
- 4 progressed over study period - recurrence with metastatic disease; treated with PD1
- 2/4 (50%) showed rapid and durable complete response to PD1 therapy
- Response data compares well in metastatic HPV+ HNSCC
  - 4% CR (8/192) Keytruda
  - 3% CR (6/240) Opdivo
- AZ conducting phase 2 studies combining MEDI0457 and durvalumab (PD-L1 inhibitor)


Data courtesy of Inovio Pharmaceuticals, Inc.
INO-5401 (3 Tumor antigens) + Libtayo (PD1) – GBM:

- SITC late breaking abstract presented Nov 6-10th 2019
  - Acceptable safety profile consistent with that of Libtayo and Inovio’s platform technology
  - Patients developed T cell immune response to tumor-associated antigens encoded by INO-5401

**Improved PFS6 relative to historical data**

<table>
<thead>
<tr>
<th>Cohort</th>
<th>N Subjects</th>
<th>N Event-free Subjects</th>
<th>PFS6 (%)</th>
<th>Historical Standard of Care PFS6 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort A (MGMT Unmethylated)</td>
<td>32</td>
<td>24</td>
<td>75</td>
<td>40</td>
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<tr>
<td>Cohort B (MGMT Methylated)</td>
<td>20</td>
<td>16</td>
<td>80</td>
<td>60</td>
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<tr>
<td>Both Cohorts Combined</td>
<td>52</td>
<td>40</td>
<td>77</td>
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</tbody>
</table>

- ASCO 2020 Annual Meeting Abstract

**Improved OS12 relative to historical data**

85% (n = 52) vs 65% for historical controls

*References:
- Chinot NJEM 2014 - Bevacizumab plus Radiotherapy–Temozolomide for Newly Diagnosed Glioblastoma
- Hegi NJEM 2005 - MGMT Gene Silencing and Benefit from Temozolomide in Glioblastoma
- Journal of Clinical Oncology 2013 - Dose-Dense Temozolomide for Newly Diagnosed Glioblastoma: A Randomized Phase III Clinical Trial

Data courtesy of Inovio Pharmaceuticals, Inc.
Key takeaways:
- Although both CD4 and CD8 T cells were induced, GENEOS platform drives strong Class I responses (predominantly CD8)
- 75% of all T cell responses generated were neoantigen specific CD8+ or both CD8+ and CD4+ T cells

FOCUSING ON HIGH AFFINITY MHC-I BINDERS (<500 nM), MHC-I PREDICTION SELECTS FOR EPITOPES THAT GENERATE CD8+ T CELL RESPONSES WHEN DELIVERED BY GENEOS PLATFORM

Key takeaway:
All (100%) of the reactive neoepitopes with MHC-I binding affinity < 500 nM yielded neoepitope specific CD8+ T cell responses

GENEOS NEOANTIGEN IMMUNOTHERAPIES DEMONSTRATE ABILITY TO COMBINE UPWARDS OF 60 NEOANTIGENS AND DRIVE SIGNIFICANT CONTROL OF TUMOR GROWTH

TC1 tumor implantation
C57Bl/6 mice
Vaccination: 7 14 21 28

Key takeaways:
- Formulations with > 60+ neoantigens
- No apparent interference seen
- Dilution of specific neoepitope dose with inclusion of additional irrelevant epitopes or control DNA does not impact tumor challenge efficacy

THE ANTI-TUMOR EFFECTOR FUNCTION IS MEDIATED BY INDUCTION OF NEOANTIGEN SPECIFIC CD8+ T CELLS

Key takeaway:
- Both CD4+ and CD8+ T cells are induced by the neoantigen plasmids.
- Neoantigen specific CD8+ T cells are sufficient to drive the anti-tumor response.

1. Biopsy specimen collected at clinical site (Day 0)

2. DNA, RNA Sequencing & somatic variant calls

3. Proprietary neoantigen prioritization, DNA insert design & sequence optimization

4. Neoantigen DNA insert synthesis, cloning & generation of seed patient-specific plasmid

5. cGMP manufacture of patient-specific DNA plasmid Drug Product

6. Patient treated Day 42-56

Specimen(s) shipped for DNA, RNA sequencing

GMP product shipped to clinical site

Seed plasmid shipped to GMP Mfg. site

Current model (Outsourced)

Total biopsy-to-treatment turnaround time for early clinical studies: 6-8 weeks

GENEOS CAN RAPIDLY IDENTIFY NEOANTIGENS AND MANUFACTURE PATIENT SPECIFIC PRODUCTS IN LESS THAN HALF THE TIME OF OUR COMPETITORS
Feb 21, 2019
Geneos Therapeutics Secures $10.5 Million in Series A Financing to Develop the Next Generation of Neoantigen-Targeting Cancer Immunotherapies

July 10, 2019
GT-10: First patient treated with GT-EPIC™ platform (Anaplastic Astrocytoma)

July 22, 2019
Manufacturing supply agreement established with CDMO VGXI, Inc.

December 31, 2019
GT-30 IND Open: Advanced HCC

February 7, 2020
GT-20 IND Open: Newly diagnosed GBM

May 19, 2020
Manufactured first GMP Clinical Lot for the GT-30 study

July 22, 2019
Manufacturing supply agreement established with CDMO VGXI, Inc.

GENEOS MILESTONES
<table>
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<tr>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tbody>
<tr>
<td><strong>GT-10:</strong> Anaplastic astrocytoma - Single patient IND for treatment GEN-PV-001 + IL-12</td>
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<td><strong>Collaboration with Wash U. School of Medicine (WUSM)</strong></td>
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<td><strong>Brain Cancer:</strong></td>
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<td><strong>GT-20:</strong> Investigator initiated IND Study in MGMT neg primary GBM – GNOS-PV01 + IL-12</td>
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<td><strong>Collaboration with Wash U. School of Medicine (WUSM)</strong></td>
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<td><strong>Liver Cancer:</strong></td>
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<td><strong>GT-30:</strong> IND Study in advanced Hepatocellular Carcinoma - GNOS-PV02 + IL-12 + PD-1 Combination</td>
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<td><strong>Geneos Sponsored Study</strong></td>
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**NOTE:** This is a summary of the clinical pipeline for Geneos Therapeutics. Details of each study, such as patient numbers, specific treatment regimens, and timelines, may vary. For more information, please refer to the original documents or contact the appropriate medical or research institutions for details.
Hepatocellular Carcinoma

6th cancer WW
Rising incidence (1-2%/yr):
• US: ~ 29,000
• EU5: ~ 34,000
• WW: ~ 800,000

4th most cancer related deaths

5-year survival: 18.4%
• 2nd behind pancreatic cancer

Checkpoint inhibitors are effective, but very limited response rates

Responders

CPI ORR: 15-17%
in 2nd line HCC

No response
Potential benefit from CD8 inducing therapy

GT-30 Trial: GNOS-PV02 + pIL12 + PD1 in 2ND L Advanced HCC

- **GT-30 Trial** - Advanced HCC patients who progress during or are intolerant to 1st L treatment with sorafenib or lenvatinib
- Patients enrolled and biopsy sample taken before or while patients are receiving 1st L TKI treatment
- Goal is to demonstrate safety, immune responses, and enhanced efficacy (ORR, PFS, OS) compared to single agent anti-PD1 therapy. Target doubling of ORR from approximately 15% for anti-PD1 alone (historical standard of care comparator)
- N = 12 Patients initial cohort
**SCIENTIFIC, CLINICAL & BUSINESS ADVISORS**

**SCIENTIFIC THERAPEUTICS TEAM**

NIRANJAN Y. SARDESAI, PH.D  
CEO & PRESIDENT, CO-FOUNDER  
- 25+y academia/biotech product development experience; Inovio, Fujirebio Diagnostics, Meso-scale Discovery/IGEN, TSRI, MIT, Caltech  
- Led development of optimized DNA-EP platform at Inovio forming the basis of GT-EPIC™; 120+ publications & multiple patents

ALFREDO PERALES-PUCHALT, MD, PH.D  
VICE PRESIDENT, RESEARCH & DEVELOPMENT  
- 10+y of academia/biotech pre-clinical & clinical research experience  
- The Wistar Institute; Tumor immunology, Immunotx. and Gene Tx. expert

FEDERICA F. O’BRIEN, CPA, CGMA  
STRATEGIC FINANCIAL CONSULTANT  
- 30+y of private and public company senior level technical accounting, financial strategy, and audit experience; Complexa, Cerecor, Cardiokine, Barrier Therapeutics, PricewaterhouseCoopers  
- Serves as audit committee chair on the board of TELA Bio.

**SCIENTIFIC, CLINICAL & BUSINESS ADVISORS**

DR. DAVID WEINER  
- W.W. Smith Endowed Chair in Cancer Research, The Wistar Institute

DR. CASEY CUNNINGHAM  
- Chief Scientific Officer, Santé Ventures

DR. CHI VAN DANG  
- Scientific Director, Ludwig Institute for Cancer Research; Professor, The Wistar Institute; Previously Director of the Abramson Cancer Center at Penn

MS. SHAWN TOMASELLO  
- BOD of Urogen, Centrexion, Oxford Biotherapeutics  
- Most recently Chief Commercialization Officer Kite Pharmaceuticals through its acquisition by Gilead; Previously CCO Pharmacyclics, Celgene

JOANN PETERS  
VICE PRESIDENT, CLINICAL & BUSINESS OPERATIONS  
- 20+y of oncology clinical development experience providing executive oversight and study strategy  
- Previously led clinical operations Linical-Accelovance, INC, PRA

BETH JUNKER PH.D  
CMC ADVISOR  
- 30+y of experience in bioprocessing of antibodies, therapeutic proteins, recombinant DNA and viral vaccines, gene therapy  
- Previously at MRK; Developed QbD and Knowledge Management frameworks for clinical, commercialization and licensure activities

SARAH ROCHESTIE – Clinical Trials Manager  
NEIL COOCH – Scientist R&D  
ELIZABETH SKALE – Associate Manager, Operations  
ILDIKO CSIKI, MD, PH.D – Clinical Advisor  
MORRISON & FOERSTER – Corporate Legal

**FEDERICA F. O’BRIEN, CPA, CGMA**  
STRATEGIC FINANCIAL CONSULTANT  
- 30+y of private and public company senior level technical accounting, financial strategy, and audit experience; Complexa, Cerecor, Cardiokine, Barrier Therapeutics, PricewaterhouseCoopers  
- Serves as audit committee chair on the board of TELA Bio.
DR. SAMUEL BRODER
DIRECTOR
- Former Head of the National Cancer Institute (NCI)
- Former Chief Medical Officer of Celera Corp., where he helped advance the human genome project
- Elected to the National Academy of Medicine of the National Academy of Sciences

DR. CASEY CUNNINGHAM
DIRECTOR
- Chief Scientific Officer, Santé Ventures
- Former Associate Director of the Mary Crowley Cancer Research Institute in Dallas, TX; The MCMRI performs early phase clinical trials in oncology and Dr. Cunningham had a particular focus on gene and immune approaches

DR. JAMES EADIE
DIRECTOR
- Partner, Santé Ventures
- Former Medical Director/Vice-Chair of Emergency Medicine at Wilford Hall Medical Ctr, level-one trauma center in San Antonio
- Air Force veteran having served two tours in Iraq as critical care transport team chief and as the emergency dept. commander

DR. J. JOSEPH KIM
DIRECTOR
- Co-founder VGX Tx; President & CEO, Inovio Pharmaceuticals
- Extensive pharmaceuticals/biotechnology management experience
- Raised over $500 M in private/public equity

DR. NIRANJAN Y. SARDESAI
DIRECTOR; PRESIDENT & CEO
- Co-founder Geneos Therapeutics
- Former COO and Head of R&D, Inovio Pharmaceuticals
- At Inovio, led corporate growth strategy; Oversaw growth of Inovio from 10-270+ employees and 0 - 20+ clinical programs; Lead program now in Phase III; As Head of R&D, led development of optimized DNA-EP platform which now forms a key component of GT-EPIC™; 120+ publications & multiple patents
- Raised over $200 M in dilutive and non-dilutive capital and drove pharma partnering deals > $1 Bn
GT-EPIC™ Platform established to develop Exquisitely Personalized Immunotherapies for Cancer

Platform backed by:
- 2,000+ patients’ safety data from licensing partner Inovio Pharmaceuticals and 6,000+ doses delivered – no signs of dose limitations
- Broad portfolio of patents (filed/issued)

Underlying DNA platform has demonstrated safety and efficacy in human clinical trials. The platform generates antigen specific CD8+ T-cell responses and TILs – Drivers of efficacy

Geneos – potential advantages to other neoantigen and personalized medicine approaches:
- Ability to drive CD8+ T cell responses
- Capacity to target 40+ tumor specific mutations per plasmid; Larger antigenic payloads achieved by combining multiple plasmids
- Reduced complexity of immunotherapy manufacturing; Favorable cost of goods
- Faster Biopsy-to-Treatment TAT relative to other neoantigen platforms (Peptides, RNA, Bacterial/Viral vectors)
  (6-8 wks vs 12-16 wks)

Streamlined product development pathway
- Geneos is in the clinic with its solid tumor programs directed at demonstrating clinical proof-of-concept

Experienced management with directly relevant clinical expertise in development of cancer immunotherapies
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