NanoVector

Plant Derived

Targeted Therapeutics for Late Stage Metastatic Cancer

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Plant Virus Nanoparticle for Drug Delivery

• NanoVector is the Federal Express of the Pharmaceutical Industry,

• Provide targeting for highly potent drugs already approved by FDA:

  [Image of FedEx truck with nanoparticles targeting tumors]
Capital Efficiency: cGMP Compliant Plant Partner

- De-risk Leverage $21M GMP Greenhouse Facility
- De-risk Only small greenhouse required for transfection

![Diagram of the cGMP Compliant Facility Vendor, Isolated RCNMV Biosynthesis Greenhouse Facility, and Inoculated Plants Harvested, Transferred to Processing Facility]
Biologic Simplifies Manufacturing

- **De-risk** Cancer drug loaded via diffusion
- **De-risk** Single step aqueous process for DOX loading and peptide attachment
Metastatic Cancer
Current Therapies Do Not Work

Problems:
Multidrug resistance (MDR)
Maximum tolerated dose (MTD) limitation
Cancer at advanced stage when diagnosed
Solution: Targeted Nanoparticle Drug Delivery

- Biologic Nanoparticle (Plant Virus)
- Doxorubicin cancer therapeutic (DOX)
- Targeting:
  - N-cadherin receptor: highly expressed on most late stage solid tumors and circulating tumor cells (CTCs)
- Potential: Single formulation to treat multiple late stage cancers – Same Cell Surface biomarker
N-Cadherin Targeting

- N-cadherin expression: universal in metastatic cancers
- On healthy cells space between N-cadherin-mediated cell junctions is too small for nanoparticle access
- N-cadherin is also highly expressed on circulating tumor cells (CTCs)
Formulation Overcomes MDR and MTD

MDR: DOX Chemotherapy agent isolated from MDR secretory pathways ➔ higher intracellular drug concentration

MTD 1: DOX Chemotherapy agent isolated from blood cells & other organs

MTD 2: N-cadherin targeting enables 10x MTD dose + longer dosing schedule

MTD 3: Nuclear targeting delivers anti-cancer drug to site of action ➔ Greater safety and efficacy
NanoVector Lead Drug: NVI-9010

- **Demonstrated Efficacy in Animals:**
  - Malignant melanoma (2011 and May 2014)
  - Ovarian cancer (July 2014)

- Applicable to cancer drugs for dogs
A375 flank tumor Xenografts in CB17 SCID Mice treated IV x1 q week. After 3 doses of agent.
In-vivo Safety/PK Testing of Plant Virus

Toxicity:
- Massive I.V. dose (more than 4 PVNs per mouse cell) showed no adverse effects.

Immunogenicity:
- No existing antibodies in human Sera and Plasma
- No antibodies after 1 week at maximum i.v. dosage in mice.
- No antibodies after Booster shot and plasma samples daily for 3 weeks

Biodistribution:
- Rapid distribution and excretion via urine
- No accumulation in organs

Conclusions:
- Nanocarrier is well tolerated
- High tolerability enables the use of more efficacious cargos
IP Barriers to Entry

Licensed technology from NCSU funded by ~$7M of Grants

1. Viral Nanoparticle Cell-Targeted Delivery Platform

2. Composition of matter provisional patent in preparation
FDA De-Risk

- Anticipate FDA’s Breakthrough Therapy Designation

- Therapeutic: Already approved by FDA
Company

- Organized August 2007
- 7 employees
- Funded by $1.8M in grants and loans
- Research Augmented
  - NCSU Sponsored Research
  - NCSU Facilities use agreement
- Seeking joint development opportunities:
  - Extend IP of existing drugs
  - To increase efficacy and specificity of new drugs
  - Joint development of new therapeutics
Partnering

- Seek joint development opportunities:
  - Extend IP of existing drugs
  - NanoVector technology to increase efficacy and specificity of new drugs
  - Joint development – Animal health applications
Management Team

Chief Executive Officer - Albert D. Bender, Ph.D.
A successful serial entrepreneur who has provided the strategic vision and leadership for 4 high technology companies.

Chief Scientific Officer - Bruce J. Oberhardt, Ph.D.
Has led and/or participated in a number of first-of-a-kind technological developments including “CoaguChek” and founded Cardiovascular Diagnostics: a successful IPO.

Board of Directors - William P. Peters, MD, PhD, MBA
CEO of Adherex, a clinical stage oncology drug company, from 2003, to 2009. Formerly Dr. Peters served on the faculty at Harvard, Duke, and Wayne State University and was Associate Director, Duke Cancer Center and Director and CEO of the Karmanos Cancer Institute in Detroit
Product Development Team

NVI - 9010 PCT
Program Manager
Bruce Oberhardt, PhD

Analytical Pharmacology/PK
Bill Zamboni, PhD

Clinical Research
Ann Gooch, PhD

GMP Production/Facility
Mark Witcher, PhD

Pharmacology/CMC
Randall Lane

Toxicology
Richard Stewart, PhD

Medical Advisor
TBD

Regulatory Affairs
Ann Gooch, PhD

Business Operations/Legal
Albert Bender, PhD

Oncology Advisor
William Peters, MD, PhD, MBA

CRO - Cato Research
CMO - TBD
# Opportunity for >$1B/yr Drug

<table>
<thead>
<tr>
<th>Cancer</th>
<th>New cases</th>
<th>Deaths</th>
<th>Metastatic at Diagnosis</th>
<th>Drug Cost</th>
</tr>
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<tbody>
<tr>
<td>Ovarian</td>
<td>22,240</td>
<td>14,030</td>
<td>85%</td>
<td>$787M/yr.</td>
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<tr>
<td>Malignant Melanoma</td>
<td>76,250</td>
<td>9,180</td>
<td>100%</td>
<td>$569M/yr.</td>
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</tbody>
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Next Steps

- Applied for $3M NCI Phase IIB grant requires match
- Use of Funds
  - Complete IND-enabling studies
  - IND submission
  - Phase 1 clinical trial metastatic cancer patients