



GENVEC



*Developing a pipeline of innovative therapeutics and vaccines  
that deliver on the promise of gene-based medicine*

# Corporate Overview

January 2017

Statements herein relating to future financial or business performance, conditions or strategies and other financial and business matters, including expectations regarding future revenues and operating expenses, are forward-looking statements within the meaning of the Private Securities Litigation Reform Act. GenVec cautions that these forward-looking statements are subject to numerous assumptions, risks and uncertainties, which change over time. Factors that may cause actual results to differ materially from the results discussed in the forward-looking statements or historical experience include risks and uncertainties, including the failure by GenVec to secure and maintain relationships with collaborators; risks relating to clinical trials; risks relating to the commercialization, if any, of GenVec's proposed product candidates (such as marketing, regulatory, patent, product liability, supply, competition and other risks); dependence on the efforts of third parties; dependence on intellectual property; and risks that we may lack the financial resources and access to capital to fund our operations. Further information on the factors and risks that could affect GenVec's business, financial conditions and results of operations are contained in GenVec's filings with the U.S. Securities and Exchange Commission (SEC), which are available at [www.sec.gov](http://www.sec.gov). The forward-looking statements speak only as of the date of this presentation, and GenVec assumes no duty to update forward-looking statements.

- Biotechnology company leveraging its proprietary AdenoVerse™ platform to develop cutting-edge gene-based medicines
- Developing a novel treatment for hemophilia A using PEC (pulmonary endothelial cell) delivery technology
- Exploring opportunities in regenerative medicine, oncology, hematology, infectious diseases, and other cell and gene therapies
- Validating partnerships demonstrating the power and value of GenVec technology including:
  - Novartis: regenerative medicine gene therapy for hearing loss
  - TheraBiologics: neural stem cell therapy for oncology indications

Program Area and Indication	Partner / Collaborator	Technology Highlights	Development Status			
			Discovery	Preclinical	Clinical	Notes
GENE AND CELL THERAPIES						
Hearing Loss and Balance Disorders	 NOVARTIS	Regenerative medicine gene therapy				First gene therapy for hearing; Phase1/2 clinical trial ongoing
Oncology	 THERABIOLOGICS	Ex vivo engineered neural stem cells				2 <sup>nd</sup> generation product to enter the Phase 1 trial in 1H2017
Hemophilia A	 Washington University in St. Louis	PEC delivery + gene editing				Proof of principle studies ongoing
INFECTIOUS DISEASE VACCINES						
RSV	Available for partnering	Prophylactic vaccine				Proof of principle established in multiple animal models
HSV-2	Available for partnering	Prophylactic and therapeutic vaccine				Proof of principle established in multiple animal models
Malaria	NMRC / NIH-LMIV	Discovery of new Malaria vaccines				Proof of principle ongoing in multiple animal models
FMD	 MERIAL	DIVA compatible vaccine				First U.S. conditionally approved FMD molecular vaccine

- Genetic disorder causing deficient production of blood clotting factor VIII (FVIII)
  - Approximately 18,000 Americans are living with hemophilia A (approximately 1 in 5,000 births)
  - About 60% of patients have severe disease (producing less than 1% of normal FVIII levels)
- Current therapy relies on prophylactic treatment with blood factors and emergency treatment for bleeding events
- Peak annual costs for treatment per patient per year of approximately \$364,000, with average costs exceeding \$160,000
- High need for curative approaches that can allow patients to live normally at lower lifetime costs

### Stages in the development of products for bleeding disorders

#### Plasma-derived clotting factors

Developed in the late 1960s into the 1970s;  
Significant safety concerns due to prevalence of contamination from viral pathogens

#### Recombinant clotting factors

Developed in the late 1980s into the 1990s;  
Eliminated the safety concerns of plasma-derived products

#### Extended half-life clotting factors

Recent and ongoing development;  
Decreased treatment frequency

*The promise for the future: **gene therapy** and other new agents*

#### Novel therapies and modalities

Notable companies with approved products or products in development in the categories shown above


- Monogenic disease, with a clear correlation between circulating blood clotting factor levels and severity of disease
- Even small increases in blood clotting factor levels from baseline can result in significant clinical improvements
- Gene therapy can potentially provide sustained levels of circulating blood clotting factors to restore normal function
- Potential to eliminate patient dependence on a lifetime of blood clotting factor injections
- While promising, choice of vector and target organ has presented challenges, particularly for hemophilia A

# Portfolio of Technologies

Combination Provides Correction of Genetic Disorders

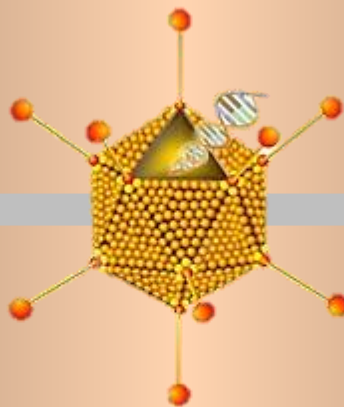
## Key technologies

PEC delivery

Gene editing

AdenoVerse™  
vectors

Proprietary product design  
incorporating all the key  
technologies



## Advantages

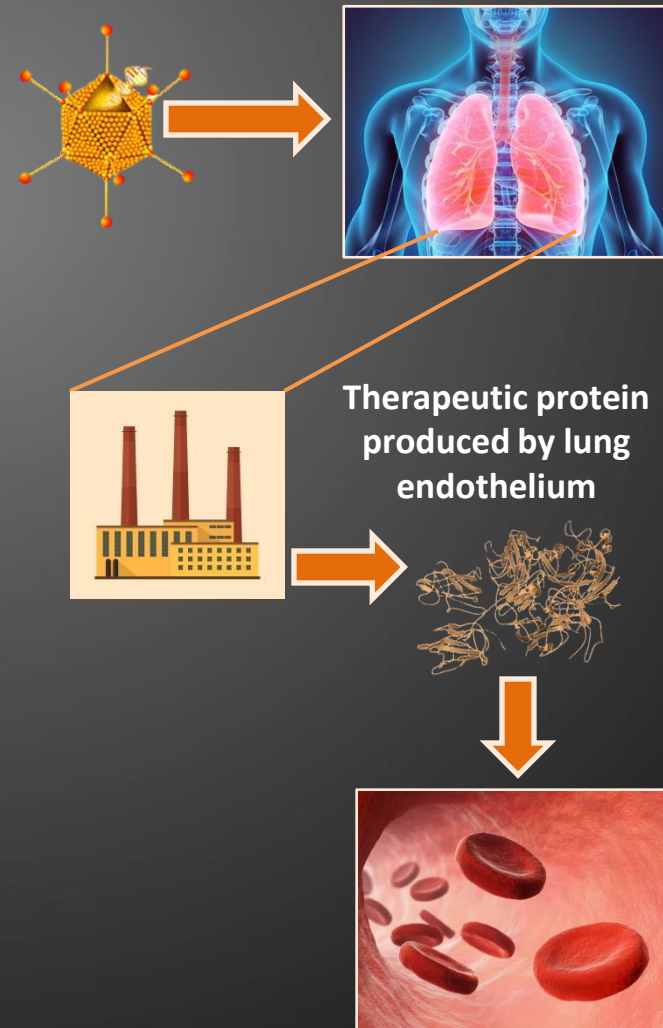
Harnessing lung  
for protein  
expression

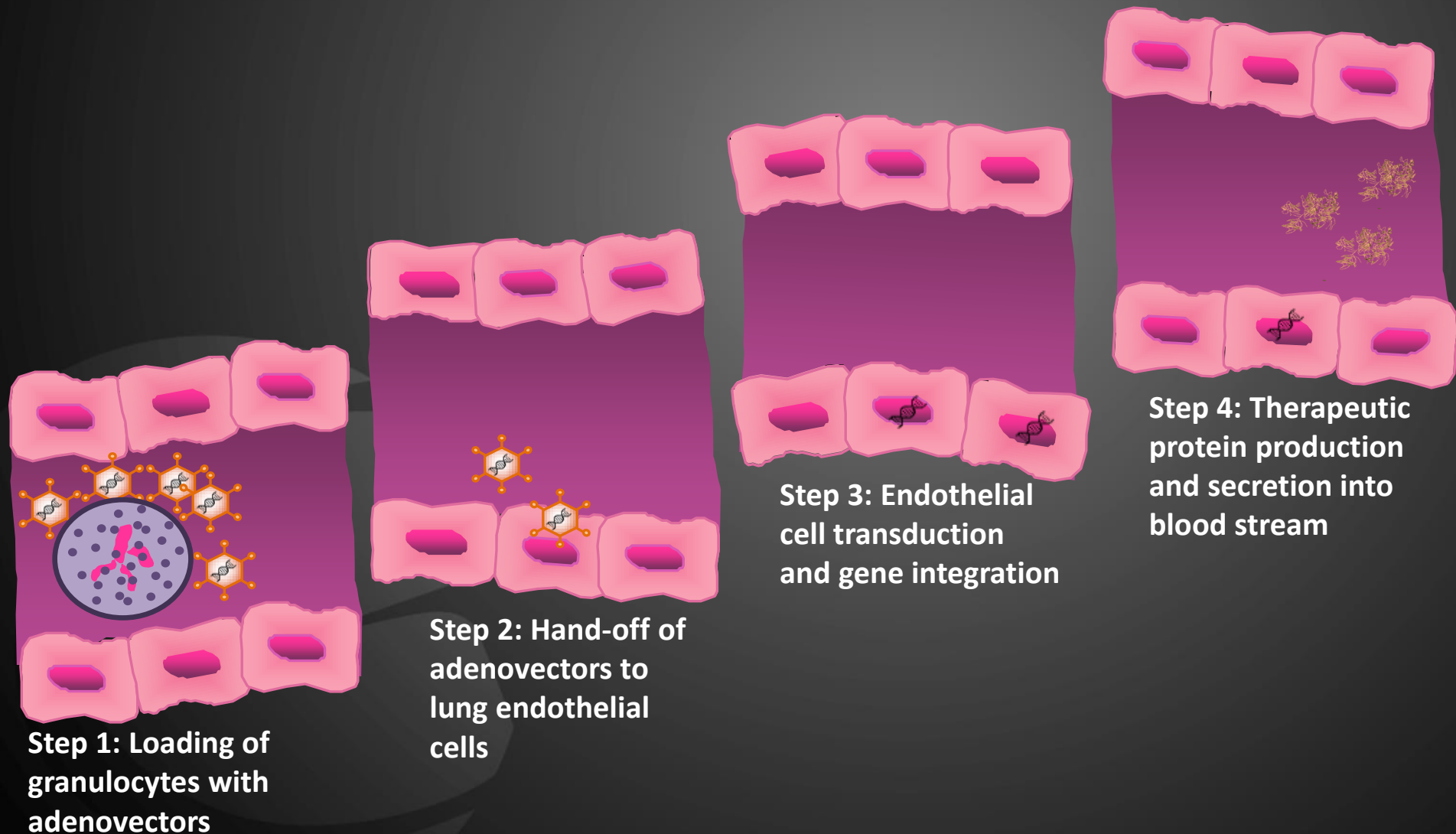
Therapeutic gene  
durable  
expression

Systemic  
administration

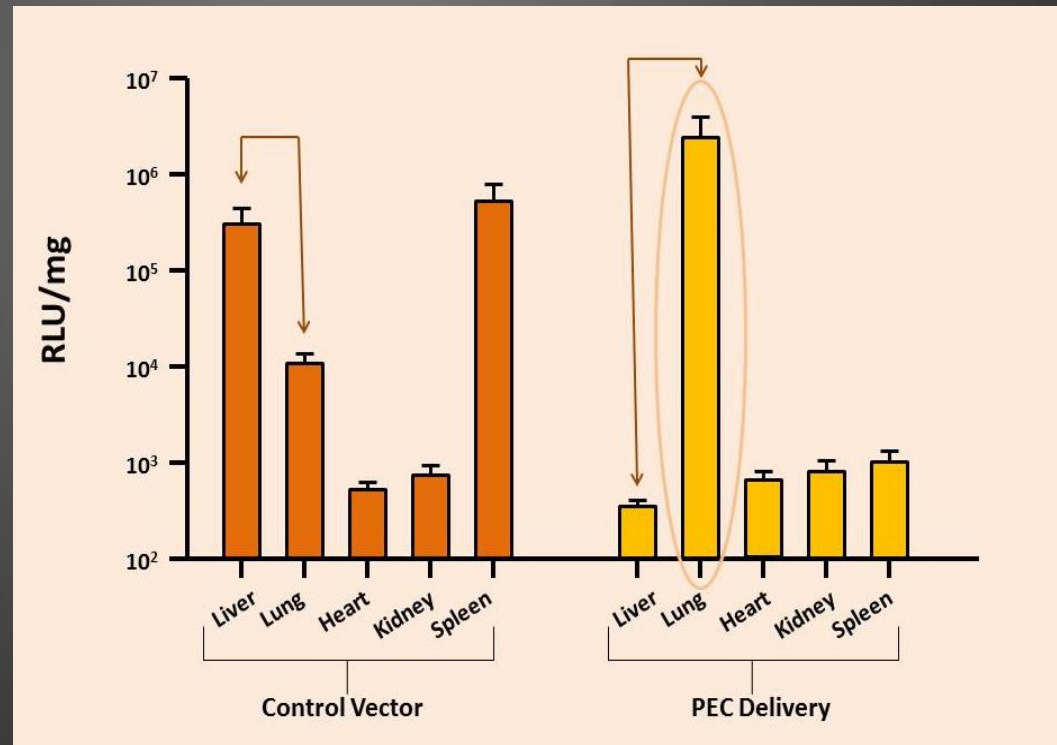


- ☉ Allows for specific gene therapeutic delivery into the lung endothelium via AdenoVerse™ vectors
- ☉ Lung endothelium is turned into a surrogate long-term production factory for therapeutic proteins
- ☉ Can be used to address multiple unmet medical needs (hemophilia, passive immunotherapies, etc.)
- ☉ PEC delivery combined with AdenoVerse™ vectors can:
  - Limit liver toxicities observed with systemic administration of more traditional gene therapeutics
  - Provide long-term production of native proteins

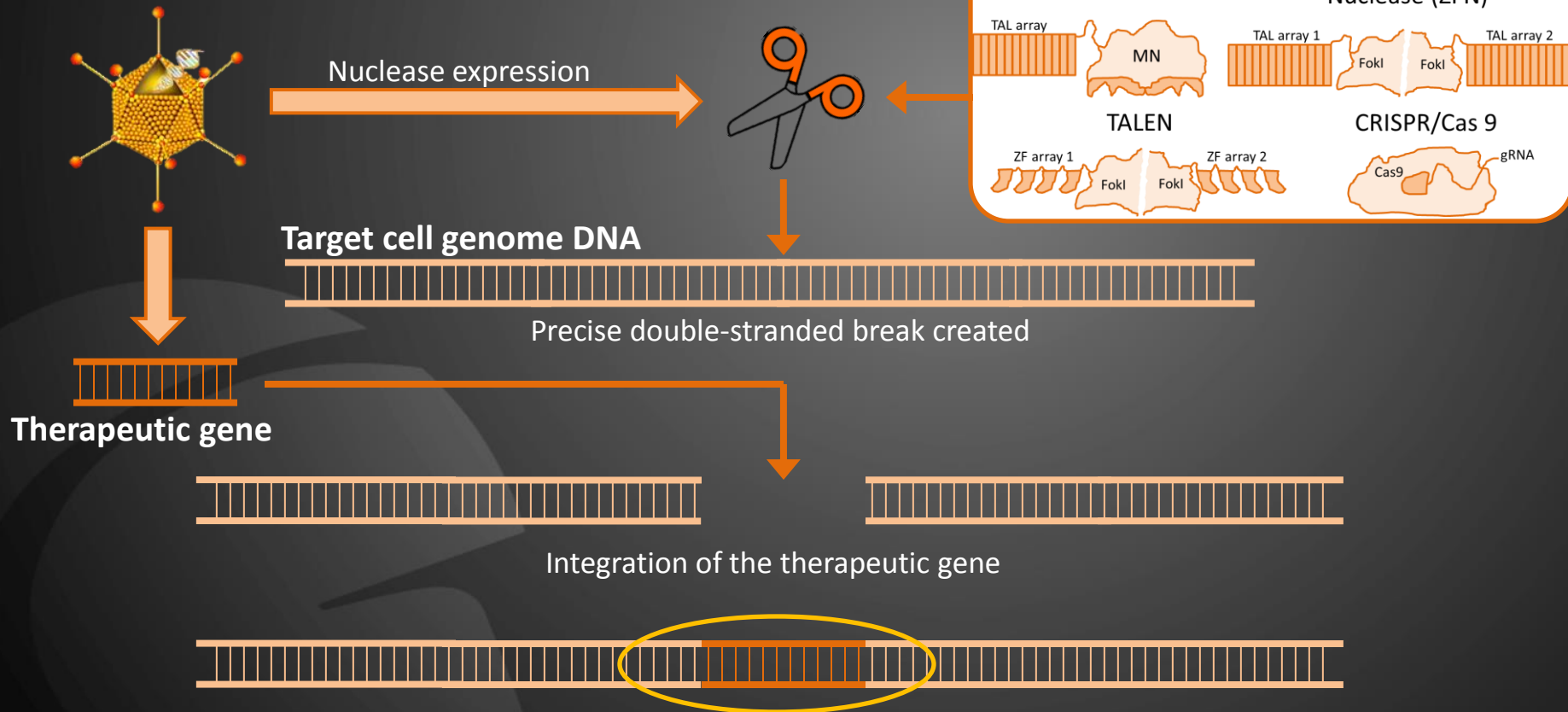




- Upon systemic administration in mice, a preferred distribution to the lung was observed
- Technology developed by David Curiel at Washington University in St. Louis
- GenVec has an exclusive option to PEC technology



**Delivery of the complete gene editing payload to targeted cells**

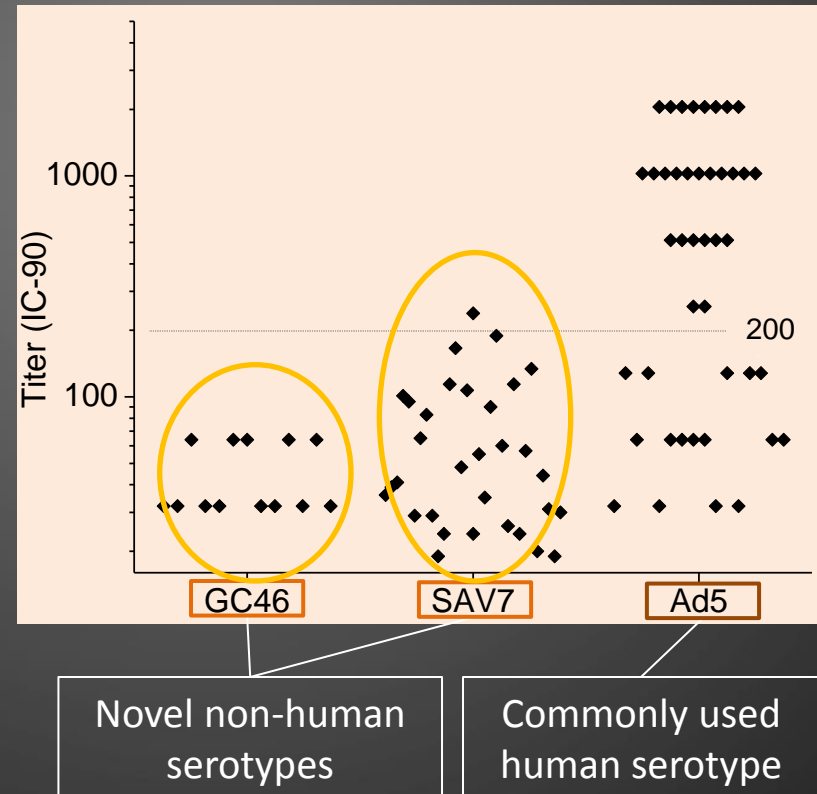


**Durable expression via permanent addition of the therapeutic gene sequence**

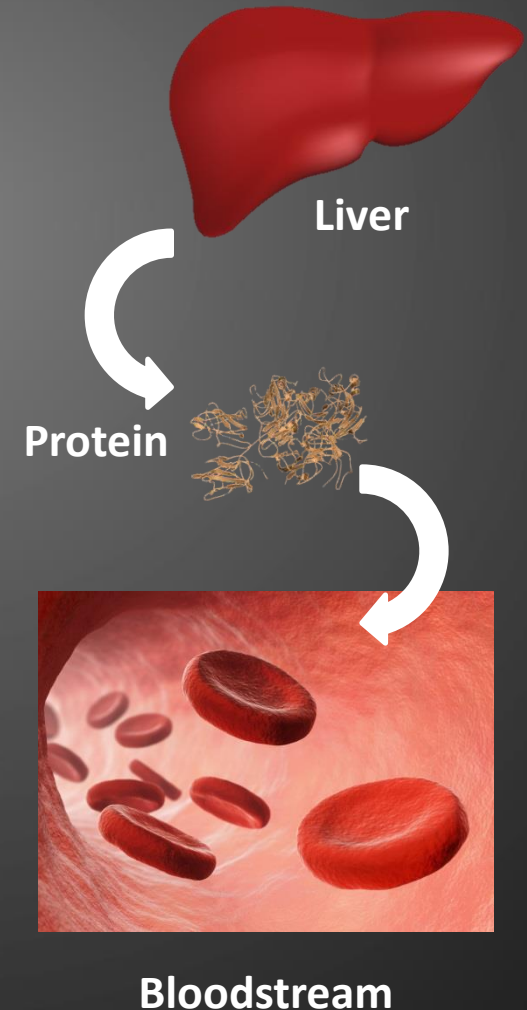
## GenVec's AdenoVerse platform provides a unique set of solutions for the key Gene Editing field requirements

Gene Editing Requirements	AdenoVerse Platform Solutions
"Hit and run" (limited off-target effects)	Non-integrating vector: <ul style="list-style-type: none"> <li>• Transient nuclease expression minimizing potential off-target cuts</li> <li>• Reduced chromosomal positional effects and risk of insertional mutagenesis</li> </ul>
Large Capacity	Delivery of large payload (up to 12Kb): <ul style="list-style-type: none"> <li>• All the components in a single vector</li> <li>• Multiple expression cassettes</li> </ul>
Low Immunogenicity	<ul style="list-style-type: none"> <li>• AdenoVerse vectors can be designed to have low immunogenicity properties</li> </ul>

- Systemic administration has been a long-standing challenge for gene therapeutics
- GenVec's AdenoVerse platform addresses this hurdle
  - No-to-low sensitivity to pre-existing neutralizing antibodies
  - Reduction of liver sequestration, minimizing hepatotoxicities



- ☉ Blood consists of cellular components (platelets, red and white blood cells) and plasma
- ☉ Plasma is a liquid, which contains numerous proteins
- ☉ Many important proteins are synthesized by the liver
- ☉ Hepatic proteins are involved in many functions:
  - Coagulation (blood factor, fibrinogen, complement, etc.)
  - Metabolism (apolipoproteins )
  - Carrier (albumin, transferrin, etc.)
  - Hormonal (hepcidin, thrombopoietin, etc.)





### Bleeding disorders

- Hemophilia A (FVIII)
- Hemophilia B (FIX)

### Metabolic disorders

- Type 1 diabetes

### Respiratory diseases

- Alpha 1-antitrypsin deficiency
- Chronic obstructive pulmonary disease

### Anemia

- Erythropoietin deficiency

### Passive Immunizations

- Anti-pathogen or anti-toxin agents



- Select preferred AdenoVerse™ platform vectors for systemic administration
- Construct program vectors incorporating PEC delivery technology
- Show proof of principle pulmonary endothelial cell delivery in *in vitro* and *in vivo* models
- Identify leads for pre-clinical development

## A library of adenoviral vectors with diverse and unique biological properties



Vectors for eliciting long-lasting adaptive immune responses

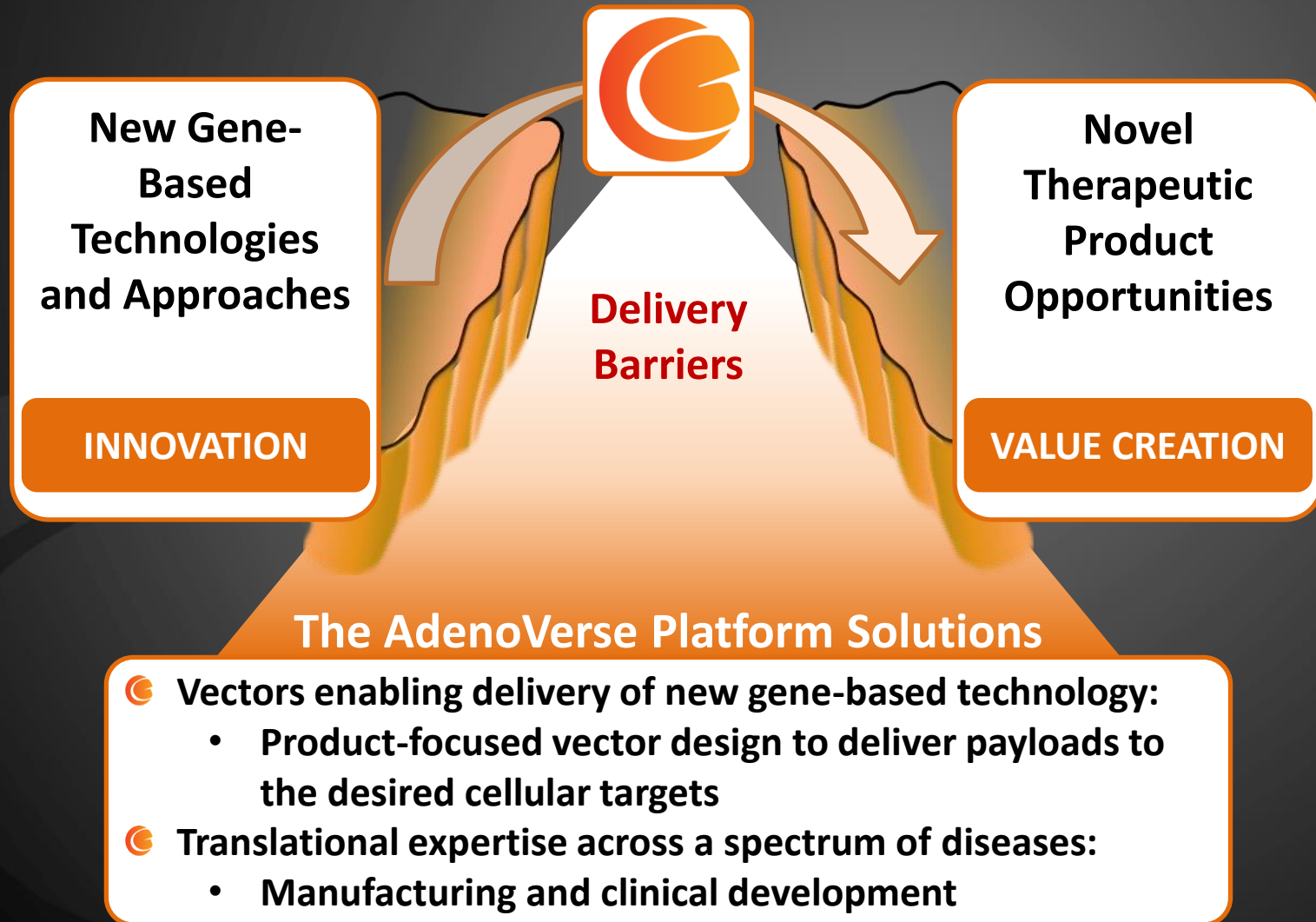


Vectors for immunologically stealth gene delivery

Multiple vectors each suited to a broad range of applications

A large set of therapeutic areas covered by the platform

Proprietary cell lines for efficient manufacturing



### Adenovector Advantages

- Efficient transduction in dividing cells and non-dividing cells
- Non-integrating transgene limits the probability of disturbance of vital cellular genes

### AdenoVerse Strengths

- Vectors with no or very low seroprevalence in the human population
- Large packaging capability (up to 12 kb) with multiple expression cassettes
- Improved safety with multiple deletions in vector genomes
- Administered to over 3,000 clinical study subjects
- Scalable platform with efficient manufacturing process and attractive cost of goods
- Strong and expanding IP position



### Standard Adenovector Known Limitations

Pre-existing  
immunity



Innate immunity  
associated toxicity



Vector liver  
sequestration



### GenVec's AdenoVerse Adenovector Superiority

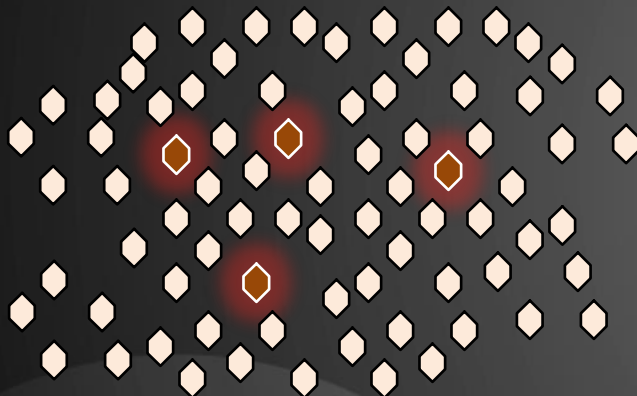
Proprietary adenovector backbones from **rare human and non-human primate serotypes** with low to no seroprevalence in the human population

Adenovector **deleted for E1, E3, and E4 regions**, limiting the expression of viral proteins mainly responsible for innate immune responses

Some of these adenovectors appear not to be sequestered in the liver and could be suitable for **systemic delivery**

**The AdenoVerse platform is the next generation of adenovector technology and has unprecedented potential for new medical treatments**

### AdenoVerse Vectors



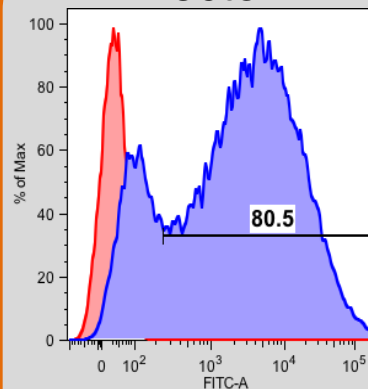
### GenVec's Screening Methodology



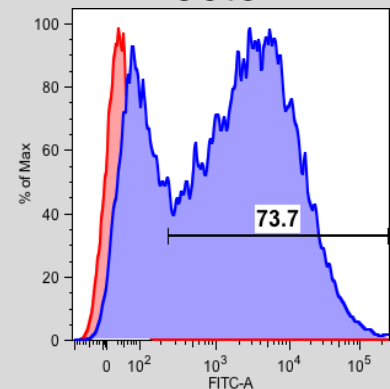
Vectors with preferred performance characteristics for any given application and unique need

*Data from screenings to identify vectors that efficiently transduce cells of interest*

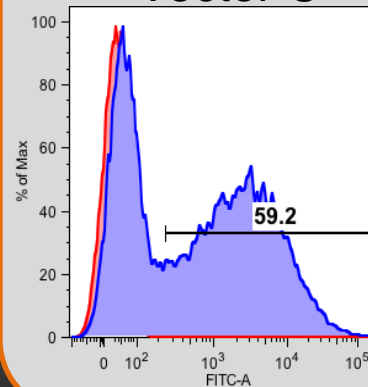
#### Vector A



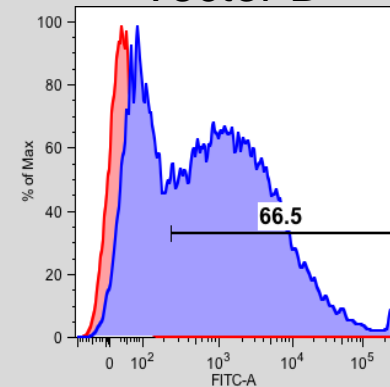
#### Vector B



#### Vector C



#### Vector D



Data shown from human primary T cell screening

## A library of adenoviral vectors with diverse and unique biological properties



**Vectors for eliciting long-lasting adaptive immune responses**



**Vectors for immunologically stealth gene delivery**

**Immuno-therapies**

**Vaccines**  
Prophylactic & Therapeutic

**Oncolytics**

**Gene Editing**

**Cell Therapies**

**Nucleic Acid Therapeutics**



Infectious Disease

Oncology

Otology

Ophthalmology

Cardiology

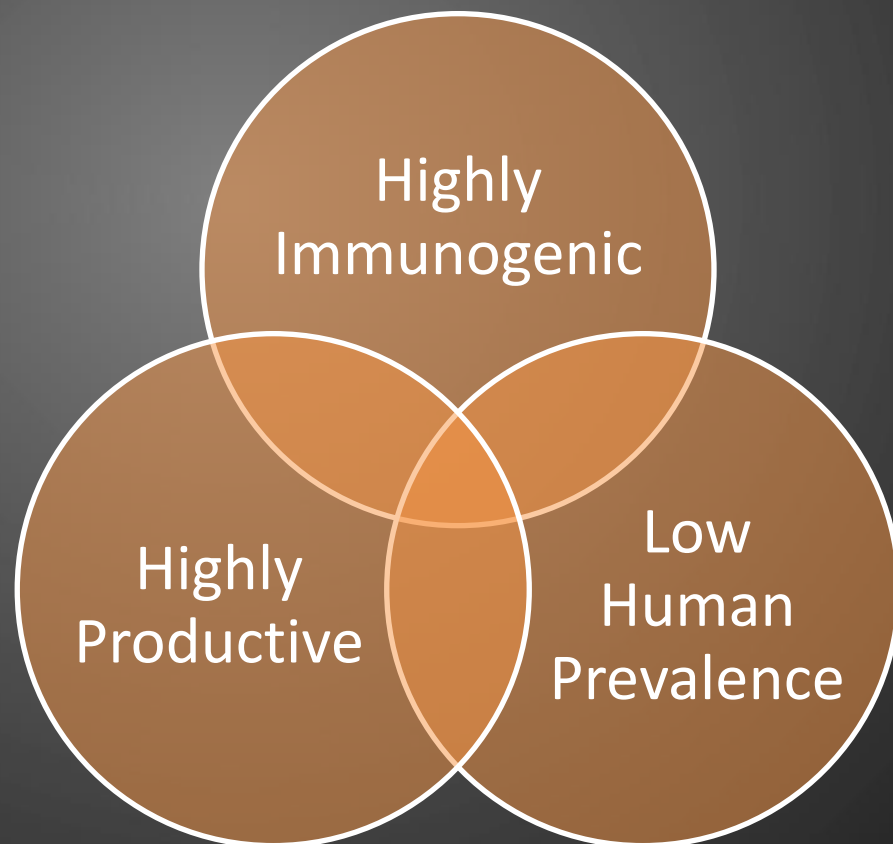
Neurology

Rheumatology

Rare Diseases

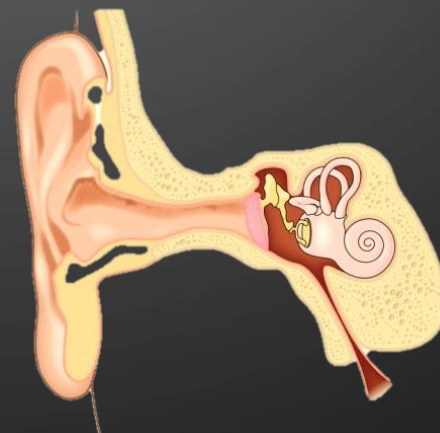


- Validated technology for vaccine applications
- Industry leading vaccine platform for generating T cell responses
- Proprietary novel adenoviral vectors with outstanding properties
- Vectors with distinct advantages for molecular vaccines
  - High-level, durable antibody responses
  - High-level T cell responses
  - Repeat administration boosts responses



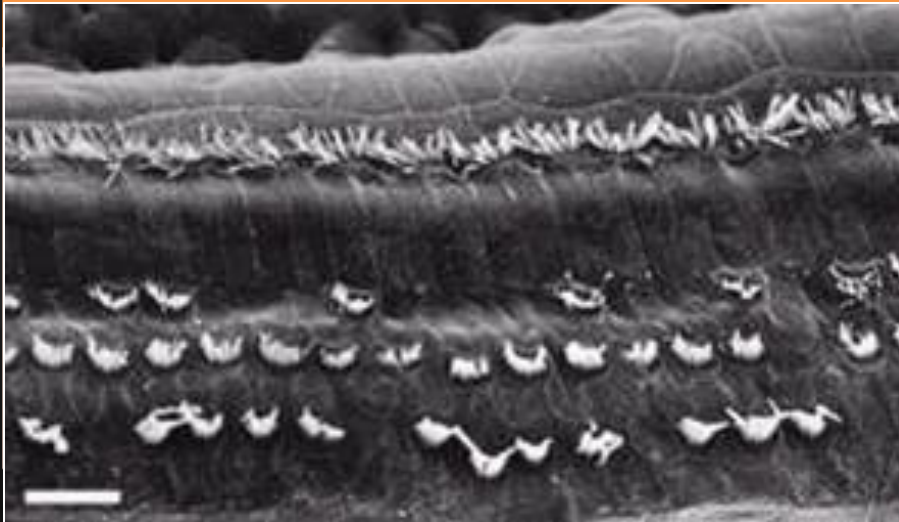


- CGF166 is currently in a Phase 1/2 clinical trial in patients with severe to profound hearing loss
- Currently recruiting patients for the fourth cohort in ongoing Phase 1/2 clinical study
- Safety and efficacy analysis from first three cohorts supports further dose escalation
- Agreement provides GenVec with up to \$206.6 million in milestone payments, in addition to royalties on sales



- Hearing loss is a multi-billion dollar market opportunity
- Disabling condition with high and increasing prevalence worldwide
- An estimated 1 in 6 adult Americans suffer from hearing loss
- 90% of hearing loss is sensorineural
- No current pharmaceutical treatment options

## Sensory Cells



## Causes of Sensory Cell Loss

- Age Related
- Infection
- Drug Induced
- Sound Trauma

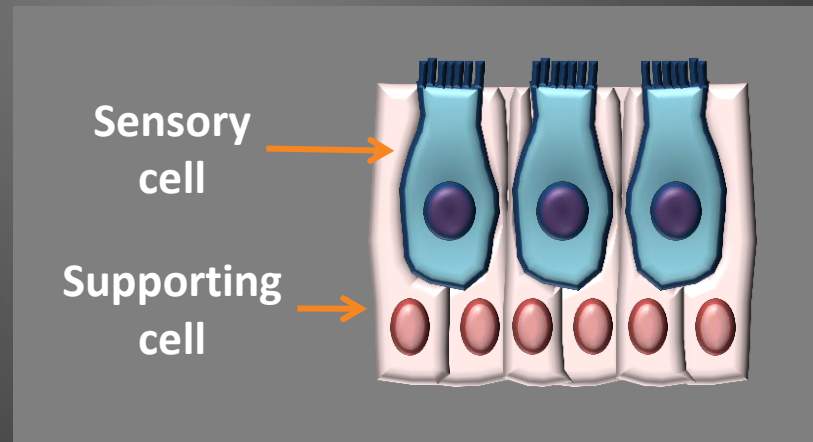
Deliver the Atonal gene to the supporting cells using an adenovector



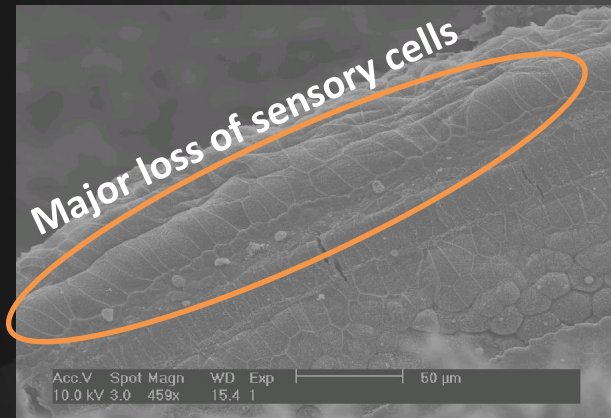
Produce Atonal protein in supporting cells



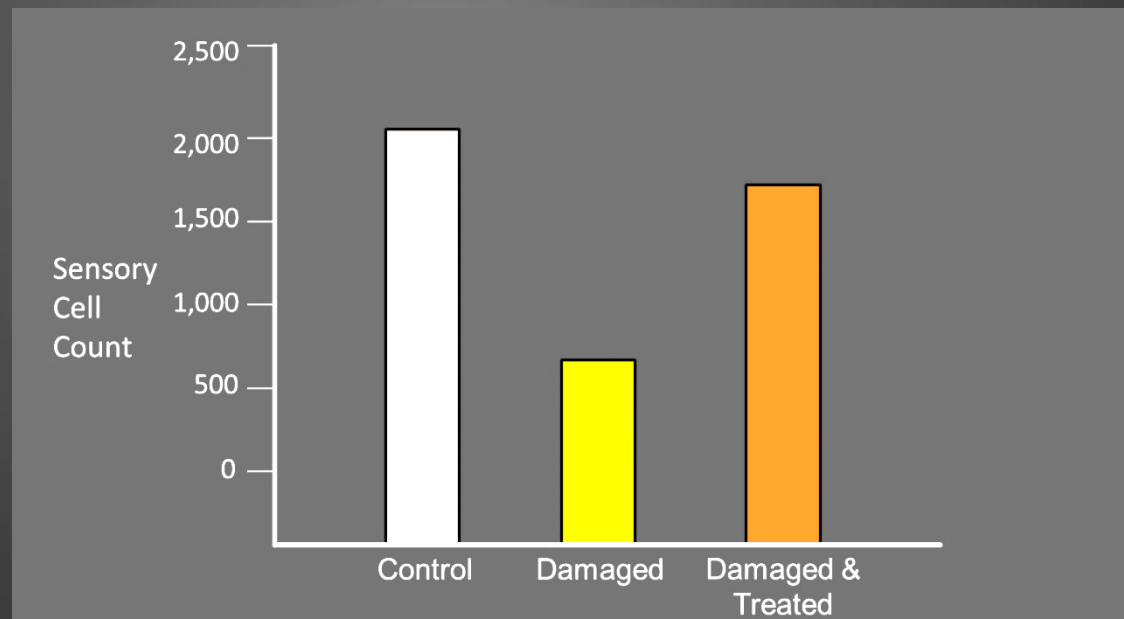
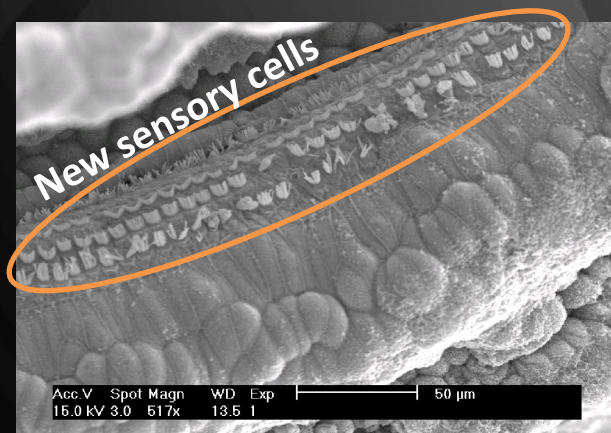
Trigger conversion of supporting cells into sensory cells



## Damaged and Untreated

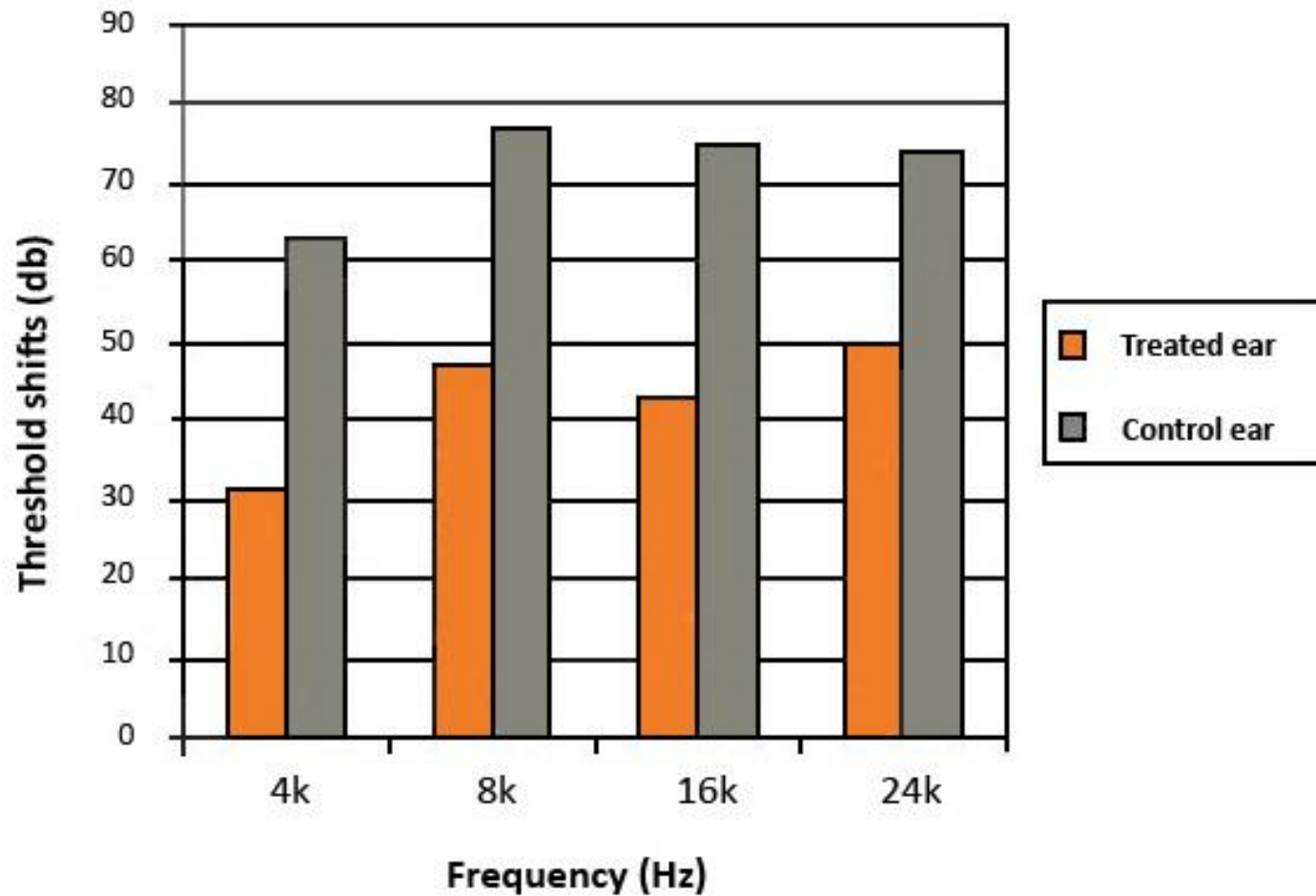


## Damaged and Treated



*Schlecker et al. Gene Therapy, 2011, 18: 884-890*

*Izumikawa et al., Nature Medicine, 2005, 11(3): 271-276*



Izumikawa *et al.* study, *Nature Medicine*, 2005, 11(3): 271-276

- Multicenter trial of 26 to 45 patients with severe to profound hearing loss

## Part A: Safety

- Single, 3-patient cohort
- Dose: 20  $\mu$ l

## Part B: Dose Volume Escalation

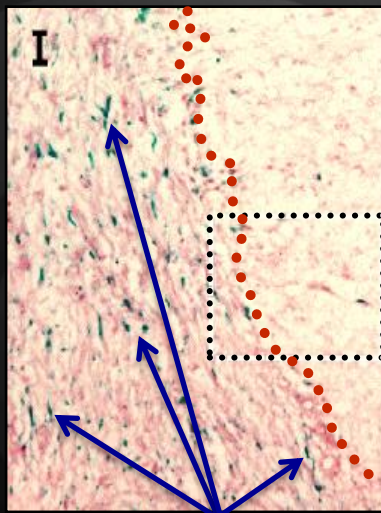
- 2-5 cohorts of 3 patients each
- Dose volume between 30  $\mu$ l and 90  $\mu$ l

## Part C: Efficacy

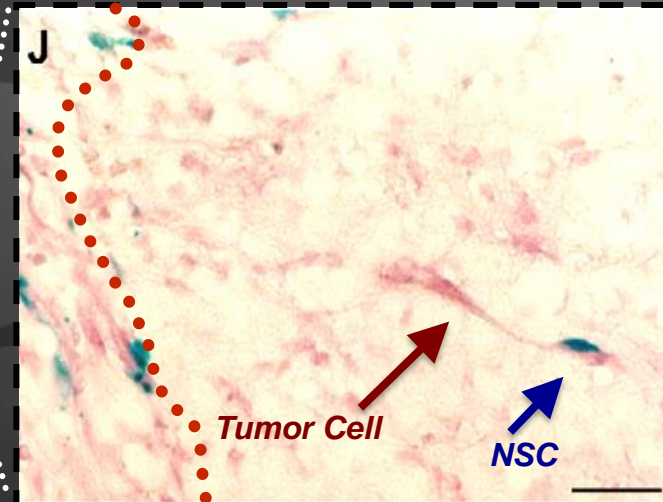
- Single cohort of 20 patients at dose determined by Part B
- Option to resize



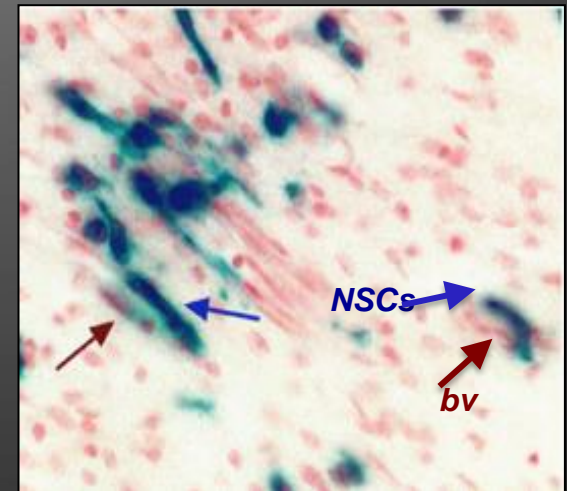
- Second generation adenovector-engineered neural stem cell (NSC) product for the treatment of primary and metastatic tumors
- NSCs selectively target tumor cells and vasculature
- TheraBiologics emerged out of the pioneering neural stem cell research and development of Dr. Karen Aboody at City of Hope



NSCs penetrate main tumor mass



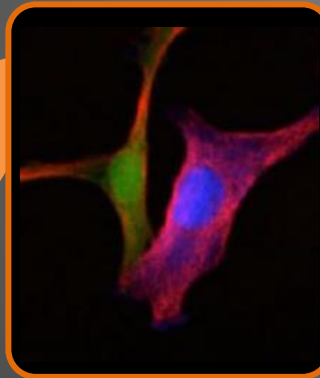
NSCs selectively target invasive tumor cells



NSCs target new blood vessels



**Two unique and synergistic biological properties make neural stems cells an ideal vehicle for targeted cancer treatment**



NSCs



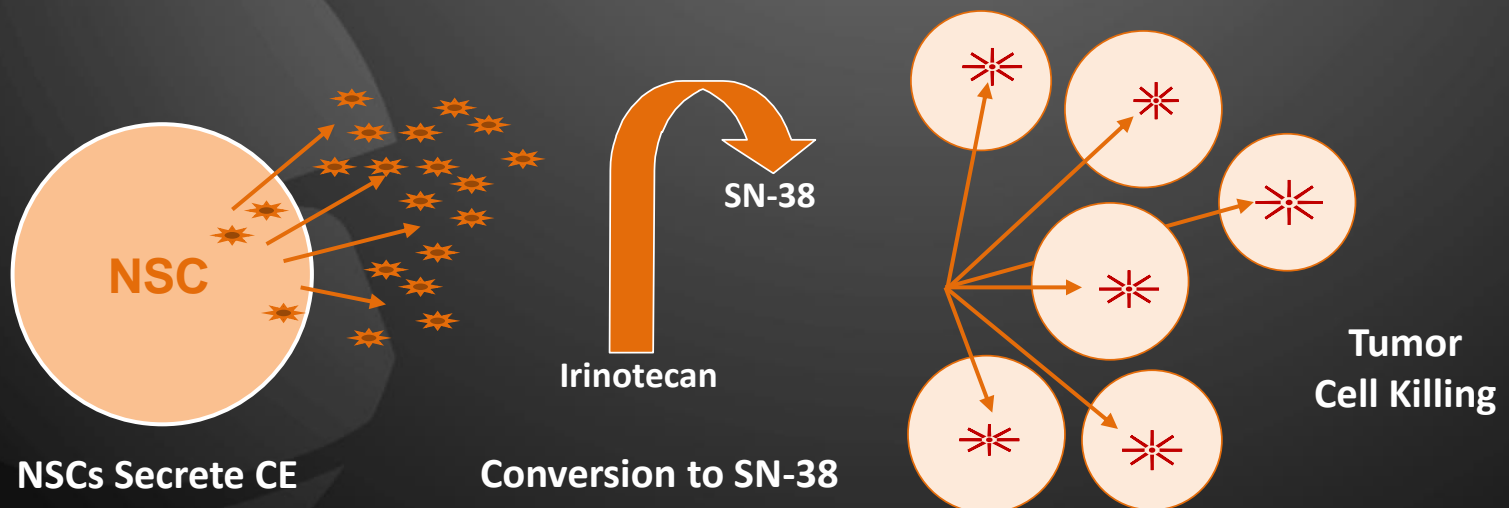
## **Homing: “GPS-like” tumor site locator**

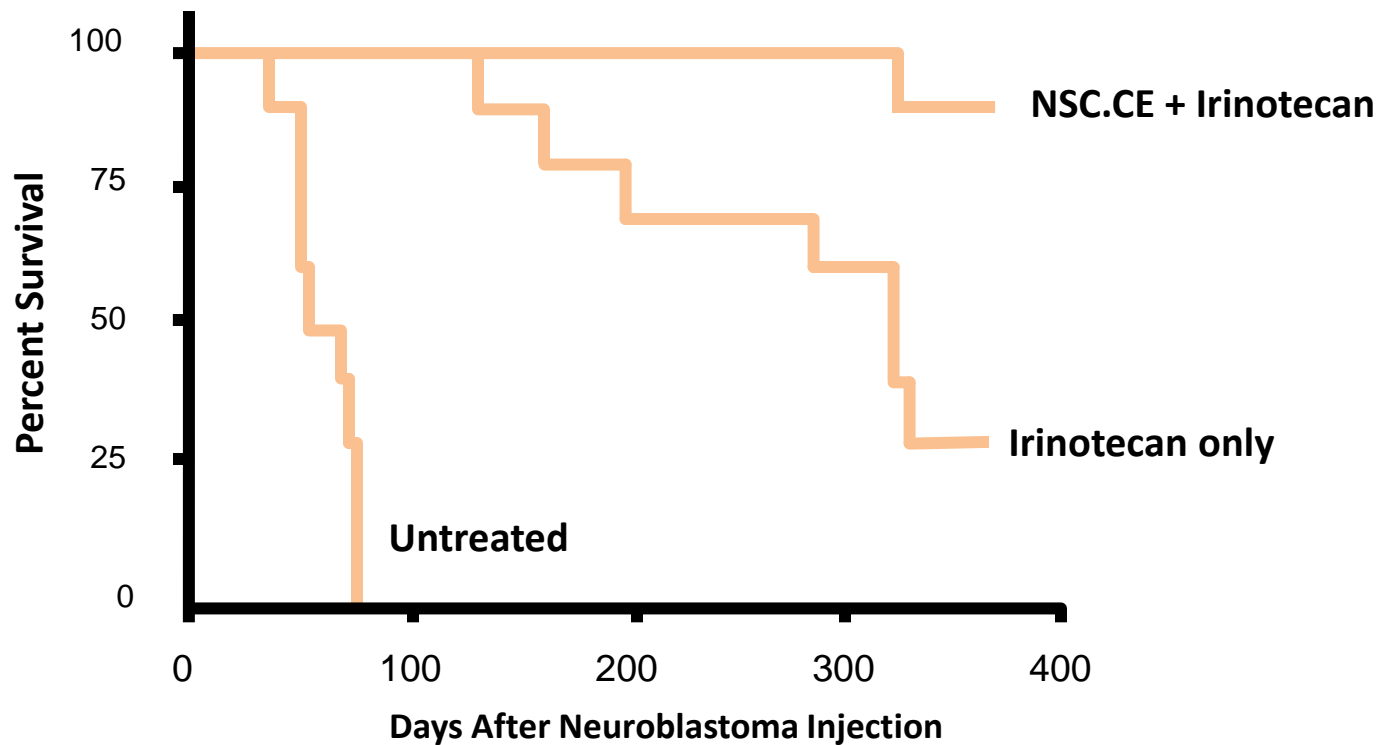
- NSCs navigate towards invasive tumor sites in various tissues, including the brain, post systemic administration
- NSCs exploit tumor angiogenesis as a homing mechanism to locate tumor and metastatic sites

## **Trojan Horse: Stealth payload delivery**

- NSCs can be genetically modified
- NSCs can carry therapeutic payloads to tumor sites, shielded within the NSC carrier
- NSCs retain the tumor homing function upon genetic modification and payload hauling

- NSCs are transduced by a proprietary GenVec adenovector to express and secrete carboxylesterase (CE) = NSC.CE
- When administered, these NSCs migrate to tumor sites where they express the CE therapeutic payload within the tumor
- The secreted CE enzyme then provides a radius of action throughout the tumor site to catalyze the conversion of irinotecan to SN-38
  - SN-38 is 1,000x more toxic to tumor cells than irinotecan





TheraBiologics Data

## ☉ First indication: Recurrent high grade glioma

- Phase 1 clinical trial ongoing currently using a first generation product
- Plan to switch to the second generation collaboration product employing GenVec's adenovector in 1H2017
- The Phase 1 clinical development is fully funded by grants

## ☉ Second indication: Metastatic neuroblastoma

- Systemic administration of the product
- Preclinical work ongoing using the second generation product
- Preclinical development is fully grant-funded

## ☉ GenVec and TheraBiologics are working closely together on:

- Process development for the production of this novel cell therapy
- Exploring additional grant funding opportunities to support the program

Common Shares  
Outstanding<sup>1</sup>

- 2.3 million shares

Exchange: Symbol

- NASDAQ: GNVC

Market  
Capitalization<sup>2</sup>

- \$13.9 million

Cash and  
Investments<sup>3</sup>

- \$8.4 million

Employees

- 15

<sup>1</sup>As of December 1, 2016; <sup>2</sup>Stock price as of January 17, 2017; <sup>3</sup>As of September 30, 2016

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