### 2009 Estimated US Cancer Cases*

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Men</th>
<th>Women</th>
<th>Treatment Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>25%</td>
<td></td>
<td>~497,000 treatable</td>
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<tr>
<td>Lung &amp; bronchus</td>
<td>15%</td>
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<td>3%</td>
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*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
Source: American Cancer Society, 2009.
Why Use Viruses?

- Self replication
- Modifiable
  - Specificity
  - Tissue
  - Replication
  - Cell lysis – goal of most oncolytic viruses
- Immune system stimulation

Issues

- Limited viral spread
- Receptor expression on cell surface
- Immune response to virus
- Virus titer toxicity
- Unintended infection
H101 – First Approved Oncolytic Virus

In November 2005, Shanghai Sunway Biotech (Shanghai, China) announced the approval of H101 by Chinese government regulators.

79% response rate with intra-tumor viral injection when combined with cisplatin chemotherapy (vs. 40% with chemo alone)

- Modified Adenovirus with deletions in the E1B and E3 genes.
- Minor side effects – similar to mild flu
  - Fever aids viral replication
- IV administration not effective
HYPR-Ad-mIL4

- Adenovirus subgroup C Type V
- E1A gene is modified
  - Hif-1 driven replication
  - IL-4 expression

Address what problems?

- Limits replication - cells expressing Hif-1
- Stimulates host immune system (IL-4)
In Vivo Viral Application

**Graph:**
- **LN229**
  - PBS ($n = 7$)
  - dL309-Ad ($n = 9$)
  - HYPR-Ad-mIL4 ($n = 8$)

**Data:**
- Fold increase in tumor volume
- Days post-tumor cell inoculation

**Legend:**
- $n$ represents the number of samples.

**Annotations:**
- 33, 35, 38
- 100 mm$^3$
- * denotes statistical significance.
In Vivo Viral Application

![Graph showing fold increase in tumor volume over days post-tumor cell inoculation for U251MG-T2 with different treatments.]

- **PBS (n = 6)**
- **HYPR-Ad#1 (n = 5)**
- **HYPR-Ad-mIL4 (n = 6)**

Key:
- **350 mm³**
- **140 mm³**

Days post-tumor cell inoculation:
- 39
- 41
- 43
- 53
- 55
- 57
- 60
- 68
- 78
Competition

• Shanghai Sunway Biotech – China
  – First approved oncolytic virus – adenovirus
  – Based on Onyx Pharmaceuticals technology (Onx-015)

• Oncolytics Biotech, Inc. – Calgary
  – 12 ongoing clinical trials - human reovirus

• Jennerex Biotherapeutics, Inc. – San Francisco, CA
  – 4 ongoing clinical trials - vaccina virus

• Neotropix, Inc. – Malvern, PA
  – 1 ongoing clinical trial - seneca valley virus/Bovine
Intellectual Property Status

• 6 issued or allowed patents
  – US – 7,285,414
  – EPO - 1328291
  – UK
  – France
  – Germany
  – Australia - 2001294793

• Pending patents
  – Canada
  – Japan
Questions?

• What is the extent of CAR expression on tumor cells?
• Longevity of virus in the body?
• Effects of repeat administration?
• Effects of co-administration with chemo?
• Others?