Targeted Therapeutics for the Treatment of Brain Cancer
Company Overview

• Singly focused on dramatically improving brain cancer survival in adults and children

• Privately-held, preclinical-stage drug development company

• Founded in 2013; 5,000-square foot lab/office in Austin, TX

• Scientific co-founder is Santosh Kesari, MD, PhD, an internationally recognized leader in the brain cancer field

• First-in-class, small molecule therapeutic with novel mechanism of action

• Major market opportunities
  • Clinical candidate for glioblastoma in adults
  • Expansion in pediatrics and metastatic disease

• Recipient of $7.6M award from CPRIT in 2014
Lead Program Highlights

**Indication:** Malignant gliomas, including glioblastoma (GBM) in adults and pediatric high-grade glioma (pHGG) in children

**Target:** Olig2, a cancer stem cell (CSC)-associated transcription factor found in nearly all gliomas

**Clinical Candidate:** CT-179, a potent oral Olig2 inhibitor

- **Efficacy:** Most effective when used in combination with chemotherapy and radiation in preclinical animal models
- **Safety:** No significant toxicities identified at therapeutic doses
- **Mechanism:** Direct binding to Olig2 protein leading to apoptosis
- **Regulatory:** Granted orphan-drug designation by the FDA
- **Development:** Initiate two Phase 1b clinical trials in newly diagnosed GBM patients in combination with RT ± TMZ in Q2 2018

Preclinical research collaborations with top brain cancer scientists
A Diagnosis Of Glioblastoma Is A Death Sentence

People who have died from brain cancer.

- Estimated 12,390 new cases of glioblastoma (GBM) in the U.S. in 2017\(^1\)
- Conventional therapy includes surgery, chemo-therapy with Temodar\(^{\circledR}\) and radiation therapy
- Median survival = 14.6 months\(^2\)
- 5-year OS rate = 9.8\%\(^2\)

$1 billion worldwide market opportunity\(^3\)

---

In Children, Pediatric High-Grade Glioma\textsuperscript{1} Has An Equally Dismal Prognosis

- \textasciitilde 700 cases per year in the US\textsuperscript{2}
- Treatment includes surgery and radiation\textsuperscript{2}
- 5-year survival less than 35\%\textsuperscript{2}
- Shorter time and lower cost to NDA vs. traditional clinical development
- Opportunity to receive a priority review voucher from the FDA worth \$300M

\textsuperscript{1} Includes anaplastic astrocytoma, anaplastic oligodendroglioma, glioblastoma, mixed glioma, and malignant glioma
Problem: Conventional Therapies Are Ineffective Against Olig2-Expressing Cancer Stem Cells, Leading To Recurrence
What Is Olig2 And Why Target It In Gliomas?

Required For Normal Brain Development
- Transcription factor
- Critical to embryologic brain development
- Typically not active in normal adult brain tissue
- Not found in normal tissues outside the CNS

Critical For Tumor Growth And Invasion
- Drives tumorigenesis
- Promotes resistance to radiation therapy
- Drives tumor invasion into healthy tissue
- CSCs are immunosuppressive
- Highly expressed in all gliomas
Solution: Eliminate The Treatment-Resistant CSCs By Targeting Olig2

- CT-179 will be given as adjunctive therapy with SOC
- Treatment goal is to debulk the tumor AND eliminate the chemo- and radiation-resistant cancer stem cells (CSC)
- As with temozolomide, maintenance therapy is planned
CT-179 Has Excellent Pharmacologic Properties

- ~60% orally bioavailable in monkeys
- Once daily dosing
- Crosses the blood-brain-barrier
- Therapeutic drug levels in brain tissue at steady-state
- Well-tolerated at therapeutic doses in preclinical studies
- Low COGS
- Straightforward manufacturing
- No major formulation issues
- Multiple patent applications
CT-179: Significantly Improves Survival In Orthotopic GBM PDX Models

- Orthotopic implantation of human Olig2-expressing GBM8 and G06 cells; cell lines selected for rapid growth rate of tumors and \textit{in vitro} sensitivity
- IP administration in GBM8 model and PO administration in G06 model
- All treatment groups with significant survival benefit
• SQ implantation of human Olig2-expressing GBM4 and GBM8 cells
• PO administration of CT-179 at 105 mg/kg ± temozolomide/radiation (TMZ/RT)
• All treatment groups with significant tumor growth inhibition (TGI)
• Combination significantly better TGI compared to either CT-179 or TMZ/RT alone

Note: Study numbers are GBM4e201 and GBM8e203
CT-179: Survival Benefit In G06 & GBM8 Orthotopic Models

- SQ implantation of human G06 and GBM8 cells
- PO administration of CT-179 at 150 mg/kg ± temozolomide/radiation (TMZ/RT) or ± TMZ
- Survival benefit from monotherapy and combination with SOC therapies
- Combination significantly better survival compared to monotherapy
- GBM8 study still in-progress; final results expected in November
CT-179: Olig2 Expression In GBM12 Tumors In Vivo Is Markedly Reduced

- Mice implanted orthotopically with GBM12 tumor cells
- Treated with CT-179 at 6 mg/kg and 20 mg/kg PO for 15 days
- Olig2 antibody stain is reddish brown
- CT-179 at 6 mg/kg and 20 mg/kg significantly reduces Olig2 staining
### 4-Year Drug Development Timeline
To Human Safety and Early Efficacy Data

<table>
<thead>
<tr>
<th>Year</th>
<th>Q3</th>
<th>Q4</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2021</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **IND submission in Q2 2018**
- **US Phase 1b clinical trial – CT-179 in combination with TMZ and RT in newly diagnosed glioblastoma (GBM) in adults (all comers)**
- **Australian Phase 1b clinical trial – CT-179 in combination with RT in newly diagnosed glioblastoma (GBM) in adults (MGMT-unmethylated only)**
- **40-patient P1/2 study planned in pediatric high grade glioma (pHGG)**
Management Team Members With Decades Of Experience Developing New And Innovative Drugs

Gregory Stein, M.D., M.B.A.
Chief Executive Officer
20+ years in clinical medicine and life science company formation and operations.

Graham Beaton, Ph.D.
VP, Medicinal Chemistry & Drug Discovery
20+ years in industrial science and pharmaceutical drug development.

Gordon Alton, Ph.D.
VP, Research and Development
20+ years of leading numerous drug discovery project teams.

Daniel Pertschuk, M.D.
VP, Clinical Development
20+ years of leading numerous clinical development programs.
Targeted Therapeutics For The Treatment Of Brain Cancer

**Unmet Medical Need**
- Glioblastoma and pediatric high grade glioma are devastating tumors with high morbidity and mortality rates
- Current standard-of-care only extends median survival by a few months

**Significant Market Opportunity**
- $1B worldwide market for glioblastoma
- Pediatric market offers increased speed and lower cost to approval along with priority review voucher
- Expansion into other primary and metastatic brain cancers

**CT-179 Differentiation**
- Novel, truly targeted mechanism of action
- Kills cancer stem cells, limits invasion, radiation sensitizer while sparing non-Olig2-expressing cells
- Excellent safety and tolerability profile