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Progenics: Targeting and Treating Cancer

- Building an oncology company with a portfolio of therapeutics and diagnostics
- Near-term opportunity with late-stage program in ultra-orphan indication
- PSMA-targeted pipeline: potential to transform clinical practice in prostate cancer
- Strong financial position

<table>
<thead>
<tr>
<th>AZEDRA</th>
<th>1404</th>
<th>PSMA ADC</th>
<th>1095</th>
<th>RELISTOR®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pivotal trial under SPA for Pheochromocytoma</td>
<td>More sensitive in detecting cancer vs. MRI in Phase 2</td>
<td>Demonstrated activity, tolerability in Phase 2</td>
<td>Potent activity in advanced cancer, MSKCC to start Phase 1</td>
<td>Marketed by Salix in US for OIC</td>
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</tbody>
</table>
### Clinical Phase

<table>
<thead>
<tr>
<th>Drug</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1404</strong></td>
<td>Preclinical - Phase 2 - Phase 3 - Reg. Filing - Market</td>
</tr>
<tr>
<td>Diagnostic Imaging Agent Prostate Cancer</td>
<td></td>
</tr>
<tr>
<td><strong>PSMA ADC</strong></td>
<td>Preclinical - Phase 2 - Phase 3 - Reg. Filing - Market</td>
</tr>
<tr>
<td>Therapeutic Prostate Cancer</td>
<td></td>
</tr>
<tr>
<td><strong>AZEDRA</strong></td>
<td>Preclinical - SPA - Reg. Filing</td>
</tr>
<tr>
<td>Theranostic Pheochromocytoma</td>
<td></td>
</tr>
<tr>
<td><strong>1095</strong></td>
<td>Preclinical - Phase 2</td>
</tr>
<tr>
<td>Small Molecule Therapeutic Prostate Cancer</td>
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### Oncology Supportive Care

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<th>Stage</th>
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<tr>
<td><strong>RELISTOR®</strong></td>
<td>Oral</td>
</tr>
<tr>
<td>Opioid-induced constipation Subcutaneous (Al)</td>
<td></td>
</tr>
<tr>
<td><strong>RELISTOR®</strong></td>
<td>Oral</td>
</tr>
<tr>
<td>Subcutaneous (CP) (US)</td>
<td></td>
</tr>
<tr>
<td><strong>RELISTOR®</strong></td>
<td>Oral</td>
</tr>
<tr>
<td>Subcutaneous (CP) (EMA)</td>
<td></td>
</tr>
<tr>
<td><strong>RELISTOR®</strong></td>
<td>Oral</td>
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<tr>
<td>Subcutaneous (Al) Japan</td>
<td></td>
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<td><strong>RELISTOR®</strong></td>
<td>Oral</td>
</tr>
<tr>
<td>Oral</td>
<td></td>
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</tbody>
</table>
AZEDRA: Ultra-Orphan Theranostic

- Novel, targeted radiotherapy candidate
- Phase 2b pivotal trial under SPA for pheochromocytomas and paragangliomas
- FDA Fast Track Status
- Pheochromocytoma and paraganglioma are rare tumors found primarily in the adrenal glands
  - Results in the release of excess hormones that control heart rate, metabolism and blood pressure
  - Left untreated, tumors most often lead to death due to high blood pressure, heart failure, stroke or metastatic disease
- No currently approved therapies in the U.S.
- Potential utility in treating neuroblastoma and other neuroendocrine diseases
# Pivotal Phase 2 Trial Under SPA

## Study Design

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>58 planned</th>
<th>41 received therapeutic dose(s)</th>
</tr>
</thead>
</table>
| Dosing regimen     | Patients receive 2 therapy doses, 3 months apart | • 7 patients have received 1 dose  
• 34 have received 2 doses |
| Primary endpoint under SPA | **25% of study patients respond** (>50% reduction in anti-hypertensive medication) | **32% responded**  
n=13 |
| Secondary objectives | Proportion of subjects with PR by RECIST criteria | 12/38 (32%) |

## Next Steps

Plan to restart enrollment in 1Q15 and complete study by end of 2015
• 85% had measurable decrease in tumor size

• Median survival as of June 2014 is 43.3 months for patients that have received 2 doses

• Long-term follow-up continues

Response rates measured by RECIST

Best change in sum of target lesion diameters from baseline at any time point

- Partial Response
- Stable Disease
- Moderate Response
- Progressive Disease

Presented at ISP September 2014
## Commercialization Strategy

### Manufacturing

- Manufacturing collaboration with Centre for Probe Development and Commercialization (CPDC)
- Innovative manufacturer allows for small doses
- Ideally suited for ultra-orphan indication

### Targeted Market

- Ultra-Orphan - Less than 1,000 cases of pheochromocytoma and paraganglioma diagnosed in the U.S. each year
- 25-30% of cases are genetic
- U.S. market can be reached with a small (3-4) specialty salesforce targeting major centers where these rare tumors are treated
PSMA Targeted Pipeline

- 1404: Diagnostic Imaging Agent Prostate Cancer
- PSMA ADC: Therapeutic Prostate Cancer
- 1095: Small Molecule Therapeutic Prostate Cancer
PSMA as an Oncology Target

PSMA has long been considered among the best oncology targets

Phase 2 data from our PSMA targeted imaging and therapeutic compounds demonstrates the potential to change clinical practice in prostate cancer through improved:

- Detection
- Imaging
- Treatment
- Monitoring response to treatment
Radiopharmaceutical product candidate targeting PSMA

Positive Phase 2 data: higher detection rate vs. MRI

Potential to transform clinical practice with improved detection and monitoring

“New molecular imaging modalities are urgently needed.”

--Jonathan W. Simons, MD
President and CEO of the Prostate Cancer Foundation
Detecting Prostate Cancer in the Gland with 1404

Gleason 4+5 Lesion

MRI

1404 SPECT/CT
1404 Phase 2 Study Design

**Patient Population**
- Biopsy confirmed adenocarcinoma of the prostate gland
- At high-risk for metastatic disease, clinically localized
- Prior neo-adjuvant therapy for prostate cancer was not excluded

**N**
- 104 evaluable patients

**Primary Endpoint**
- Detection of disease; gland level disease vs. histopathology

**Secondary Endpoint**
- Location, extent of disease within gland; lymph nodes/regions vs. histopathology; comparison to MRI (gland & lymph nodes)

Surgeons and pathologists blinded to 1404 results

**MRI/ Bone Scan**

**99mTc-MIP-1404 Dosing**

**SPECT/ CT Imaging**

**Prostatectomy with EPLND**

**Histopathology of prostate & LN**
Phase 2 Results: 1404 Has Higher Detection Rate vs. MRI

1404 detected cancer in the prostate gland with a high degree of sensitivity

- Higher detection rate than matched MRI
- Identified 8 more patients with cancer than MRI

1404 readers identified 14 (19%) more patients with suspicious lymph node sites than MRI

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR Reader</td>
<td>86%</td>
<td>(0.79-0.90)</td>
</tr>
<tr>
<td>(84/98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECT/CT Readers</td>
<td>94%</td>
<td>(0.88-0.97)</td>
</tr>
<tr>
<td>(92/98)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1404 Uptake Correlates with Gleason Score

Gleason Score at Prostatectomy [Lobes]

- No Pca
- 3+3
- 3+4
- 4+3
- 4+4
- 4+5
- 5+4
- 5+5

Aggressive Disease
1404 May Have Utility In Monitoring The Effect of Prostate Cancer Treatments

- Previously treated patients had significantly lower uptake of 1404 in gland (p<0.0001) and primary tumor (p<0.0001)

- Corresponding decrease in PSA measured over time observed in these patients

- Demonstrates potential to track patient’s response to treatment by monitoring PSMA levels

Uptake in Gland Significantly Lower in Treated Pts.

Each error bar depicted 95% confidence interval of the mean

\[ P<0.0001 \]
Opportunity for 1404 at Multiple Points in the Treatment Path

1404: Potential for Broad Utility

- Improve Detection
  - Build on Phase 2 data demonstrating higher detection rate than standard of care
  - Detecting cancer missed on biopsies
- Guide Biopsy
- Determine Staging
- Develop Treatment Plan
- Enable Active Surveillance
  - Discriminate between indolent and clinically significant disease
  - Pursuing a software toolkit
- Assess Biochemical Relapse

Potential Phase 3 Design
PSMA ADC: First-in-Class Targeted Therapeutic

**Targets PSMA**
Fully human antibody to PSMA linked to MMAE

**Highly Active**
Robust and potent activity with favorable tolerability profile in Phase 2

**Biomarkers Identified**
Low NE and High PSMA

**Next Steps**
Design pivotal trial with input from FDA/potential partners
## Phase 2 Open Label Study in Advanced Prostate Cancer

<table>
<thead>
<tr>
<th>Cohorts</th>
<th>After Chemotherapy</th>
<th>Chemotherapy Naïve</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Status</strong></td>
<td>• Enrollment complete&lt;br&gt;• Data presented at ASCO GU, ASCO</td>
<td>• Enrollment complete&lt;br&gt;• Data to be presented at upcoming medical meeting</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>84</td>
<td>35</td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>• Progressed on abiraterone and/or enzalutamide&lt;br&gt;• Previously treated with taxane</td>
<td>• Progressed on abiraterone and/or enzalutamide</td>
</tr>
<tr>
<td><strong>Dosing regimen</strong></td>
<td>Every 3 weeks IV for up to 8 cycles</td>
<td></td>
</tr>
<tr>
<td><strong>Primary outcome measures</strong></td>
<td>Anti-tumor response&lt;br&gt;• Changes in serum PSA and circulating tumor cells (CTCs)&lt;br&gt;• Changes in tumor assessments (RECIST 1.1 criteria)</td>
<td></td>
</tr>
</tbody>
</table>
CTC Responses in Taxane-Resistant Patients

CTC reductions of greater than or equal to 50% in greater than 70% of patients
Measuring CTCs Increasingly Recognized Amongst Broader Clinical Community

Circulating Tumor Cells Predict Survival Benefit from Treatment in Metastatic Castration-Resistant Prostate Cancer

Johann S. de Bono, Howard I. Scher, R. Bruce Montgomery, Christopher Parker, M. Craig Miller, Henk Tissing, Gerald V. Doyle, Leon W.W.M. Terstappen, Kenneth J. Pienta, and Derek Raghavan

Published in Clin Cancer Res 2008;14:6302-6309.

Abstract

Purpose: A method for enumerating circulating tumor cells (CTC) has received regulatory clearance. The primary objective of this prospective study was to establish the relationship between posttreatment CTC count and overall survival (OS) in castration-resistant prostate cancer (CRPC). Secondary objectives included determining the prognostic utility of CTC measurement before initiating therapy, and the relationship of CTC to prostate-specific antigen (PSA) changes and OS at these and other time points.

Experimental Design: Blood was drawn from CRPC patients with progressive disease starting a new line of chemotherapy before treatment and monthly thereafter. Patients were stratified into predetermined Favorable or Unfavorable groups (<5 and ≥5 CTC/7.5mL).

Results: Two hundred thirty-one of 276 enrolled patients (84%) were evaluable. Patients with Unfavorable pretreatment CTC (57%) had shorter OS (median OS, 11.5 versus 21.7 months; Cox hazard ratio, 3.3; P < 0.0001). Unfavorable posttreatment CTC counts also predicted shorter OS at 2 to 5, 6 to 8, 9 to 12, and 13 to 20 weeks (median OS, 6.7-9.5 versus 19.6-20.7 months; Cox hazard ratio, 3.6-6.5; P < 0.0001). CTC counts predicted OS better than PSA decrement algorithms at all time points; area under the receiver operator curve for CTC was 81% to 87% and 58% to 68% for 30% PSA reduction (P = 0.0218). Prognosis for patients with (a) Unfavorable baseline CTC who converted to Favorable CTC improved (6.8 to 21.3 months); (b) Favorable baseline CTC who converted to Unfavorable worsened (>26 to 9.3 months).

Conclusions: CTC are the most accurate and independent predictor of OS in CRPC. These data led to Food and Drug Administration clearance of this assay for the evaluation of CRPC.
Experts Believe That CTC Reductions Correlate with Improved OS

Experience from Johann de Bono’s Work

OS According to CTC Status Throughout Follow-Up

Data from: https://www.cellsearchctc.com/clinical-applications/mpc-clinical-trials-case-studies
## Biomarkers That Predict Response to PSMA ADC

### High PSMA

- **Marker**: High PSMA
- **Description**: Measurement of PSMA on the CTCs of the patient and on the tissue of the patient
- **Response**: Best CTC percent change
- **Spearman Correlation P-value**: 0.0192

### Low NE

- **Marker**: Low NE
- **Description**: Combination of easily obtainable neuroendocrine blood tests
- **Response**: Best PSA percent change
- **Spearman Correlation P-value**: 0.0116
PSMA Targeted Small Molecule Therapeutic (1095) for Prostate Cancer

- Targeted small molecule radiotherapeutic that selectively binds to PSMA
- Delivers lethal dose of radiation directly to prostate cancer cells with minimal impact on surrounding healthy tissue
- Compassionate use study in advanced prostate cancer
- Primary study site for Phase 1: Memorial Sloan Kettering, the Coordinating Center for the Prostate Cancer Clinical Trials Consortium (PCCTC)

Courtesy of Prof. U. Haberkorn, University Hospital Heidelberg
1095: Effect on Serum PSA

Best PSA Response in 25 patients

- Published in the *European Journal of Nuclear Medicine and Molecular Imaging*
- 1095 markedly reduced PSA levels in a healthy pretreated group of 25 evaluable patients, and reduced bone pain

RELISTOR
Opioid-induced constipation
RELISTOR®
Economics of 2011 Salix Collaboration

- Marketed by Salix in the U.S.
- Subcutaneous formulation approved for treatment of OIC in patients with:
  - Advanced illness who are receiving palliative care; or,
  - Chronic, non-cancer pain
- Salix to file NDA for RELISTOR Oral by end of 2Q15

<table>
<thead>
<tr>
<th>Royalty scale based on WW net sales, ranging from 15%-19%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial milestones totaling up to $200M, including $10M on first $100M in sales</td>
</tr>
<tr>
<td>Entitled to receive 60% of revenues received by Salix from ex-U.S. sub-licensees</td>
</tr>
<tr>
<td>$50M milestone upon U.S. approval of RELISTOR Oral</td>
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$50M milestone upon U.S. approval of RELISTOR Oral
## Financial Highlights

**As of 09/30/2014**

<table>
<thead>
<tr>
<th>Shares outstanding</th>
<th>Net cash decrease</th>
</tr>
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<tbody>
<tr>
<td>69.6 M</td>
<td>$0.1 M</td>
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</table>

**Q3 2014**

<table>
<thead>
<tr>
<th>Net income</th>
<th>Net income/share, diluted</th>
</tr>
</thead>
<tbody>
<tr>
<td>$37.0 M</td>
<td>$0.51</td>
</tr>
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</table>

**$87.4 M**

- Cash & securities on 9/30
- Received from Salix on 10/6
- $40 M
Upcoming Milestones

- Restart pivotal Phase 2 AZEDRA Trial
  - Q1 2015
- Meet with FDA to determine next steps for 1404
- Present Data from Phase 2 PSMA ADC Trial (Chemo Naïve Cohort)
- NDA Filing for RELISTOR Oral (Salix)
  - Q2 2015
- Initiate Phase 1 Trial for 1095
  - 2015
- Complete enrollment in pivotal Phase 2 AZEDRA trial
  - 4Q 2015
Progenics: Targeting and Treating Cancer

- AZEDRA progressing toward commercialization
- Phase 2 clinical data for 1404 and PSMA ADC demonstrates potential to change clinical practice in prostate cancer
- Evaluating next steps for 1404 program
- Exploring partnership opportunities & registration path forward for PSMA ADC
- 1095 Phase 1 trial to initiate at Memorial Sloan Kettering
- Strong cash position, fueled by royalties/milestones from RELISTOR

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