Background: Archexin® (RX-0201) is a 20-mer oligonucleotide that is complementary to AKT1 messenger ribonucleic acid (mRNA). The specificity of Archexin mediated effect on AKT1-mRNA levels, in human renal cell carcinoma (von Hippel-Lindau protein deficient renal cell carcinoma line) LNCaP cells results in a reduction of AKT1-mRNA levels. In a single agent phase I study the maximum tolerated dose of Archexin was 200 mg/m²/day.

Methods: The current study is a proof of concept phase 1/2, multicenter, open label study for subjects who have progressed on at least 1 VEGF-targeted therapy (e.g., sunitinib, pazopanib, axitinib). Stage 1 is an open-label, dose-escalation phase I study of Archexin administered in combination with everolimus. Archexin is administered by a 24 hour continuous intravenous infusion for 14 days followed by 7 days of rest. It is Archexin administered in combination with everolimus. Archexin is administered by a study for subjects who have progressed on at least 1 VEGF-targeted therapy.

Conclusions: The RX-0201 dose (125, 200 and 250 mg/m²/day) will be escalated until the maximum tolerated dose or target dose is achieved. The dose of RX-0201 identified in Stage 1 will be used in the dose expansion portion (Stage 2).

Primary Objectives:
• To determine the maximum tolerated dose (MTD) of RX-0201, up to a target dose of 250 mg/m²/day, when given in combination with everolimus.

Secondary Objectives:
• To assess the pharmacokinetics of RX-0201 in combination with everolimus versus everolimus alone.

Stage 1 Demographics

• 7 Males; 3 Females
• Median Age: 60 years; Range: 44-78 years
• 7 Males; 3 Females
• Median Number of Prior Therapies: 1

Stage 1 Study Design and Objectives

Stage 1 Response Data

- At the lowest dose level (125 mg/m²/day) one subject has had stable disease for more than 1 year and experienced a 16% reduction in a right adrenal lesion after 4 cycles of treatment.

- At the second dose level (200 mg/m²/day) one subject’s hypervascular mass just anterior to the nephrectomy bed has decreased 36% in size after 2 cycles of treatment.

- Treatment at the third dose level (250 mg/m²/day) is ongoing.

Previous Therapies (Best Response)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Best Response</th>
<th>Days of Stable Disease</th>
<th>Reduction</th>
<th>Reason for Discontinuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sunitinib (PD)</td>
<td>125</td>
<td>383</td>
<td>16%</td>
<td>Subject Withdrawal</td>
</tr>
<tr>
<td>Pazopanib (PD)</td>
<td>200</td>
<td>16</td>
<td>NE</td>
<td>Unrelated AE</td>
</tr>
<tr>
<td>Pazopanib (NE)</td>
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<td>51</td>
<td>PD</td>
<td>PO</td>
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<tr>
<td>Axitinib (PD)</td>
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<td>PD</td>
<td>PO</td>
</tr>
<tr>
<td>Pazopanib (PD)</td>
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<td>87</td>
<td>36%</td>
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<tr>
<td>Pazopanib (PR)</td>
<td>250</td>
<td>23</td>
<td>NA</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Sunitinib (PD)</td>
<td>250</td>
<td>9</td>
<td>NA</td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

Stage 1 PK Data

- The pharmacokinetics of RX-0201 is dose proportional and declines rapidly upon cessation of infusion. Exposure of RX-0201 is safe and well-tolerated at doses up to 250 mg/m²/day.

- Disease activity and imaging of patients are assessed every 4 weeks during the dosing period.

- Upon cessation of the 14-day infusion, plasma concentrations decreased rapidly.

- The mean T1/2, AUC last, Cmax and Tmax for RX-0201 were 3.0 hours, 234.1 hours·ng/ml, 2997 ng/ml and 8.3 hours, respectively.

- RX-0201 exposure is dose proportional and appears to slightly accumulate during the dosing period. Upon cessation of the 14-day infusion, plasma concentrations decreased rapidly with mean T1/2 of 3.98 hours (125 mg/m²/day) and 2.65 hours (200 mg/m²/day).

- PK-Parameter:
  - Day 1:
    - Dose: 125 mg/m²/day
    - AUC last (ng·hr/ml): 234.1 ± 116.0
    - Cmax (ng/ml): 2897 ± 889
    - Tmax (h): 6 ± 5.2

- Day 15:
  - Dose: 125 mg/m²/day
  - AUC last (ng·hr/ml): 4395 ± 2153
  - Cmax (ng/ml): 4590 ± 2153
  - Tmax (h): 3 ± 2.8

Stage 1 Preliminary PK Data

PK Parameter

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 1</th>
<th>Day 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>125 mg/m²/day</td>
<td>125 mg/m²/day</td>
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<tr>
<td>AUC last (ng·hr/ml)</td>
<td>234.1 ± 116.0</td>
<td>4395 ± 2153</td>
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<tr>
<td>Cmax (ng/ml)</td>
<td>2897 ± 889</td>
<td>4590 ± 2153</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>6 ± 5.2</td>
<td>3 ± 2.8</td>
</tr>
</tbody>
</table>

Methodology:

- This study is a 2-stage multi-center, open-label study to assess the safety and tolerability of RX-0201 in combination with everolimus versus everolimus alone to treat subjects with advanced renal cell carcinoma.

- Stage 1 is an open-label, dose-escalation phase I study of Archexin administered in combination with everolimus. Archexin is administered by a 24 hour continuous intravenous infusion for 14 days followed by 7 days of rest. It is hypothesized that 250 mg/m²/day or a lower dose of Archexin will be identified as the safety and tolerability of RX-0201 when given in combination with everolimus.

- Treatment: RX-0201 is administered by continuous IV infusion for 14 days followed by 7 days of rest. It is hypothesized that 250 mg/m²/day or a lower dose of Archexin will be identified as safe and tolerable when administered in combination with everolimus.

- The dose of Archexin identified in Stage 1 will be studied further in Stage 2 which is the randomized, open-label, 2-arm study of Archexin in combination with 10 mg of everolimus. Stage 2 is an open-label randomized Stage 2 portion of the study.

- Archexin to be studied further in Stage 2 (randomized) when combined with everolimus.

- Stage 2 (randomized) when combined with everolimus.

- The dose of Archexin identified in Stage 1 will be studied further in Stage 2 which is the randomized, open-label, 2-arm study of Archexin in combination with 10 mg of everolimus.

- Stage 2 is an open-label randomized Stage 2 portion of the study.

- Archexin to be studied further in Stage 2 (randomized) when combined with everolimus.

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- Archexin to be studied further in Stage 2 (randomized) when combined with everolimus.