Phase I Trial of AVN944 in Patients with Advanced Hematologic Malignancies
Safe Harbor Statement

This announcement contains, in addition to historical information, certain forward-looking statements that involve risks and uncertainties, in particular, related to clinical progress in the development of AVN944. Such statements reflect the current views of Avalon management and are based on certain assumptions. Actual results could differ materially from those currently anticipated as a result of a number of factors, risks and uncertainties including the risk that AVN944 will not progress successfully in its clinical trials, and other risks described in our SEC filings. There can be no assurance that our development efforts will succeed, that AVN944 will receive required regulatory clearance or, even if such regulatory clearance is received, that any subsequent products will ultimately achieve commercial success. The information in this Release should be read in conjunction with the Risk Factors set forth in our 2006 Annual Report on Form 10-K and updates contained in subsequent filings we make with the SEC.
AVN944 Overview

- Oral pan-cancer agent
- More potent inhibitor of IMPDH than other agents with similar MoA
- *In vitro* evidence for efficacy with additive/synergistic activity in combination; non-additive toxicity profile
- Good animal toxicology profile
- Healthy volunteer study:
  - human pharmacokinetics
  - no toxicity signal over a dose range of 25 - 250 mg
  - 90% inhibition of IMPDH enzyme activity at doses ≥ 150 mg
- Ongoing Phase I study in hematologic malignancies with no safety signal to date
- Phase II studies to start during 2007
IMPDH is a validated target for cancer therapy

- IMPDH is over-expressed in proliferating cells
- Catalyzes the rate-limiting step in GTP synthesis
- AVN944 has fewer off-target effects than other drugs in class
- Depleted GTP pools affect nucleic acid synthesis & cell regulation

Sintchak, Cell 1996
IMPDH-2 is overexpressed in hematologic & solid cancers

IMPDH 1

= mean level of mRNA expression

Hematological Cancer WBC (n=290)

Normal WBC (n=1345)

IMPDH 2

Hematological Cancer WBC (n=290)

Normal WBC (n=1345)

= mean level of mRNA expression

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IMPDH inhibition suppresses guanosine triphosphate (GTP)

DNA synthesis

RNA synthesis

Regulatory proteins

GMP - guanosine monophosphate
IMP = inosine monophosphate
XMP = xanthine monophosphate
Phase I Study Design

- Open label, sequential, dose escalation study
- All patients have advanced, refractory disease
- 3-6 patient dose levels; 10-12 dose levels (25 mg bid – 350 mg twice a day, orally x 21 d every 28 d)
- Cohort 1: AML, ALL, or CML-BP
  Cohort 2: MM, CLL, NHL, HD, WM
- Endpoints: safety, pharmacokinetics, biomarkers, efficacy
Phase I Clinical Summary

- 25 mg b.i.d. - 200 mg b.i.d.: well tolerated
- Pharmacokinetic profile is dose-dependent
- 46% of patients have achieved stabilization of disease
- 24% of patients have had more extended benefit from treatment (up to 1 year)
- Biomarker assessments substantiate observations of clinical activity
- Biomarkers offer potential to accelerate development
Dose escalation is progressing well
46 total subjects; 104 cycles administered

<table>
<thead>
<tr>
<th>Patient enrollment</th>
<th>Cohort 1</th>
<th>Cohort 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML: 23</td>
<td>MM: 15</td>
<td></td>
</tr>
<tr>
<td>ALL: 2</td>
<td>CLL: 5</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Dose Levels</th>
<th>Cohort 1</th>
<th>Cohort 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-200 mg bid: completed</td>
<td>25-100 mg bid: completed</td>
<td></td>
</tr>
<tr>
<td>250 mg bid: accruing</td>
<td>150 mg bid: accruing</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># Cycles completed</th>
<th>Cohort 1</th>
<th>Cohort 2</th>
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<tbody>
<tr>
<td>41</td>
<td>53</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient status</th>
<th>Cohort 1</th>
<th>Cohort 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 of 19 evaluable AML stable ≥ 2 cycles; 1 AML on cycle 9</td>
<td>9 of 15 evaluable MM stable ≥ 2 cycles; 2 completed 5 mos. 2 completed 12 mos.</td>
<td></td>
</tr>
</tbody>
</table>
AVN944 pharmacokinetics are dose-dependent.
AVN944 has been well-tolerated

- **Drug-related Symptoms (not dose-related)**
  - loose stool
  - dehydration
  - fatigue and/or dizziness
  - anorexia
  - fever, neutropenia

- **Lab:**
  - No drug-related or dose-related abnormal labs
  - Abnormal CBCs consistent with disease state
  - Transient grade 1-2 transaminases or creatinine elevations attributed to disease state or to concurrent meds
Safety: Side effects have not limited dose escalation

- 20 SAEs in 12 subjects (10 w/AML)
- 18 SAEs “unrelated to treatment”:
  - 8 fever w or w/o neutropenia &/or sepsis (all AML)
  - 2 pneumonia w/ hypoxia
  - 2 dehydration
  - 2 progressive disease
  - 2 syncope (dizziness)
  - 1 hyperglycemia
  - 1 ataxia p single dose (CSF+ for malignancy)
- 2 SAEs “possibly” related to AVN944
  - upper GI bleeding
  - dehydration and dizziness with urinary tract infection
Protocol response criteria are rigorously defined

Response Criteria for Acute Myeloid Leukemia

Complete Remission (CR)

**Peripheral Blood Counts:**
- No leukemic blasts in the peripheral blood
- ANC > 1,000/µL
- Platelet count > 100,000/µL
- Transfusion independent

**Bone Marrow:**
- <5% blasts
- No cells with Auer rods

Partial Remission (PR)

Must meet all the criteria for CR but with a decrease of at least 50% in the percentage of blasts to 5 – 25% blasts in the bone marrow.
## Consensus Response Criteria: Multiple Myeloma

<table>
<thead>
<tr>
<th></th>
<th>Complete Response</th>
<th>Partial Response</th>
<th>Minimal Response</th>
<th>Plateau Phase</th>
<th>Progressive Disease</th>
<th>Relapse After CR</th>
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</thead>
<tbody>
<tr>
<td><strong>Serum M-protein</strong></td>
<td>Absence</td>
<td>+</td>
<td>≥ 50% reduction</td>
<td>↑ or ↓ 25%</td>
<td>Increase &gt; 25% and &gt; 5g/L</td>
<td>Reappearance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>25 – 49% reduction</td>
<td></td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td><strong>Urine light chains</strong></td>
<td>Absence</td>
<td>+</td>
<td>≥ 90% reduction or 200 mg</td>
<td>↑ or ↓ &lt; 25%</td>
<td>Increase &gt; 25% and &gt; 200 mg</td>
<td>Reappearance</td>
</tr>
<tr>
<td>(mg/24 hours)</td>
<td></td>
<td>+</td>
<td>50 – 89% reduction and &gt;200 mg</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td><strong>Bone marrow plasma cells (%)</strong></td>
<td>&lt; 5%</td>
<td>+</td>
<td>≥ 50% reduction</td>
<td>↑ or ↓ &lt; 25%</td>
<td>Increase &gt; 15% and &gt; 10%</td>
<td>&gt; 5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>25 – 49% reduction</td>
<td></td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td><strong>Bone lytic lesions</strong></td>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>+</td>
<td>Stable</td>
<td>Stable</td>
<td>Increase</td>
<td>or</td>
</tr>
<tr>
<td><strong>Extramedullary plasmacytomas</strong></td>
<td>Absence</td>
<td>+</td>
<td>≥ 50% reduction</td>
<td>Absence</td>
<td>Increase</td>
<td>Increase</td>
</tr>
</tbody>
</table>
Clinical Benefit

- Stabilized disease seen in 46% of evaluable patients
- No protocol-defined responses seen to date
- Biomarkers correlate with clinical biological activity
Critical contributions of biomarkers in AVN944 clinical development

- Does AVN944 reach the ‘target’?
- Is there biologic activity to AVN944 treatments?
- Is AVN944 activity dose-responsive?
- Are there biomarker correlates to AVN944 clinical activity?
Biomarker Take-home messages

- AVN944 is inhibiting the IMPDH enzyme.
- IMPDH inhibition results in depletion of GTP.
- IMPDH inhibition and GTP depletion correlate with specific genetic biomarker changes.
- Gene biomarker changes correlate with clinical biologic activity.
- Genetic signature biomarkers distinguish patients who experience stable disease from those with progressive disease.
AvalonRx Guiding AVN944 Development

IMPDH enzyme analysis

GTP Pool Depletion

Comprehensive Biomarkers

Targeted Pathway Biomarkers

Clinical activity predictors

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AVN944 is inhibiting the IMPDH target enzyme in a dose-dependent manner.

Inhibition of IMPDH enzyme at 4 hours post-dose is seen consistently at 200 mg dose, where it was rarely seen at lower doses.
AVN944 causes GTP depletion, with greater duration at higher doses

Depletion at 4 hours only at 50 mg dose

Depletion at 4 and 8 hours with 200 mg dose
Inhibition of IMPDH enzyme correlates with genetic markers of activity

GTP levels differ across patients

<table>
<thead>
<tr>
<th>Patient ID#</th>
<th>% GTP (t=4 hr)</th>
<th>GTP depletion</th>
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<tbody>
<tr>
<td>1005</td>
<td>26</td>
<td>N</td>
</tr>
<tr>
<td>1007</td>
<td>15</td>
<td>N</td>
</tr>
<tr>
<td>1008</td>
<td>18</td>
<td>N</td>
</tr>
<tr>
<td>1006</td>
<td>122</td>
<td>Y</td>
</tr>
<tr>
<td>1010</td>
<td>86</td>
<td>Y</td>
</tr>
<tr>
<td>1011</td>
<td>328</td>
<td>Y</td>
</tr>
</tbody>
</table>

N, GTP depletion >50% of Cycle 1 day 1 time 0 value
Y, GTP depletion < 50% of Cycle 1 day 1 time 0 value

Biomarkers respond to depletion of GTP pools

>2 fold change in expression

Oncogene marker3

Nucleotide metabolism marker 1
Gene biomarkers are dose-responsive

Gene Ontology (GO) contains 8 genes; Z score of 2.0 is equal to p<0.05

<table>
<thead>
<tr>
<th>Patient ID#</th>
<th>Dose Level</th>
<th>Z score</th>
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<tr>
<td>1005</td>
<td>50mg</td>
<td>ns</td>
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<tr>
<td>1006</td>
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</tr>
<tr>
<td>1007</td>
<td>50mg</td>
<td>ns</td>
</tr>
<tr>
<td>1008</td>
<td>75mg</td>
<td>ns</td>
</tr>
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<td>1009</td>
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<tr>
<td>1010</td>
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<td>1011*</td>
<td>75mg</td>
<td>3.7</td>
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<tr>
<td>1018</td>
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<td>1020</td>
<td>200mg</td>
<td>5.2</td>
</tr>
<tr>
<td>1021</td>
<td>200mg</td>
<td>2.5</td>
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<tr>
<td>1022</td>
<td>200mg</td>
<td>5.5</td>
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<tr>
<td>1024**</td>
<td>200mg</td>
<td>ns</td>
</tr>
<tr>
<td>1025</td>
<td>200mg</td>
<td>4.4</td>
</tr>
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</table>
Significant genetic biomarker response correlates with patient benefit

Gene Expression Averaged over 15 Genes

Apoptosis Pathway marker 2

Patient groups distinguished by signature trend

Patient groups distinguished by a single gene
Specific genetic biomarkers correlate with patient benefit

Use of 11-gene predictor
For patient identification

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>NB</th>
<th>Total</th>
<th>Percent Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>No patient enrichment</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>38</td>
</tr>
<tr>
<td>Retrospective enrichment</td>
<td>5</td>
<td>2</td>
<td>7</td>
<td>71</td>
</tr>
</tbody>
</table>
Biomarker summary and conclusions

- AVN944 is inhibiting the IMPDH enzyme
- IMPDH inhibition results in depletion of GTP
- IMPDH inhibition and GTP depletion correlate with specific genetic biomarker changes
- Gene biomarker changes correlate with clinical biologic activity
- Genetic signature biomarkers distinguish patients who experience stable disease from those with progressive disease
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Clinical development is directed toward rapid approval

- Single agent activity and limited combination studies as a rational foundation for further studies
- Unmet medical needs in myeloma, leukemia, and pancreatic cancer
- Assessing expanded clinical trial opportunities through NCI collaborations
- Each Phase II study will include multiple sites to achieve rapid accrual of subjects
Additional effect on IMPDH inhibiton: AVN944 inhibits new blood vessel formation (angiogenesis)

- C57BL/6 mice (4 per group) implanted with 2 Matrigel plugs each
- VEGF (50ng/ml) and FGFb (50ng/ml) added to stimulate blood vessel growth
- Mice treated with compound for 12 days
- Plugs stained with H&E. Blood vessel density analyzed with Image Pro-Plus software.
AVN944 inhibits pancreatic and other solid tumor cells at clinically achievable concentrations.
AVN944 inhibits pancreatic and other solid tumor cells at clinically achievable concentrations

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Mean IC50 (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic Cancer</td>
<td>80 nM (60 – 180 nM)</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>70 nM (30 – 120 nM)</td>
</tr>
<tr>
<td>NSCLC</td>
<td>125 nM (40 - 230 nM)</td>
</tr>
<tr>
<td>Breast</td>
<td>60 nM (30 – 80 nM)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>110 nM (30 – 280 nM)</td>
</tr>
</tbody>
</table>
AVN944 is Active in Gemcitabine-resistant Pancreatic Tumor

Percent inhibition of proliferation

AVN944 concentrations

Gemcitabine
Opportunities for AVN944 in Pancreatic Cancer

- Able to accelerate initiation of Phase II plans with pancreatic cancer
  - we are within a clinically active dose range for AVN944
  - not at MTD; appropriate for combining with another cytotoxic agent

- Phase II study in 1st line patients with newly diagnosed pancreatic cancer

- AVN944 active in pancreatic cell lines and in gemcitabine resistance cells

- Pre-clinical studies show at least additive effects of AVN944 + gemcitabine

- AVN944 adds to gemcitabine effect by changing gene related to gemcitabine mechanism of action and metabolism
2007 Clinical Development
Phase II Avalon sponsored studies

- Solid:
  - Phase I/II AVN944 + gemcitabine in 1st-line pancreatic ca.

- Hematologic:
  - Determination of single agent Phase II dose will be data driven
  - May require 1 or several more Phase I dose levels
  - Phase II AML in elderly and in refractory
  - Phase II in refractory myeloma

- Tissue acquisition studies (NSCLC, NHL, prostate, et al.)
  - Pre-treatment predictors of benefit/acclual enrichment
  - Surrogate endpoint for response or survival
  - Benign tissue as surrogate for cancer biopsies
  - Correlations with efficacy and/or safety over time (phase II component)

- Phase II CTEP sponsored studies
Timelines for 2007 - 2008

■ 2H07:
  • Complete Phase I
  • Start AVN944 + gemcitabine Phase II
  • Start tissue acquisition studies
  • Initiate sites for myeloma and AML Phase II studies
  • Accrual to all active studies
  • Ongoing biomarker evaluations for hypothesis validation

■ 1H08
  • Evaluation of pancreatic, myeloma and AML studies
  • Planning for end-of-phase II and pivotal studies