Overview of AN2728 in Psoriasis

- Target Product Profile
  - Safe and effective topical therapy for mild-to-moderate psoriasis affecting all areas of the body, including sensitive skin
  - Efficacy in the range of mid-potency steroids or Vitamin D analogs
  - Safer than topical steroids and without the irritation of Vitamin D analogs

- 14 clinical studies to date have demonstrated a strong safety profile

- AN2728 has demonstrated efficacy in the range of mid-potency steroids and vitamin D analogs

- Results of Local Tolerability Study confirm potential to expand indication to patients with inverse psoriasis which involves the face, skin folds, recesses, and genitalia

- Plans to initiate Phase 3 in psoriasis to follow Phase 2 results in atopic dermatitis
Three Types of Psoriasis Studies

- **Microplaque Studies**
  - Establish initial human proof of concept for efficacy
  - Efficacy of multiple comparators can be examined on one subject

- **Bilateral trials**
  - Patient treats 2 similar lesions – one with active and one with vehicle
  - Measures efficacy of active compared to vehicle on one person

- **Whole-body studies**
  - Patients are randomized to treat lesions with either active or vehicle
  - Efficacy of active relative to vehicle is evaluated between patients

Phase 2a (201 Study) Trial Overview

- **Purpose**
  - Assess efficacy and safety of AN2728 Ointment, 5%

- **Design**
  - Randomized double-blind bilateral trial
  - 35 patients
  - Non-occluded twice daily patient applied for 28 days
  - AN2728 Ointment, 5% vs. vehicle

- **Clinical evaluations**
  - Overall Target Plaque Severity Score
  - Individual signs of psoriasis

- **Primary endpoint**
  - Overall Target Plaque Severity Score at Day 28
Phase 2a (201 Study)
AN2728 Demonstrated Efficacy Under Non-Occluded Patient Self Application

Proportion of Plaques Achieving Clear or Almost Clear with ≥ 2-Grade Improvement from Baseline (OTPSS scale)

- Phase 2a (201 Study): AN2728 Demonstrated Efficacy Under Non-Occluded Patient Self Application
- Proportion of plaques achieving clear or almost clear with ≥ 2-grade improvement from baseline (OTPSS scale)
- Baseline
- Day 14
- Day 28

<table>
<thead>
<tr>
<th>Time</th>
<th>5% AN2728</th>
<th>Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 week</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>2 weeks</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>3 weeks</td>
<td>17%</td>
<td>3%</td>
</tr>
<tr>
<td>4 weeks</td>
<td>40%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Phase 2 (201 Study)

- Ointment Vehicle
- AN2728 Ointment, 5%
- Baseline
- Day 14
- Day 28

OTPSS = 2
OTPSS = 3
OTPSS = 4
OTPSS = 1
### Phase 2 (201 Study)

#### Trial Overview

- **Purpose**
  - Define optimal duration of therapy

- **Design**
  - Randomized double-blind bilateral trial
  - 30 patients
  - Bilateral design
  - Patient applied AN2728 Ointment, 5% BID for 12 weeks

- **Clinical evaluations**
  - Overall Target Plaque Severity Score
  - Individual signs of psoriasis

- **Primary endpoint**
  - Overall Target Plaque Severity Score at Day 28
**Phase 2 (202 Study)**
AN2728 Demonstrated Efficacy Plateau at 6-10 Weeks

**Proportion of Plaques Achieving Clear or Almost Clear with ≥ 2-Grade Improvement from Baseline**

(OTPSS scale)

<table>
<thead>
<tr>
<th></th>
<th>1 wk</th>
<th>2 wks</th>
<th>4 wks</th>
<th>6 wks</th>
<th>8 wks</th>
<th>10 wks</th>
<th>12 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% AN2728</td>
<td>0%</td>
<td>3%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>7%</td>
<td>3%</td>
</tr>
<tr>
<td>Vehicle</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Phase 2 (202 Study)**
Cases of Complete Clearance

**Visit 2 (Baseline)**
- OTPSS = 0
- Ointment Vehicle

**Visit 9 (Day 84)**
- OTPSS = 2
- AN2728 Ointment, 5%
- OTPSS = 4
Phase 2 (202 Study) Cases of Complete Clearance

<table>
<thead>
<tr>
<th>Ointment Vehicle</th>
<th>AN2728 Ointment, 5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit 2 (Baseline)</td>
<td></td>
</tr>
<tr>
<td>OTPSS = 2</td>
<td>OTPSS = 3</td>
</tr>
<tr>
<td>Visit 9 (Day 84)</td>
<td></td>
</tr>
<tr>
<td>OTPSS = 2</td>
<td>OTPSS = 0</td>
</tr>
</tbody>
</table>

Phase 2b (203 Study) Trial Overview

- **Purpose**
  - Determine optimal concentration and dosing of AN2728

- **Design**
  - Randomized, double-blind bilateral trial
  - 145 patients
  - Bilateral design
  - Patient applied AN2728 or vehicle for 12 weeks
  - 4 cohorts
    - 0.5% QD vs Vehicle
    - 2.0% QD vs Vehicle
    - 0.5% BID vs Vehicle
    - 2.0% BID vs Vehicle

- **Clinical evaluations**
  - Overall Target Plaque Severity Score
  - Individual signs of psoriasis

- **Primary endpoint**
  - Improvement in Overall Target Plaque Severity Score at Day 42
Phase 2b (203 Study)
Clear Dose Response Over 12 Weeks of Treatment

Example of Complete Clearance

AN2728 Ointment, 0.5%, BID  Ointment Vehicle

V2 (Baseline)  
OTPSS = 4  
OTPSS = 4

V9 (Day 84)  
OTPSS = 0  
OTPSS = 2
Phase 2b (203 Study)
Example of Complete Clearance

Phase 2b (204 Study)

- **Key objectives**
  - Provide data to inform plans for anticipated Phase 3 trial design and End of Phase 2 meeting with FDA
    - Safety and tolerability with larger body surface area treated than previous Phase 2 trials
    - Level of efficacy with subject to subject comparison, rather than bilateral
    - Time to peak efficacy with whole body treatment
  - Not intended to demonstrate statistical differentiation of treatment from vehicle, but to inform a fully-powered pair of pivotal Phase 3 trials

- **Design**
  - 12 week, double-blind, subject-to-subject comparison
  - 68 patients randomized 2:1
  - AN2728 Ointment, 2%, vs. Vehicle BID

- **Clinical evaluations**
  - Safety, efficacy and duration of treatment under anticipated Phase 3 conditions
Phase 2b (204 Study)
AN2728 Demonstrated Improvement Over Vehicle at Each Recorded Timepoint

Proportion of Subjects Achieving Clear or Almost Clear with ≥ 2-Grade Improvement from Baseline (PGA scale)

- **Phase 2b (204 Study)**
- AN2728 Demonstrated Improvement Over Vehicle at Each Recorded Timepoint

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>AN2728 (n=46)</th>
<th>Vehicle (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 wks</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>4 wks</td>
<td>9%</td>
<td>5%</td>
</tr>
<tr>
<td>6 wks</td>
<td>26%</td>
<td>18%</td>
</tr>
<tr>
<td>8 wks</td>
<td>18%</td>
<td>14%</td>
</tr>
<tr>
<td>10 wks</td>
<td>14%</td>
<td>17%</td>
</tr>
<tr>
<td>12 wks</td>
<td>17%</td>
<td>14%</td>
</tr>
</tbody>
</table>

Phase 2b (204 Study)

Day 1 | Day 42 | Day 84

Day 1

Day 42

Day 84
### Overview of Three Most Recently Approved Topical Psoriasis Drugs

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Trial Size (Active vs Vehicle)</th>
<th>Efficacy Endpoint</th>
<th>Efficacy (Active/Vehicle)</th>
<th>Active Ingredient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sorilux</strong></td>
<td>8 223 vs 113 214 vs 109</td>
<td>“clear” or “almost clear” with 2+ grade improvement in PGA</td>
<td>14%/7% 27%/16%</td>
<td>Calcipotriene (vitamin D analog)</td>
</tr>
<tr>
<td><strong>Vectical</strong></td>
<td>8 209 vs 209 210 vs 211</td>
<td>“clear” or “minimal” with 2+ grade improvement in PGA</td>
<td>23%/14% 21%/7%</td>
<td>Calcitriol (vitamin D)</td>
</tr>
<tr>
<td><strong>Taclonex</strong></td>
<td>4 490 vs 157 476 vs 157</td>
<td>“Absent” or “very mild” with 2-grade improvement</td>
<td>48%/8% 26%/8%</td>
<td>Combination of: 1) Calcipotriene 2) Betamethasone Dipropionate</td>
</tr>
</tbody>
</table>

**Components**

- Betamethasone Dipropionate (high potency steroid)
- Calcipotriene (vitamin D analog)
Local Tolerability Trial Demonstrates Potential for Wider Use in Psoriasis

- AN2728 Ointment, 2% was applied to sensitive areas BID for 21 days
  - Elbows and knees
  - Groin, axillae, gluteal cleft, retroauricular areas
  - Face / hairline
- AN2728 Ointment, 2% appears to be safe and well-tolerated when applied to sensitive skin areas
  - Adverse events occurred at a low rate and were generally mild
  - None of the treated anatomic areas appeared to be particularly sensitive to irritation by the study drug
- Reduces risk of treating areas of “inverse” psoriasis in Phase 3; increasing potential for non-restrictive psoriasis indication
- Increases probability of safe and well-tolerated treatment of areas typically affected by atopic dermatitis

Local Tolerability: Mean Change from Baseline

- **Burning & Stinging**
  - Mean change from baseline for different anatomical areas
- **Pruritus**
  - Mean change from baseline for different anatomical areas
Conclusions

- AN2728 has demonstrated efficacy in the range of mid-potency steroids and vitamin D analogs
- Safety has been demonstrated in 14 clinical trials
- Plans to initiate Phase 3 in psoriasis to follow Phase 2 results in atopic dermatitis
- Additional opportunity in inverse psoriasis
  - Significant unmet medical need for topical therapy to treat psoriasis that involves the face, skin folds, recesses and genitalia
  - No topicals currently approved for inverse psoriasis
  - Results of the Local Tolerability Study indicate that AN2728 could meet that need
AN2728 Market Opportunity

Geoff Parker, CFO

Initial Sales Ramp of Protopic and Elidel
Demonstrated Demand for Safe Non-steroidal
Topical Treatment for Atopic Dermatitis

Protopic and Elidel Generated Over $500M in Sales Prior to FDA Black Box Warning in 2005

Protopic and Elidel WW Sales
($ in millions)

Source: SEC filings and company reports
## Assumptions for Peak U.S. Sales

<table>
<thead>
<tr>
<th></th>
<th>Atopic Dermatitis</th>
<th>Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence (U.S.)</strong> (a)</td>
<td>6.6 - 15.8 million</td>
<td>~7 million</td>
</tr>
<tr>
<td><strong>Total Rx’s for A.D.</strong> (c)</td>
<td>~6 million</td>
<td>~4 million</td>
</tr>
<tr>
<td><strong>AN2728 Rx Share</strong> (d)</td>
<td>25% (50% of survey results)</td>
<td>10% (50% of survey results)</td>
</tr>
<tr>
<td><strong>AN2728 Rx’s for A.D.</strong></td>
<td>1.5 million</td>
<td>400K</td>
</tr>
<tr>
<td><strong>Price per Rx</strong> (e)</td>
<td>$350</td>
<td>$350</td>
</tr>
<tr>
<td><strong>Estimated Peak U.S. Sales</strong></td>
<td>$525M</td>
<td>$140M</td>
</tr>
</tbody>
</table>

(a) NIH. U.S. incidence is based on prevalence of 1%-3% in adults and 10% - 20% in children
(b) National Psoriasis Foundation
(c) IMS (topical treatments)
(d) Results of two surveys based on current target product profile - 1) Atopic dermatitis survey included 53 dermatologists and 2) psoriasis survey included 75 dermatologists.
(e) Represents a blended price for 30g, 60g, and 100g tubes

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**Overview of Cost Assumptions**

Geoff Parker, CFO
Low COGS and Specialty Salesforce Costs Should Lead to Strong Operating Margins

### Estimated Cost of Goods Sold (a)

<table>
<thead>
<tr>
<th>Product</th>
<th>Cost per Course of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tavaborole</td>
<td>~$40 per course of therapy (12 bottles)</td>
</tr>
<tr>
<td>AN2728</td>
<td>~$6 - $12 per course of therapy (30g or 60g tube)</td>
</tr>
</tbody>
</table>

### Estimated Salesforce Cost

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Podiatrists</td>
<td>~10,000</td>
</tr>
<tr>
<td># of Dermatologists</td>
<td>~15,000</td>
</tr>
<tr>
<td>Salesforce size to cover</td>
<td>60-120</td>
</tr>
<tr>
<td>dermatologists and podiatrists</td>
<td></td>
</tr>
<tr>
<td>Annual cost per salesperson</td>
<td>$200K to $250K</td>
</tr>
<tr>
<td>Total annual salesforce cost</td>
<td>$12M to $30M</td>
</tr>
</tbody>
</table>

(a) Estimates based on costs as of June 2012

Q&A and Panel Discussion

Karl Beutner, M.D., Ph.D.
Lawrence Eichenfield, M.D.
Mark Lebwohl, M.D.
Richard Pollak, D.P.M., M.S.
Jonathan Wilkin, M.D.