Illuminating Science...Empowering Patients

COMPANY OVERVIEW

Dr. Neal Walker
President and CEO

November 2017
Any statements contained in this presentation that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "believe", "expect", "may", "plan," "potential," "will," and similar expressions, and are based on Aclaris' current beliefs and expectations. These forward-looking statements include expectations regarding Aclaris' use of cash through the first quarter of 2019, development programs in skin and hair conditions, and the clinical development of JAK inhibitors. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the conduct of clinical trials, Aclaris' reliance on third parties over which it may not always have full control, and other risks and uncertainties that are described in the Risk Factors section of Aclaris' Annual Report on Form 10-K for the year ended December 31, 2016, Form 10-Q filed for the quarter ended September 30, 2017, and other filings Aclaris makes with the U.S. Securities and Exchange Commission from time to time. These documents are available under the "Financial Information" section of the Investors page of Aclaris' website at http://www.aclaristx.com. Any forward-looking statements speak only as of the date of this presentation and are based on information available to Aclaris as of the date of this release, and Aclaris assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.
Our Corporate Strategy: Building a Fully-Integrated Biopharmaceutical Company

**APPLY UNIQUE LEADERSHIP INSIGHTS**

- Founded and partnered multiple companies
- 250+ years of relevant experience in dermatology
- Combined 300+ years of drug discovery experience in immunology
- Board-certified dermatologists as CEO and CSO
- Key leadership with track record of executing across multiple development and commercial stage companies

**ACCELERATE NOVEL, DIVERSE PIPELINE**

- **A-101**
  - A-101 40%
    - Seborrheic Keratosis
    - December 24, 2017 PDUFA
    - MAA submission July 2017
  - A-101 45%
    - Common Warts
    - Initiated Phase 2 clinical trials June 2017
- **Immunology Portfolio**
  - JAK 1/3 Inhibitors (ATI-50001/ATI-50002)
    - Alopecia Areata
    - Vitiligo
  - MK-2 inhibitor (ATI-450)
    - Psoriasis, Psoriatic Arthritis
  - Soft JAK inhibitor
    - Androgenetic Alopecia (AGA)
  - ITK inhibitor
    - Atopic Dermatitis, Psoriasis

**ASSET AND COMMERCIAL STRATEGY**

- Time and capital efficient
- Offer physicians opportunity to expand practice with new self-pay aesthetic treatments
- Focus on large, underserved market segments in dermatology and adjacent therapeutic areas with no FDA-approved medications and/or where treatment gaps exist
## Pipeline

*Diversified Aesthetic and Medical Immuno-dermatology/Immunology Portfolio*

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication(s)</th>
<th>Discovery</th>
<th>Pre-Clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Filed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A-101 (40%) Topical</strong></td>
<td>Seborrheic Keratosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A-101 (45%) Topical</strong></td>
<td>Common Warts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATI-50002 Topical</strong></td>
<td>Alopecia Areata</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATI-50001 Oral</strong></td>
<td>Alopecia Areata</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATI-50002 Topical</strong></td>
<td>Vitiligo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Soft” JAK Inhibitor</td>
<td>Hair Loss - androgenetic alopecia (AGA), Inflammatory Skin Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Topical</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MK-2 Inhibitor</strong></td>
<td>Psoriasis, Psoriatic Arthritis, RA, Inflammatory Bowel Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Oral</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ITK “Oral anti-IL17”</strong></td>
<td>Atopic Dermatitis, Psoriasis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Oral</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ITK “Topical anti-IL17”</strong></td>
<td>Atopic Dermatitis, Psoriasis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Topical</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Additional Compounds</strong></td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novel Targets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: The pipeline includes compounds targeting various skin and immunological conditions, with phases ranging from Discovery to Filed.*
Markets Poised for Continued Growth: Self-Pay Aesthetic and Medical Dermatology

Global dermatology market valued at **$20 billion** in 2015, growing at CAGR of 7.7%\(^1\)...

Global aesthetic market expected to reach **$13.29 billion** by 2021, growing at CAGR of 10.8%\(^2\)...

...and non-surgical procedures increased by 650% from 1997-2016\(^3\)

“The types of procedures being performed is changing. Most of the growth has been in minimally invasive cosmetic procedures.”
- *The Washington Post, March 2, 2016*

---


Focus on Conditions with Significant Treatment Gaps

SEBORRHEIC KERATOSIS (SK)

83.8MM people
in U.S.\(^1\); current treatments invasive or painful\(^2\), no FDA-approved medications

COMMON WARTS (VERRUCA VULGARIS)

22+MM people
in U.S.\(^3\); current treatments show only modest therapeutic effect and have significant limitations\(^4,5\)

ALOPECIA AREATA (AA)

6.8+MM people
in U.S. have had or will develop AA\(^6\); current available Rx treatment options used off label and have significant limitations

PATTERN HAIR LOSS (ANDROGENETIC ALOPECIA)

35MM men and 21MM women
in U.S. suffered from hair loss in 2012\(^7\); demand for treatment high

VITILIGO

1-2% overall global
population impacted\(^8\), no FDA-approved medication to repigment the skin\(^9\)

---

9 ASDReports. The Vitiligo Therapeutics Market is Expected to Show Moderate Growth up to 2019. 08.22.2012.
A-101 40% Topical Solution
LEAD CANDIDATE FOR SEBORRHEIC KERATOSIS
Favorable Market Dynamics for a New Seborrheic Keratosis (SK) Topical Treatment

Large Market

SEBORRHEIC KERATOSIS (SK)

83.8M people

in U.S.\(^1\); 8.3 million SK treatments by dermatologists annually\(^2\)

Motivated Patient Base

- SK associated with aging; 72% of affected patients are between ages 40-74\(^3\)
- Large number of SK patients motivated to treat SKs due to concerns about appearance and health, especially when SKs appear on the face or neck\(^4\)
- Number of minimally invasive aesthetic procedures up more than six-fold from 1997-2015\(^5\)

Concentrated Physician Targets

- Dermatologists manage a majority of SK cases (~80%), primary care refers to derm\(^3\)
- ~5K dermatologists most active in treating SK; many believe current treatment options have limitations\(^2\)

SK Distribution\(^4\)
% of Patients who Have SKs on the:

- FACE or NECK 80%
- TRUNK 85%
- ARMS 61%

80%

83.8M people

Concentrated Physician Targets

- Dermatologists manage a majority of SK cases (~80%), primary care refers to derm\(^3\)
- ~5K dermatologists most active in treating SK; many believe current treatment options have limitations\(^2\)

3 IMS National Disease and Therapeutic Index 2016.
Significant Unmet Need in SK Treatment

CURRENT TREATMENT OPTIONS ARE OFTEN INVASIVE OR PAINFUL…¹

- No FDA-approved medications
- Around two-thirds of SK treatments are performed through cryosurgery
- Other less common treatments include:
  - Curettage
  - Electrodesiccation
  - Excision, usually shave

A-101 IS AN APPEALING CONCEPT FOR SK TREATMENT

- Topical, non-invasive
- Minimal discomfort / Minimal downtime
- Reduced risk of pigmentary changes and scarring
- Can treat larger numbers of lesions
- Ability to hand off to ancillary staff
- MOA: Drives an apoptotic and necrotic cell death

¹ Jackson et al, Current Understanding of Seborrheic Keratosis: Prevalence, Etiology, Clinical Presentation, Diagnosis, and Management, Journal of Drugs in Dermatology; 14:10, 2015; 1119-1125
A-101 40% Topical Solution Phase 3 Data
# A-101 40% Topical Solution Phase 3 Pivotal Trials SEBK-301 and SEBK-302

## Trial Design
- Two identical multi-center, randomized double-blind, placebo-controlled trials conducted in the U.S., which enrolled a total of 937 patients
- Assessed safety, efficacy, and tolerability of A-101 40% topical solution versus placebo
- Patients were 18 years and older, and received up to two treatments on four target lesions, 21 days apart

## Primary Endpoint
- Primary efficacy endpoint was the percentage of patients with clearance (PLA=0) of all four target lesions at 106 days after first treatment

## Secondary and Other Endpoints
- Secondary efficacy endpoint was the percentage of patients with clearance (PLA=0) in at least three of the four target lesions
- Mean per-patient percentage of target lesions judged to be clear/near-clear (PLA≤1)
- Percentage of all target lesions of the face judged to be clear/near-clear (PLA≤1)

## Safety
- Safety – assessed adverse events, local skin reactions, vitals and clinically-relevant abnormal lab results
A-101 Patients Achieved the Primary Endpoint of Clearance of All 4 Target SK Lesions and the Secondary Endpoint of Clearance of at Least 3 of 4 Target SK Lesions

Day 106

<table>
<thead>
<tr>
<th>Study</th>
<th>Vehicle</th>
<th>A-101 40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-101-SEBK-301</td>
<td>0</td>
<td>4.0%</td>
</tr>
<tr>
<td>A-101-SEBK-302</td>
<td>0</td>
<td>7.8%</td>
</tr>
</tbody>
</table>

(US PRIMARY REGULATORY ENDPOINT)

(US PRIMARY REGULATORY ENDPOINT)

Day 106

<table>
<thead>
<tr>
<th>Study</th>
<th>Vehicle</th>
<th>A-101 40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-101-SEBK-301</td>
<td>0</td>
<td>13.5%</td>
</tr>
<tr>
<td>A-101-SEBK-302</td>
<td>0</td>
<td>23.0%</td>
</tr>
</tbody>
</table>

(EU PRIMARY REGULATORY ENDPOINT)

(EU PRIMARY REGULATORY ENDPOINT)
A-101 Patients Had Significantly More Target Lesions of the Face Judged to Be Clear/Near Clear (PLA<1)

**Study A-101-SEBK-301**

Day 106

- **Vehicle**: 14.7%
- **A-101 40%**: 64.6%

**P<0.001**

**Study A-101-SEBK-302**

Day 106

- **Vehicle**: 6.2%
- **A-101 40%**: 65.9%

**P<0.001**
Phase 3 Patient Photos: PLA 3 to PLA 0 (Clear)

Pre-Treatment with A-101

Final Visit Follow-Up

Male

Skin Type: 3

Location: Face

Male

Skin Type: 3

Location: Face
Phase 3 Patient Photos: PLA 1 (Near Clear)

Female
Skin Type: 2
Location: Back

Pre-Treatment with A-101

Final Visit Follow-Up
Phase 3 Patient Photos: PLA 1 (Near Clear)

Pre-Treatment with A-101

Final Visit Follow-Up

**Female**
**Skin Type:** 1
**Location:** Back

**Female**
**Skin Type:** 2
**Location:** Face

**Female**
**Skin Type:** 3
**Location:** Back
Local Skin Reactions Were Mostly Mild/Moderate in Severity (Study 301+302; percentage of lesions, at Day 106)

<table>
<thead>
<tr>
<th>Condition</th>
<th>A-101 40%</th>
<th>0 = No Reaction</th>
<th>1 = Mild</th>
<th>2 = Moderate</th>
<th>3 = Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperpigmentation</td>
<td>A-101 40%</td>
<td>92.2%</td>
<td>7.0%</td>
<td>0.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>99.8%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Hypopigmentation</td>
<td>A-101 40%</td>
<td>97.0%</td>
<td>2.9%</td>
<td>0.1%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>99.9%</td>
<td>0.1%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Scarring</td>
<td>A-101 40%</td>
<td>99.6%</td>
<td>0.4%</td>
<td>0.1%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Atrophy</td>
<td>A-101 40%</td>
<td>99.8%</td>
<td>0.2%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Crusting</td>
<td>A-101 40%</td>
<td>94.6%</td>
<td>4.7%</td>
<td>0.6%</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>95.6%</td>
<td>3.1%</td>
<td>1.2%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Edema</td>
<td>A-101 40%</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Erosion</td>
<td>A-101 40%</td>
<td>99.9%</td>
<td>0.1%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Erythema</td>
<td>A-101 40%</td>
<td>89.9%</td>
<td>9.7%</td>
<td>0.4%</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>99.2%</td>
<td>0.8%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Scaling/Dryness</td>
<td>A-101 40%</td>
<td>92.0%</td>
<td>7.7%</td>
<td>0.2%</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>93.1%</td>
<td>6.5%</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Ulceration</td>
<td>A-101 40%</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>99.9%</td>
<td>0.1%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Vesicles/Bullae</td>
<td>A-101 40%</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>A-101 Vehicle</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
Favorable Market Dynamics: High Level of Patient Interest in SK Treatment

83.8M People in the US with SK\(^1\)

18.5M visits to Derm for SK\(^2\)

8.3M SK treatments\(^2\)

Opportunity to Engage Motivated Patients via DTC

83% of SK patients are interested in treatment and willing to pay out-of-pocket\(^3\)

73% of female SK patients are so bothered by SK that they have tried to hide, disguise or remove their lesions on their own\(^3\)

42% of male SK patients are so bothered by SK that they have tried to hide, disguise or remove their lesions on their own\(^3\)

Reasons for Not Removing SKs Include\(^3\):

- Risk of scarring
- Risk of hypopigmentation
- Want to avoid pain or discomfort

---

## A-101 Market Strategy

### Buy and Bill Model
- Self-pay, minimally invasive procedure
- Lower cost relative to other aesthetic treatments (Botox®, fillers, lasers)
- Number of minimally invasive aesthetic procedures up six-fold from 1997-2015

### A-101 Positioning
- A-101 positioned for SKs located in highly visible areas
- Providers more risk-averse when treating cosmetically sensitive areas
- Patients most motivated to treat SKs in highly visible areas

### Commercial Launch
- 50-60-person specialty sales team focused on high-tier targets
- Comprehensive promotional campaign to include peer-influence programs

### Patient Engagement
- DTP/DTC Campaigns focused on driving awareness and furthering interest in treatment options

---

A-101 45% Topical Solution Candidate For Common Warts
Existing Patient Base Offers Significant Market Potential

2+ million patient visits to HCPs annually for treatment of common warts

- 43% of patients have more than one wart
- Patients with warts have a higher risk of developing new warts

59% of visits are to a dermatologist

25% of visits are to a pediatrician

11% of visits are to a family/general practitioner

1 IMS National Disease and Therapeutic Index 2016.
## Summary of A-101 Phase 2 Wart Clinical Trial Results

<table>
<thead>
<tr>
<th>Trial</th>
<th>Common Wart Area</th>
<th>Topline Data</th>
<th>Trial Objective and Design</th>
<th>Trial Outcome</th>
</tr>
</thead>
</table>
| WART–201 (n=98) Phase 2 | Trunk and Extremities | August 2016 | - Multicenter, parallel group  
- One wart treated  
- A-101 concentrations: 40%, 45% compared to vehicle  
- 8 applications  
- Duration: 56 days | - Efficacy: Statistically significant clearance with 45% concentration  
- Favorable safety profile |

### Primary Endpoint:

Mean change from baseline in the Physician’s Wart Assessment (PWA) score at Visit 10 using an analysis of covariance

### Secondary Endpoints:

- Responder analysis: The proportion of subjects whose target wart is judged to be clear on the PWA at Visit 10.
- Responder analysis: The proportion of subjects whose target wart is judged to be clear or mild on the PWA at Visit 10.
- Durability of Response analysis: For each active treatment group, the proportion of those subjects whose target wart is judged to be clear at Visit 10 who also remain clear at Visit 13 will be calculated and presented, along with the lower bound of the 95% confidence limit around each proportion.
Statistical Significance Achieved on Secondary Endpoints in Clearance of Common Warts With A-101 45% Concentration

Responder Analysis

Proportion of Subjects Achieving Wart Clearance at Visit 10

- Vehicle: 3.7%
- A-101 40.0%: 3.1%
- A-101 45.0%: 25.8%

Proportion of Subjects Achieving Clear or Barely Evident on PWA at Visit 10

- Vehicle: 14.8%
- A-101 40.0%: 15.6%
- A-101 45.0%: 41.9%

P = 0.02
### Study WART-201: Skin Reactions Similar to Vehicle at Visit 10

<table>
<thead>
<tr>
<th>Condition</th>
<th>A-101 40%</th>
<th>A-101 45%</th>
<th>A-101 Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Edema</strong></td>
<td>100.0%</td>
<td>100.0%</td>
<td>96.3%</td>
</tr>
<tr>
<td><strong>Erosion</strong></td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Erythema</strong></td>
<td>75.0%</td>
<td>80.7%</td>
<td>92.6%</td>
</tr>
<tr>
<td><strong>Excoriations</strong></td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Scabbing</strong></td>
<td>81.3%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Ulceration</strong></td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Vesicles/Bullae</strong></td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

0 = No Reaction  
1 = Mild  
2 = Moderate
Patient Treated with A-101 45% Concentration in Study WART-201

Pre-Treatment with A-101

Visit 2 (PWA 3)

Visit 10 (PWA 0)

Post-Treatment with A-101
Study WART-201: Based on Results, A-101 45% Concentration to be Further Developed as Treatment for Common Warts

### 45% Concentration of A-101 Met Phase 2 Objectives

| Efficacy and Durability | • Achieved both statistical and clinical significance on the primary endpoint  
                          | • Achieved statistical significance in complete clearance of the warts  
                          | • Only 1 incidence of recurrence 3 months post-treatment |
|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| Safety Profile          | • Favorable safety profile was observed under the conditions of this study  
                          | • Occasional mild, transient local skin reactions observed during treatment; skin reactions were similar to vehicle |
| Next Steps              | • Develop A-101 45% concentration as the initial commercial dosage form for common warts  
                          | • Develop as Rx drug for patient to use at home  
                          | • Two ongoing Phase 2 studies in which patients self-administer A-101 45% |
Core Intellectual Property: A-101

- **Issued US Patent # 7,381,427**
  - Directed to high concentration H$_2$O$_2$ methods of use for treating/removing SK.
  - Orange Book listed for SK indication - estimated expiry date w/ potential PTE of 2½ yrs ~ 2025.

- **Issued US Patent # 9,675,639**
  - Encompasses Formulations / MOU / Applicators for A-101 ~ total of 70 claims
  - Eligible for listing in Orange Book for A-101 Topical Solution
  - Expires July 2035

- **US Provisional Application**
  - Directed to methods and compositions for the treatment of warts.
  - Filed upon obtaining Aclaris Wart-201 Study data - Natural expiry 2037.

- **Potential NCE Exclusivity for at least 7½ years from approval**
  - No ANDA/505(b)(2) for same active moiety for any indication can be reviewed or approved for 5 years.
    - 30 months from notice (after year 5)

- **Exclusive supply agreement with only cGMP manufacturer of Active Pharmaceutical Ingredient**
  - Exclusivity for 10 years from time of 1st commercial sale of product.
JAK Inhibitor Candidates
ATI-50001 and ATI-50002 – Selective JAK 1/3 inhibitor

Additional topical JAK inhibitors in development
- Oral and topical rights
- Known MOA and biological response in humans
- Promoted hair regrowth in mouse model
- Broad IP estate
- Know how and methods of use covering JAK inhibitors for the treatment of:
  - Alopecia areata
  - Androgenetic alopecia (male and female pattern hair loss)
  - Additional hair loss disorders

ATI-50001
Oral treatment for alopecia totalis, alopecia universalis and vitiligo

ATI-50002
Topical treatment for patchy alopecia areata and vitiligo

Topical JAK inhibitors
Topical treatment for androgenetic alopecia

Portfolio and IP Estate:

ATI-50001 and ATI-50002: JAK Inhibitors in Alopecia Areata, Vitiligo and Androgenetic Alopecia

1 Data on File. Aclaris Therapeutics Inc.
Alopecia Areata (AA)

- 6.8+ million people in the U.S. have had or will develop AA during their lives
  - 25-50% of patients have persistent patchy AA
  - 14-25% of patients progress to alopecia totalis or universalis
- AA is an autoimmune condition characterized by patchy, non-scarring hair loss on the scalp and body
  - Alopecia Areata – patchy hair loss on scalp
  - Alopecia Totalis – complete hair loss on scalp
  - Alopecia Universalis – complete hair loss on scalp, face and body
- 2/3 of affected individuals ≤30 years old at disease onset
- Translational research work by Dr. Angela Christiano at Columbia University

---

Mechanism of Action: JAK Inhibitors in Alopecia

Ruxolitinib (Incyte) and Tofacitinib (Pfizer) in Alopecia Areata

Baseline

Week 24

RUXO - Baseline SALT 64%. Duration of hair loss 12 years. 6 months 20mg BID. Last SALT 1%

TOFA - Baseline SALT 100%, 5 months 5mg BID, 2 months 10/5 mg BID, 3 months 10mg BID ongoing. Last SALT 39%.

TOFA - Baseline SALT 84%, 6 months 5mg BID, 0 months 10/5mg, 0 months 10mg. Last SALT 0%.

TOFA - Baseline SALT 46%, 5 months at 5mg BID, 2 months at 10/5mg, 2 months 10mg ongoing. Last SALT 12%.
ATI-50001 Prevents and Reverses Alopecia Areata

ATI-50001 Prevents AA

ATI-50001 chow: 0.5g ATI-50001 disodium/kg diet

ATI-50001 reverses AA

#1

Baseline   6WK

N=10

#2

Baseline   6WK

N=4

Control

N=10

ATI-50001 chow

N=4
Topical JAK Inhibitors are Effective \textit{In Vivo} (ATI-50002)

Topical Small Molecule JAK Inhibitors Reversed Established AA in Mouse Model*
ATI-50001 Targets IFN-γ producing CD8+ Cytotoxic T cells

<table>
<thead>
<tr>
<th>Skin Draining Lymph Nodes</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated AA</td>
<td>AA treated w/ ATI-50001</td>
</tr>
<tr>
<td>CD4</td>
<td>CD4</td>
</tr>
<tr>
<td>3.71</td>
<td>2.14</td>
</tr>
<tr>
<td>0.060</td>
<td>0.027</td>
</tr>
<tr>
<td>95.7</td>
<td>97.5</td>
</tr>
<tr>
<td>0.54</td>
<td>0.34</td>
</tr>
<tr>
<td>CD8</td>
<td>CD8</td>
</tr>
<tr>
<td>52.5</td>
<td>23.4</td>
</tr>
<tr>
<td>0.54</td>
<td>0.031</td>
</tr>
<tr>
<td>47.0</td>
<td>76.5</td>
</tr>
<tr>
<td>0.038</td>
<td>0.039</td>
</tr>
<tr>
<td>IFN-γ</td>
<td>IFN-γ</td>
</tr>
<tr>
<td>18.0</td>
<td>4.58</td>
</tr>
<tr>
<td>IL-17</td>
<td>CD8</td>
</tr>
<tr>
<td>42.9</td>
<td>22.1</td>
</tr>
</tbody>
</table>

Major IFN-γ producing T cells are CD8+ T cells in AA mice. ATI-50001 targets IFN-γ producing CD8+ T cells.
Vitiligo is a common autoimmune disease where melanin (pigment) is absent, causing lighter patches of skin to appear on various parts of the body.\(^1,2\)

- Vitiligo impacts 1-2% of the overall global population irrespective of sex, race or age.\(^3\)
- Disease onset occurs in about one-half of sufferers between the ages of 10 and 30.\(^3\)
- Product candidates: Oral (ATI-50001) and topical (ATI-50002) JAK inhibitors

---

1 Roddick, J. Autoimmune Diseases. Healthline. 07.22.2015.
2 Oakley, A. Vitiligo. DermnetNZ. 08.2015.
Additional Potential Indications - AGA

- Androgenetic alopecia (male/female pattern hair loss)
- AGA, a genetic disorder, is the most common cause of hair loss\(^1\)
- Experienced by 70% of men and 40% of women at some point in their lives.\(^1\) In 2012, 35 million men and 21 million women suffered hair loss.\(^2\)
- Sufferers are highly motivated to seek treatment.\(^1\)
- Product candidate: Topical “Soft” JAK inhibitors in development


Core Intellectual Property: JAK inhibitor

- US & Global JAK IP estate consisting of >150 patents/applications (issued and/or pending)
- Exclusive license with Rigel Pharmaceuticals for ATI-50001 & ATI-50002 (COM) in dermatology
  - US Natural expiry dates 2030-2034 + potential applicable PTE
  - Corresponding patents & applications in 18 additional jurisdictions (EU, AU, CA, IN, JP, others) - Natural expiry dates 2030 + potential applicable PTE
- Exclusive license under Columbia University
  - Covers the use of certain JAK inhibitors for the treatment of AA, AGA, and other hair loss disorders and biomarkers to identify potential responders
  - This portfolio includes a recently issued U.S. patent and recently allowed U.S. applications directed to methods of treating AA, AGA and other hair loss disorders by administering ruxolitinib, baricitinib, decernotinib, or tofacitinib, and a recently issued patent in Japan directed to pharmaceutical compositions comprising ruxolitinib, baricitinib, or tofacitinib for use in treating AA, AGA and other hair loss disorders.
  - Natural expiry date 2031
  - Pending applications in Europe, Japan and Korea
Confluence Life Sciences

**Assets**
- JAK inhibitors - oral and topical - (next generation)
- ITK inhibitors - oral and topical - (“anti-IL-17”)
- MK-2 inhibitor - oral - (“anti-TNF”)

**Platform**
- KINect™ platform – drug discovery engine
- Proprietary compound library and computational chemistry capability
- Medicinal chemistry, disease biology, immunology, pharmacology and preclinical development expertise

**People**
- Co-inventors of tofacitinib and former leaders of Pfizer kinase program (including JAK inhibitors)
- Kinome experts - chemists and biologists; combined 300+ years of drug discovery experience
- Significant experience in small molecule drug discovery through Phase II
Confluence Expected to Drive Future Growth

*Short term and Long term*

- Synergies in drug discovery through Phase 2
  *Internalizes preclinical research and development services which are currently outsourced*

- CRO business facilitates cutting edge technology and disease expertise in immunology, pharmacology and biochemistry
  *
  *Cash neutral in near-term*

- Supports and extends Aclaris’ JAK kinase inhibitor programs

- Enables targeted development of novel therapeutics for inflammation and immunology in dermatology and adjacent therapeutic areas
Confluence Assets

**MK-2 Pathway Inhibitor ATI-450 “Oral Anti-TNF”**
- Psoriasis / Psoriatic Arthritis, RA, CAPS, Chronic Inflammation
- Highly potent and designed to escape tachyphylaxis associated with global p38 kinase inhibitors

**JAK Inhibitors**
- Alopecia Areata, Vitiligo, AGA, Inflammatory Disorders
- Highly selective, covalent and non-covalent. Oral and soft topical formulation

**ITK Inhibitors “Oral Anti-IL17”**
- Atopic Dermatitis, Psoriasis
- Oral and soft topical formulation

**Early Discovery Portfolio**
- Leverage mechanisms in play to maximize opportunities
- Utilize KINect™ platform for exciting new kinase targets
Platform - KINect™ Innovation Engine

- Concentrated effort in immunology: autoimmune disease and chronic inflammation
- Cysteinome targeted chemical library (60% of the kinome)
- Focused on a number of important but hard-to-drug kinases
- Structural analysis, KINect™ chemical library, screening in validated bioassays, SBDD (Schrödinger enabled) and medicinal chemistry
- KINect™ library interrogates both Type 1 and Type 2 kinases vs competitors who focus only on a few subgroups of Type 1 kinases
- KINect™ addresses both reversible and irreversible inhibitors
Platform - Research and Development Capabilities

**BIOCHEMISTRY & ENZYMEOLOGY**
- Leaders in Mechanistic Enzymology
- Custom Assay Development
- Compound: Target Interaction
- Enzyme Inhibitor Mechanisms
- Direct Binding Kinetics
- High Throughput Screening

**CELL & MOLECULAR BIOLOGY**
- Target Clone/Express/Purification
- Translatable Cellular Assays
- Target Modulation/Disease Assays
- Cell Pathway Interrogation
- Custom Assay Development
- Multiple Assay Platforms

**TRANSLATIONAL RESEARCH**
- Biomarker Assay Development
- Clinical Biomarker Assessment
- In vivo Efficacy and PK Studies
- PK/PD Relationship
- Release Assay Validation

**IMMUNOLOGY & IMMUNO-ONCOLOGY**
- Cytokine Expression
- Th Cell Differentiation/Activation
- CTL Differentiation and Function
- B Cell and NK cell Function
- Ag Specific Cell and In Vivo Models
- HWB/PBMC/Monocyte Assays

**BIOANALYTICAL CHEMISTRY**
- Non-GLP Analytical
- Bioanalytical Method Development
- Bioanalytical Method Validation
- Pharmacokinetic/Toxicokinetic Analysis
- Ab Solubility and Aggregation

**COMPUTATIONAL & MEDICINAL CHEMISTRY**
- Schrödinger™ Enabled Structure Based Drug Design
- Computational Chemistry
- Library Design
- Compound Synthesis
Confluence People - Ex-Pfizer “Kinase and JAK experts”

**Walter Smith**
CEO
Former VP Research & Global Head, Pfizer Inflammation, co-leader of Pfizer Licensing Team
Delivered 8 clinical candidates, 6 INDs and 1 NDA in inflammation and cancer

**Joseph Monahan, PhD**
CSO/Founder
Former Executive Director, Pfizer Inflammation Research and Leader of Global Kinase Technology Team
>95 publications and patents (>30 total on kinases)

**Jon Jacobsen, PhD**
Chemistry Director
Former Research Fellow and Director, Pfizer Chemistry
>100 publications and patents (15 total on kinases)
Project Lead for PFE JAK Program

**Paul Changelian, PhD**
Biology Director
Immunologist/drug discovery leader at pharma (Pfizer) & biotech (Lycera, Infinity)
Validated JAK 1/3 as target for transplant/RA/psoriasis, leading to approval of Xeljanz®

---

<table>
<thead>
<tr>
<th>Program Initiation</th>
<th>Hit</th>
<th>Lead</th>
<th>Candidate</th>
<th>IND</th>
</tr>
</thead>
</table>

**BIOLOGY and COMPOUND PROFILING**
- Enzyme/Cellular assay development and screening
- Immunology models
- *In vivo* efficacy studies
- *In vitro* ADME
- *In vitro /In vivo* Metabolite profiling
- *In vivo* DMPK
- *In vivo* toxicology

**CHEMISTRY**
- Structure based drug design
- Medicinal Chemistry
- API synthesis
- Process Development
- Pre-Clinical cGMP API production
- CMC generation
- Patent filing

**PRE-CLINICAL IND ENABLING STUDIES (GLP)**
- GLP Analytics
- Drug-Drug Interaction
- Genetic toxicology
- Safety pharmacology
- Definitive PK
- General toxicology
- Biomarker development
The Kinase Opportunity – Rational Targeted Drug Discovery

Creating New Medicines Targeting Previously Inaccessible Parts of the Kinome

KINect™ Technology Platform

Proprietary chemical library and integrated capabilities for interrogating the Kinome

• Solves challenges encountered in the class
  • Selectivity
  • Biochemical efficiency
• Validity of targeting kinases is commercially established
• Plethora of validated kinase targets are inadequately drugged
• Kinect™ platform allows rational targeting of validated kinase targets

Kinase Drugs Represented $240B in Aggregate Global Sales from 2011-2015

500 member class, representing 2% of the human genome
Confluence Pipeline

**MK2:** Innate immune response – clinically validated by Humira®, Actemra®, Kineret®

**ITK:** T-cell receptor dependent autoimmune disease – clinically validated by Neoral®, Prograf®, Orencia®

**JAK:** Inflammatory cytokine dependent inflammation – clinically validated by Xeljanz®, Jakifi®
Confluence Pipeline: Antigen and Cytokine Receptor Signaling Inhibitors for Dermatology

- **Alopecia Areata**: IFN$_{\gamma}$ (JAK1/2) and IL-15 (JAK1/3)
- **Vitiligo**: IFN$_{\gamma}$ (JAK1/2) and IL-15 (JAK1/3)
- **Psoriasis**: IFN$_{\gamma}$ (JAK1/2), IL-12/23 (JAK2/Tyk2), IL-22 (JAK1/Tyk2) and IL-21 (JAK1/3)
- **Atopic Dermatitis**: IFN$_{\gamma}$ (JAK1/2), TSLP (JAK1/2), IL-22 (JAK1/Tyk2) and IL-4/IL-21 (JAK1/3)
- All autoimmune disease driven by antigen recognition/T cell receptor (ITK)
Building a Fully Integrated Biopharmaceutical Company

Executive Team
Proven track record of R&D, commercial execution, and business development

Commitment to Patients
Focus on “white-space” or underserved diseases where treatment gaps exist

Pipeline
Multiple therapeutic programs ranging from discovery to NDA filed

Strong Cash Position
~$240 million pro forma June 30, 2017

Commercial Infrastructure
50-60 person sales force with expected launch 2018

Research and Development
Scientific leadership in immuno-dermatology and immunology- innovative clinical and regulatory strategies

KINect™ Technology Platform
Proprietary discovery engine enables targeted design of novel drug candidates

Intellectual Property
US & Global IP estate consisting of >150 patents/applications (issued and / or pending)
## Milestones

<table>
<thead>
<tr>
<th>Milestone</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A-101 SK</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Submit NDA</td>
<td>Q1</td>
<td></td>
</tr>
<tr>
<td>Submit MAA</td>
<td>Q2</td>
<td>Q3</td>
</tr>
<tr>
<td>Expected U.S. Approval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expected U.S. Launch</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A-101 Common Warts</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate Two Additional Phase 2 Trials</td>
<td>Q1</td>
<td>Q2</td>
</tr>
<tr>
<td>Additional Phase 2 data</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATI-50001/ATI-50002 Alopecia Areata</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate Phase 2 (ATI-50001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Submit IND (ATI-50002)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate Phase 2 (ATI-50002)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATI-50001/ATI-50002 Vitiligo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate Phase 2 (ATI-50002)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
THANK YOU

www.aclaristx.com