

EMPOWERING PATIENTS THROUGH  
**REVELATIONARY**  
SCIENCE

## Company Overview

Dr. Neal Walker  
President and CEO  
June 2019



# Cautionary Note Regarding Forward-Looking Statements

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' development of its drug candidates, including the timing for initiation and completion of clinical trials, the availability of data from these trials and the timing of its regulatory submissions related to these trials, and the growth opportunity for ESKATA and RHOFADÉ. 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, 2018, and other filings Aclaris makes with the U.S. Securities and Exchange Commission from time to time. These documents are available under the "SEC filings" 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 presentation, 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.

# Corporate Strategy: Building a Fully-Integrated Biopharmaceutical Company



## LEADERSHIP

- Physician-founded
- Key leadership with track record of executing across multiple development and commercial stage companies
- Kinome experts - chemists and biologists; combined 300+ years of drug discovery experience

Leverage core expertise in drug development and kinase inhibition to develop small molecule therapeutics



12

**ACTIVE**  
CLINICAL TRIALS



2

**FDA-APPROVED**  
**MEDICINES**



**KINect™** PLATFORM  
Proprietary discovery engine

# Pipeline

Program	Indication(s)	Preclinical	Phase 1	Phase 2	Phase 3
A-101(45%) <i>Topical</i>	Common Warts	▶			
ATI-502 JAK1/JAK3 Inhibitor <i>Topical</i>	Alopecia Areata	▶			
	Vitiligo	▶			
	Androgenetic Alopecia	▶			
	Atopic Dermatitis	▶			
ATI-501 JAK1/JAK3 Inhibitor <i>Oral</i>	Alopecia Areata	▶			
ATI-450 MK2 Pathway Inhibitor <i>Oral</i>	RA (Psoriasis, Hidradenitis Suppurativa, CAPS, Pyoderma Gangrenosum, Oncology)	▶			
ATI-1777 JAK1/JAK3 Inhibitor <i>Soft Topical</i>	Atopic dermatitis, Vitiligo, Alopecia Areata	▶			
ITK/JAK3 Inhibitor <i>Soft Topical</i>	Psoriasis, Inflammatory Dermatoses	▶			
ITK/JAK3 Inhibitor <i>Oral</i>	Psoriasis, Inflammatory Dermatoses	▶			
ITK/JAK3 Inhibitor <i>Oral, gut-restricted</i>	Ulcerative colitis / Crohn's Disease	▶			
MK2 Pathway Inhibitor <i>Oral</i>	Oncology	▶			

RA = rheumatoid arthritis, CAPS = cryopyrin-associated periodic syndromes

# Conditions with Significant Treatment Gaps

## SEBORRHEIC KERATOSIS (SK)

83+MM people in U.S.\*<sup>1</sup>

ESKATA® (hydrogen peroxide) topical solution, 40% (w/w), first FDA-approved topical treatment for raised SKs in adults



## ALOPECIA AREATA (AA)

5-7MM people in U.S.

have or will develop AA<sup>2,7</sup>  
Currently available Rx treatment options often used off-label and have significant limitations<sup>7</sup>



## VERRUCA VULGARIS (COMMON WARTS)

19-22MM people in U.S.<sup>2,3</sup>

Currently available treatments have modest therapeutic effect and significant limitations<sup>4</sup>



## ANDROGENETIC ALOPECIA (MALE / FEMALE PATTERN HAIR LOSS)

~50MM men / ~30MM women

in U.S. affected by AGA hair loss<sup>8</sup>



## VITILIGO

1-2% of global population impacted<sup>5</sup>

No FDA-approved medication to repigment the skin<sup>6</sup>



## ROSACEA

16+MM people in U.S.<sup>9</sup>

RHOFADE® (oxymetazoline hydrochloride) cream, 1% FDA-approved for the topical treatment of persistent facial erythema (redness) associated with rosacea in adults, a symptom experienced in about 71% of patients with rosacea<sup>9</sup>



\*Includes all types of SKs <sup>1</sup>Bickers et al. The Burden of Skin Disease. *J Am Acad Dermatology*. 2006;55:490-500. <sup>2</sup>Data on file, Aclaris Therapeutics, Inc. <sup>3</sup>Nguyen et al. Laser Treatment of Nongenital Verrucae A Systematic Review. *JAMA Dermatology*. 2016;152(9):1025-1033. <sup>4</sup>Kwok et al. Topical treatments for cutaneous warts (Review). Cochrane Database of Systematic Reviews. 2012. Art. No.: CD001781. <sup>5</sup>Fitzpatrick T, et al. <http://www.avrf.org/facts/frequently-asked-questions.html>. Last accessed March 30, 2019. <sup>6</sup><https://www.asdreports.com/news-217/vitiligo-therapeutics-market-expected-show-moderate-growth-up-2019>. Last accessed March 30, 2019. <sup>7</sup>National Alopecia Areata Foundation. <https://www.naaf.org/alopecia-areata>. Last accessed March 30, 2019. <sup>8</sup>National Institute of Health Androgenetic Alopecia. <https://ghr.nlm.nih.gov/condition/androgenetic-alopecia#statistics>. Last accessed March 30, 2019. <sup>9</sup>National Rosacea Society, <https://www.rosacea.org/rosacea-review/2010/summer/new-survey-unveils-wide-range-of-potential-signs-and-symptoms>. Last accessed on March 30, 2019.

# COMMERCIAL PORTFOLIO

RHOFADE<sup>®</sup> (oxymetazoline HCl) cream, 1%

ESKATA<sup>®</sup> (hydrogen peroxide) topical solution, 40% (w/w)



# RHOFADE Cream

**Rhofade**  
(oxymetazoline HCl)  
cream, 1%

IMPORTANT SAFETY INFORMATION • PRODUCT INFORMATION • FOR HEALTHCARE PROFESSIONALS

SAVINGS & UPDATES FIND A DERMATOLOGIST MENU

ABOUT  
**RHOFADE® CREAM**

RHOFADE® cream reduced persistent facial redness due to rosacea in adults all day, through 12 hours on day 29.<sup>1</sup>

BEFORE AND AFTERS

**BEFORE** **AFTER**

Illustration only.

On day 29, results seen in 12%–18% of people using RHOFADE® cream vs 5%–9% of people using vehicle cream. Individual results may vary.

TAKE THE NEXT STEP

Find a dermatologist, savings, and condition information.

LEARN MORE

- National Rosacea Society estimates more than 16 million Americans are affected by rosacea<sup>1</sup>
- Persistent facial erythema (PFE) is the most common sign or symptom of rosacea, experienced in about 71% of rosacea patients according to a survey conducted by this same Society<sup>1</sup>
- RHOFADE Growth Opportunity:
  - Increase prescribing by current RHOFADE prescribers
  - Recapture lost share from HCPs who decreased their prescribing in 2018
  - Capitalize on untapped potential within rosacea-treating HCPs who are not yet prescribing a medication to treat PFE

#### INDICATION

RHOFADE cream is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults.

#### IMPORTANT SAFETY INFORMATION AND WARNINGS

##### WARNINGS AND PRECAUTIONS

##### Potential Impacts on Cardiovascular Disease

Alpha-adrenergic agonists may impact blood pressure. RHOFADE cream should be used with caution in patients with severe or unstable or uncontrolled cardiovascular disease, orthostatic hypotension, and uncontrolled hypertension or hypotension. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension/hypotension to seek immediate medical care if their condition worsens.

The most common side effects of RHOFADE® Cream include application-site reactions of: skin reactions (dermatitis), worsening of rosacea pimples, itching, redness, and pain.

<sup>1</sup>National Rosacea Society, <https://www.rosacea.org/rosacea-review/2010/summer/new-survey-uncovers-wide-range-of-potential-signs-and-symptoms>, Last accessed on March 30, 2019.

# Core Intellectual Property: RHOFADE

- **Three-year CI market exclusivity until January 18, 2020**
- **Five Orange Book Patents**
  - **USP No. 7,812,049 (Exp 5/2/28 with 1562 days PTA)**
    - Method of treating erythema resulting from rosacea comprising administering topically a composition comprising about 0.05-30% of oxymetazoline as the sole active agent
    - Exclusively licensed from Allergan
  - **USP No. 8,420,688 (Exp 8/02/24 with 193 days PTA)**
    - Same as '049, but recites “therapeutically effective amount” of oxymetazoline
    - Exclusively licensed from Allergan
  - **USP No. 8,815,929 (Expires: 1/22/24)**
    - Same as '688, but recites oxymetazoline and other alpha-1 agonists
    - Exclusively licensed from Allergan
  - **USP No. 8,883,838 (Exp 12/1/31)**
    - A cream composition with certain % of oxymetazoline, % of certain emollient/emulsifier/excip/ etc. (the stabilized cream)
  - **USP No. 9,974,773 (Exp 6/11/35)**
    - Method of treating facial erythema associated with rosacea comprising topically administering once daily to the site of erythema on the face of the patient a pharmaceutical composition comprising 1.0% or 1.5% w/w oxymetazoline HCl thereof as the sole active ingredient
- **Pending applications**
  - Families related to Orange Book listed patents have pending applications in the U.S.
  - Pending applications are directed to, for example, methods of treating facial erythema using 1.0% oxymetazoline administered once daily; cream formulations of oxymetazoline; method of treating erythema, telangiectasia or inflammatory lesions associated with rosacea comprising topically administering formulations of oxymetazoline
  - Corresponding pending/issued applications in major international jurisdictions

# ESKATA

**83+MM** People in the US with SK\*<sup>1</sup>

**18+MM** visits to Derm for SK<sup>2</sup>

**8+MM** SK treatments<sup>2</sup>

## Reasons for Not Removing SKs Include<sup>3</sup>:

- High risk of **scarring**
- High risk of **hypopigmentation**
- Want to avoid **cutting, freezing** or **burning**
- Moved to second position in the detail schedule
- Sales team focused on top ESKATA accounts based on productivity in each territory, with the objective of increasing utilization
- Received recent European approvals for ESKATA / ESKERIELE and in active discussions with potential commercial partners



\*Includes all types of SKs <sup>1</sup>Bickers et al. The Burden of Skin Disease. *J Am Acad Dermatology*. 2006;55:490-500. <sup>2</sup>Data on File. Aclaris Therapeutics, Inc. Burke Screener of 594 dermatologists. 2014. <sup>3</sup>Data on File. Aclaris Therapeutics, Inc. In-Office SK Treatment Study. Final Report. 2016.

A-101 (hydrogen peroxide) 45%  
Topical Solution (Investigational  
Drug Candidate) -  
Phase 3 for the Treatment of  
Common Warts



# Common Warts - Patient/Physician Surveys



People with Common Warts in the US

19–22 MM<sup>1,2</sup>



61%

treated by  
**Primary Care  
Physicians**  
(2.5 avg. visits)<sup>1</sup>



39%

treated by  
**Dermatologists**  
(2.6 avg. visits)  
31% of pts are referrals<sup>1</sup>

- 50% of all patient visits for warts are for common warts<sup>3</sup>
- 3x more patient visits than genital warts<sup>3</sup>
- 50% of patients report moderate to extreme discomfort<sup>4</sup>
- 39% of patients say warts impact social/leisure activities<sup>4</sup>
- Unmet Needs<sup>1</sup>:
  - Would prefer pain-free treatments which work faster and do not have unwanted side effects

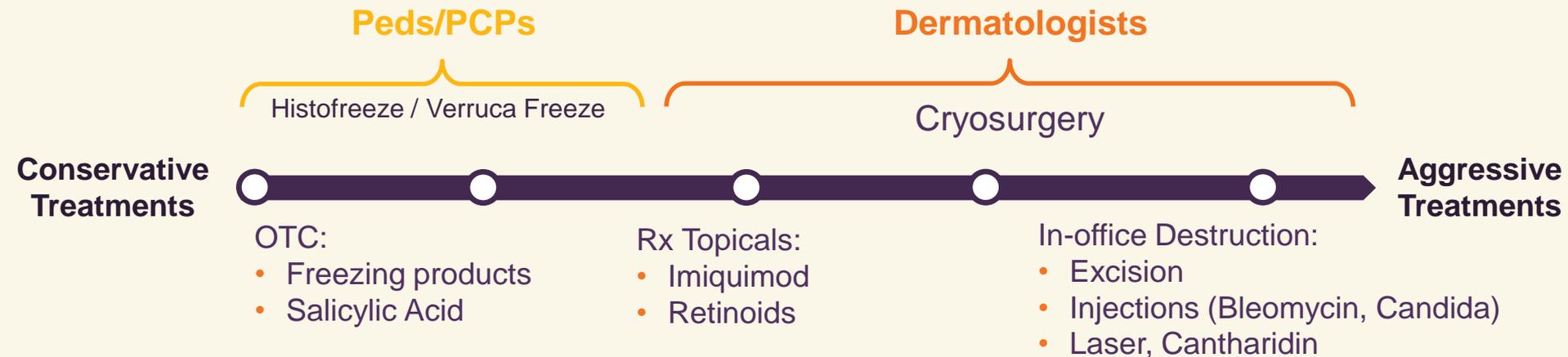
<sup>1</sup>Data on file, Aclaris Therapeutics, Inc.

<sup>2</sup>Nguyen et al. Laser Treatment of Nongenital Verrucae A Systematic Review. *JAMA Dermatology*. 2016;152(9):1025-1033.

<sup>3</sup>IMS National Disease and Therapeutic Index 2016.

<sup>4</sup>Lipke M., An Armamentarium of Wart Treatments, *Clinical Medicine & Research*,4:4, 2006; 273–293.

# Common Warts: Treatment Paradigm



## Peds/PCPs:

- Difficult and recalcitrant cases are typically referred to dermatologists
- Less likely to utilize in-office procedures but more likely to utilize take-home Rx/OTC

## Dermatologists:

- Viewed as the specialists in the treatment of warts; other specialties follow dermatologists' lead
- More likely to utilize both in-office procedures and take-home Rx/OTC

- Patient burden comes from the duration of treatment, time commitment, pain and discomfort, as well as the cost of treatments
- Opportunity to position A-101 45% as Rx treatment with convenience of home use

# Summary of WART-203 Phase 2 Trial Results

Trial	Trial Design	Trial Outcome
<b>WART-203 (N=159)</b>	<ul style="list-style-type: none"><li>• A randomized, double-blind, vehicle-controlled, parallel-group study of investigational drug A-101 45% topical solution in subjects with 1-6 common warts</li><li>• Self-treated twice weekly for a total of 16 treatments</li></ul>	<ul style="list-style-type: none"><li>• Efficacy: Statistically significant results on all primary and secondary endpoints</li><li>• Favorable safety profile</li></ul>

## Primary Endpoint:

- Mean change from baseline in the Physician's Wart Assessment (PWA)<sup>™</sup> score on target wart at day 56 (visit 10) using an analysis of covariance.

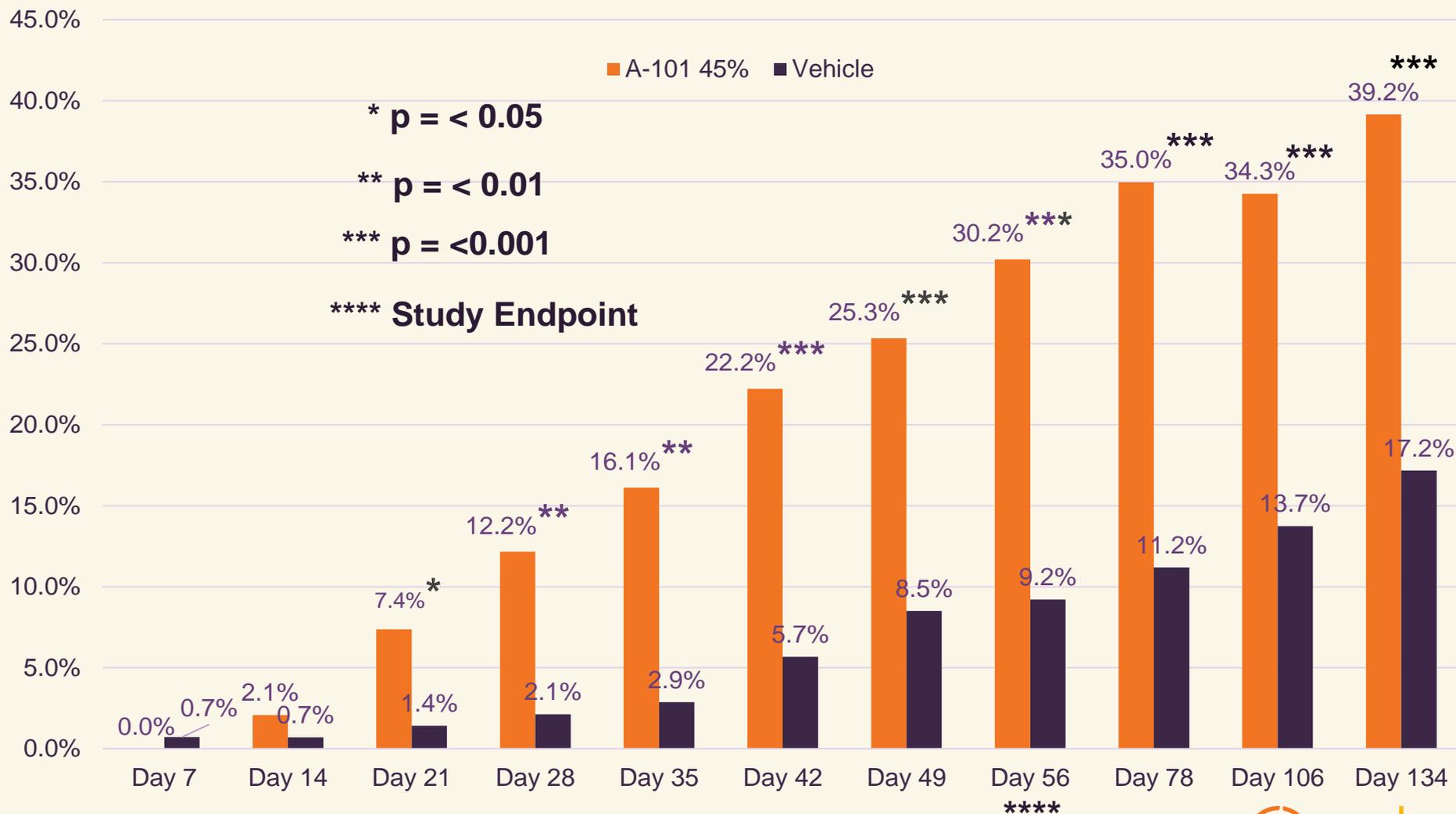
## Secondary Endpoints:

- The proportion of subjects whose target wart is judged to be clear (PWA=0) at day 56.
- The proportion of subjects with all treated wart(s) clear, stratified by baseline number of warts at day 56.
- The percentage of all treated warts that were clear at day 56.

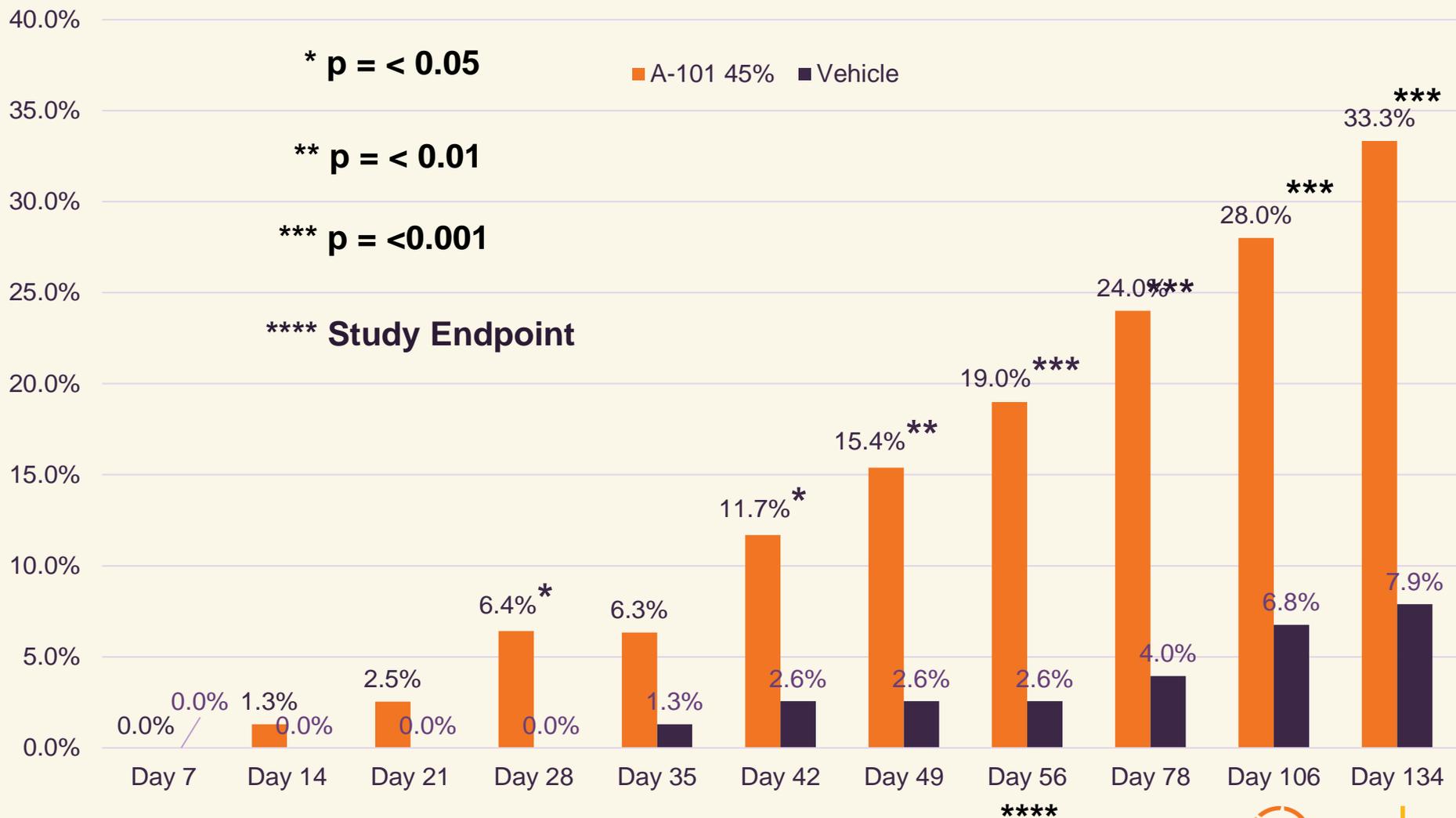
## Current Status

- Phase 3 Data expected 2H19.

# WART-203: The Percentage of All Treated Warts that are Clear on the PWA for Each Post-baseline Visit (N=159)



# WART-203: Proportion of Subjects with all treated Wart(s) (1-6) Clear, Stratified by Baseline Number of Warts, at each Post-Baseline Visit (N=159)



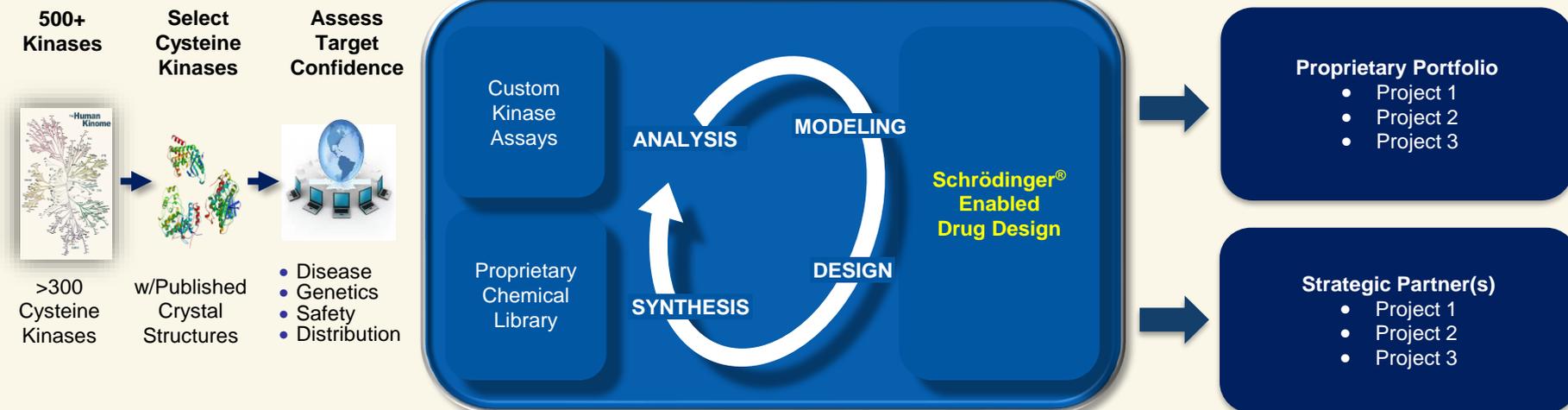
# Inflammation and Immunology Platform

# KINect™ Platform – Developing Better Kinase Drug Candidates Rapidly & Efficiently

TARGET SELECTION & VALIDATION

KINect™ Platform – LEAD GENERATION

ASSET GENERATION



Leveraging key opinion leaders, data in public domain and internal validation

High affinity/selective drug scaffolds more rapid target to candidate selection

## 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 2

# 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<sup>1</sup>



**500 member class, representing 2% of the human genome**

<sup>1</sup> [https://www.nature.com/nrd/posters/druggablegenome/nrd\\_druggablegenome.pdf](https://www.nature.com/nrd/posters/druggablegenome/nrd_druggablegenome.pdf). Last Accessed March 30, 2019

# Investigational Selective JAK 1/3 Inhibitors

## Portfolio and IP Estate:

### **ATI-501 (oral) and ATI-502 (topical) – Selective JAK 1/3 inhibitor**

#### **Additional topical JAK inhibitors in development**

- Known MOA and observed biological response in humans
- Promoted hair regrowth in mouse model<sup>1</sup>
- Broad IP estate - Methods of use covering JAK inhibitors for the treatment of:
  - Alopecia areata
  - Androgenetic alopecia (male and female pattern hair loss)

## **ATI-501 JAK1/JAK3 inhibitors**

Oral treatment for severe alopecia areata (alopecia totalis and alopecia universalis)

## **ATI-502 JAK1/JAK3 inhibitors**

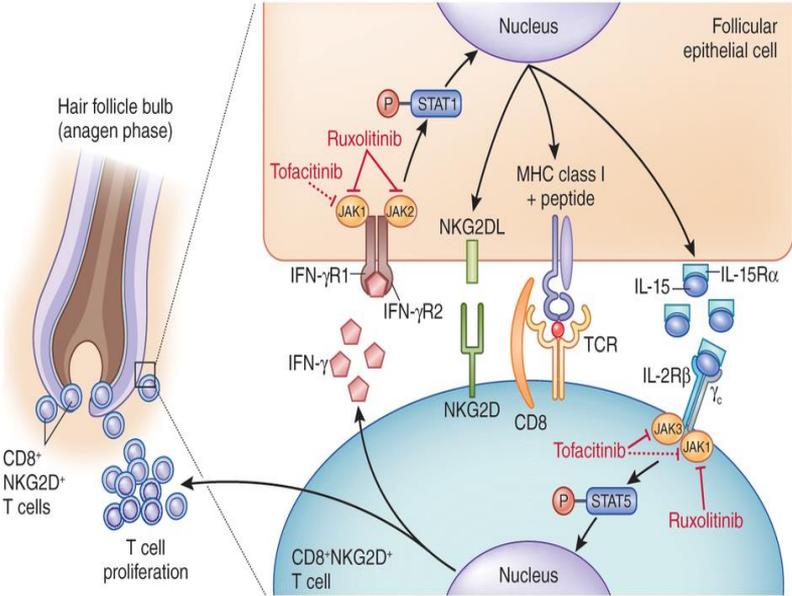
Topical treatment for hair loss disorders: mild to moderate alopecia areata (patchy alopecia areata) and androgenetic alopecia

## **ATI-1777 JAK1/JAK3 inhibitors**

“Soft Topical” treatment for atopic dermatitis, alopecia areata, and vitiligo

<sup>1</sup> Data on File. Aclaris Therapeutics, Inc.

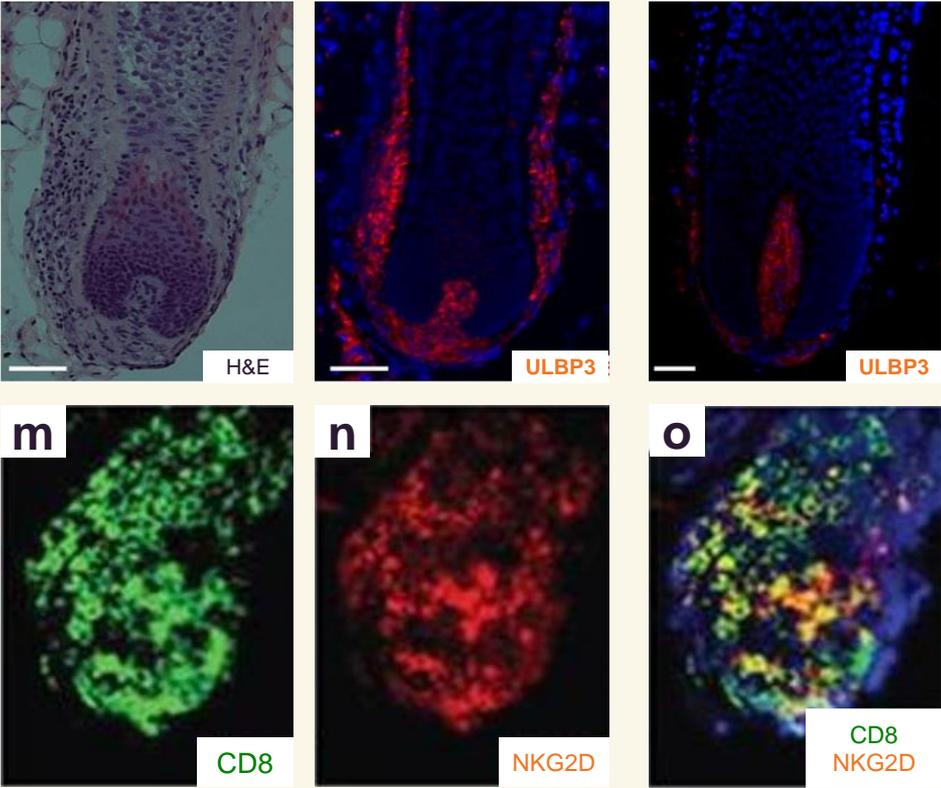
# Mechanism of JAK Inhibitors in Alopecia Areata



Divito & Kupper, *Nature Medicine* 20, 989–990 (2014).

HF of an AA patient

Control Individual



Christiano Laboratory, Columbia University

# ATI-502 – Topical Proof of Concept

Baseline

Follow up

33/M



(334 Days on Drug)

23/F



(353 Days on Drug)

45/F



(385 Days on Drug with a 47 day gap)

- Of the 8 patients who received at least 6 months of drug, 3 had evidence of eyebrow hair regrowth (defined by at least a 2 grade categorical shift in eyebrow score in at least 1 eyebrow [scale 1-5]).
- The 3 patients pictured above were the only patients who completed ~12 months of drug treatment.

# Alopecia Areata - Patient/Physician Surveys



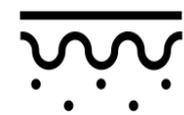
Patients with Alopecia Areata in the US

5-7 MM<sup>12</sup>



42%

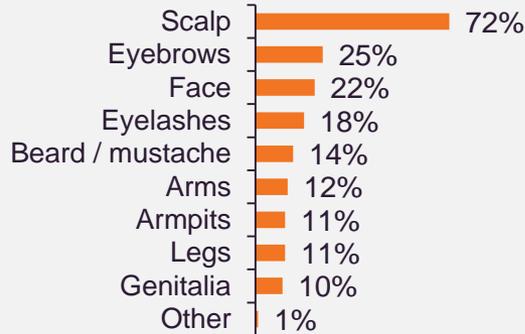
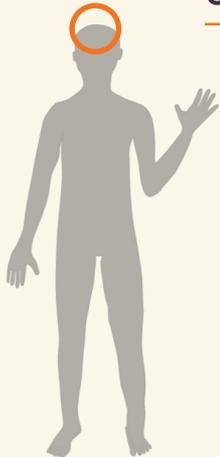
treated by  
**Primary Care Physicians**  
(6.7 avg. visits)<sup>1</sup>



54%

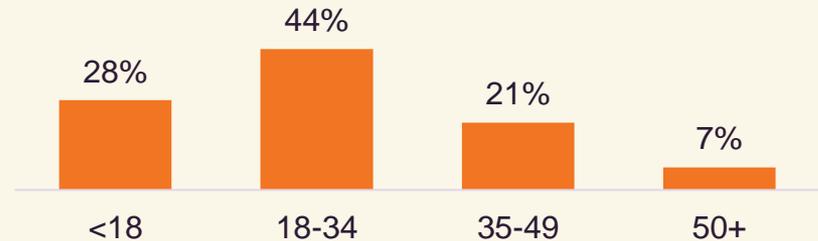
treated by  
**Dermatologists**  
(7.1 avg. visits)  
43% of pts are referrals<sup>1</sup>

## COMMON BODY LOCATIONS<sup>1</sup>



## AGE & OTHER DEMOGRAPHICS<sup>1</sup>

Average age = 25.7 years



<sup>1</sup>Data on file, Aclaris Therapeutics, Inc.

<sup>2</sup>National Alopecia Areata Foundation. <https://www.naaf.org/alopecia-areata>.

# Spectrum of Hair Loss

24%



34%



43%



51%



100%

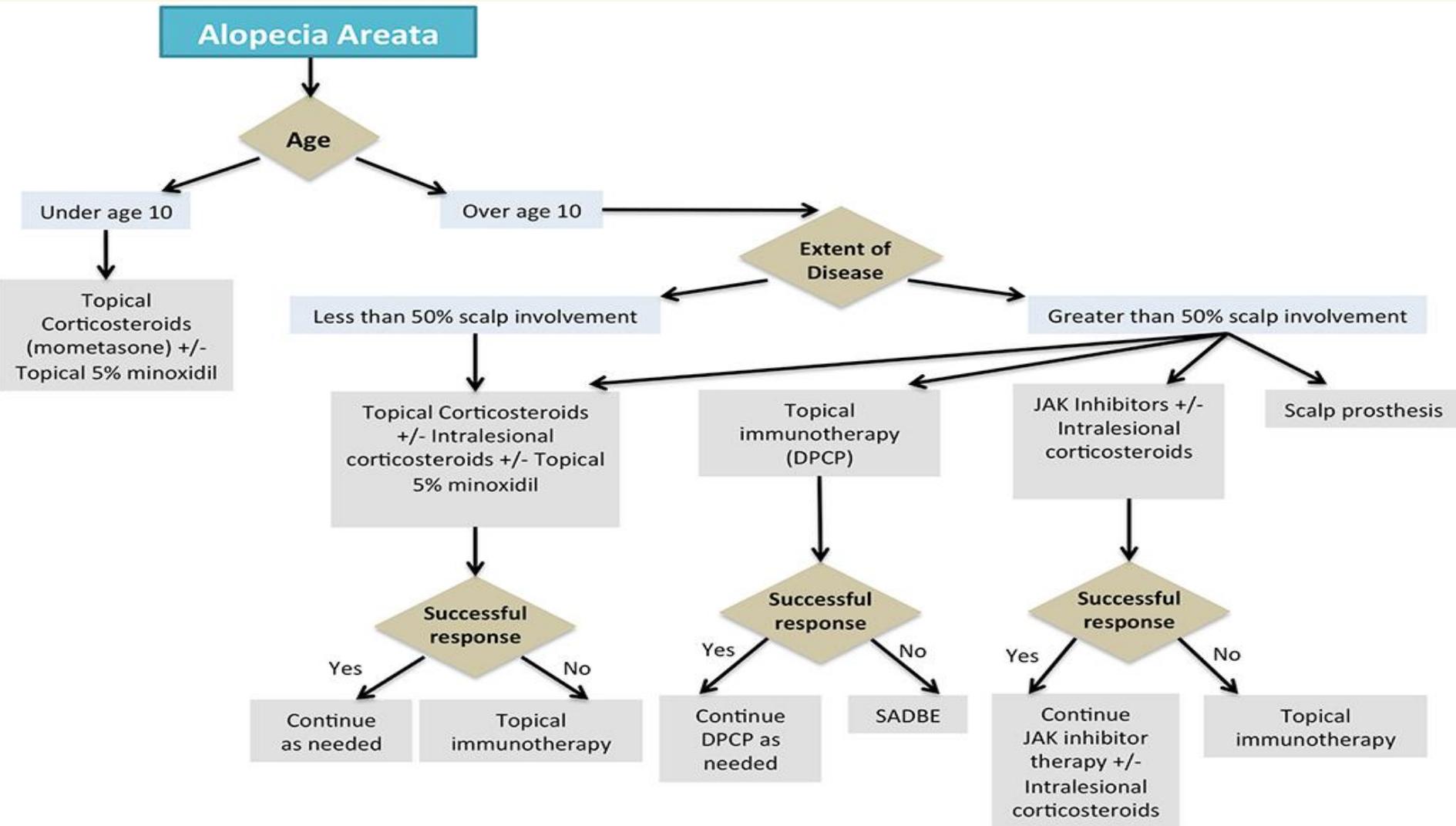


- 25-50% of patients have mild to moderate alopecia areata (patchy)<sup>1</sup>
- 14-25% of patients progress to severe alopecia areata (alopecia totalis or universalis)<sup>1</sup>

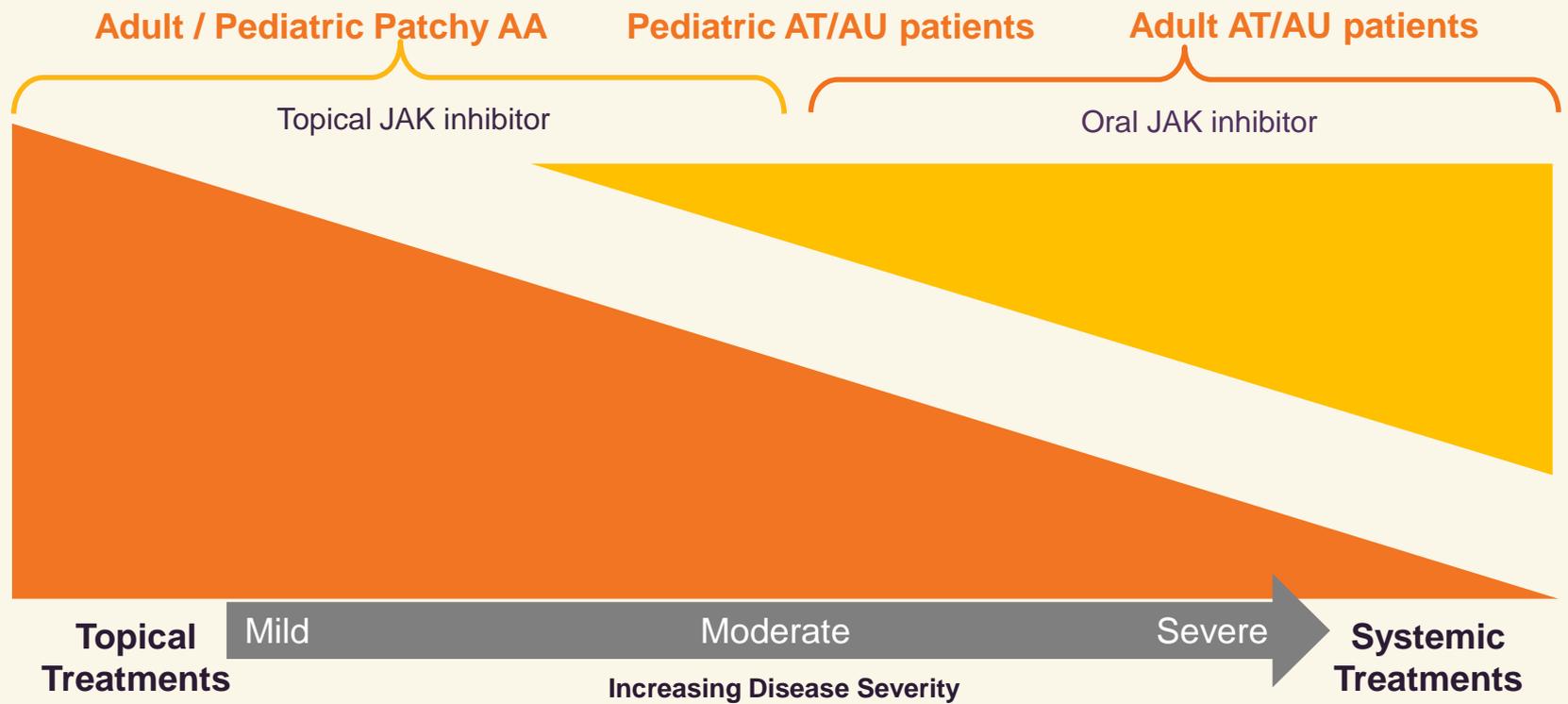
<sup>1</sup>MacDonald, et al. Guidelines for the Management of Alopecia Areata. *Brit J Derm.* 2003

\*Pictures from data on file

# Current treatment paradigm



# Alopecia Areata: Potential Treatment Paradigms



## INDUCTION:

Topical JAK inhibitor may be efficacious in patients with less severe patchy AA

Oral JAK inhibitor may be best option in patients with more severe AT/AU phenotypes

## MAINTENANCE:

AT/AU patients may be able to maintain hair with topical JAK inhibitor

Concomitant topical therapy may decrease reliance on longer term oral therapy in some patients

# Androgenetic Alopecia (AGA)

# Androgenetic Alopecia (AGA): Male/Female pattern hair loss

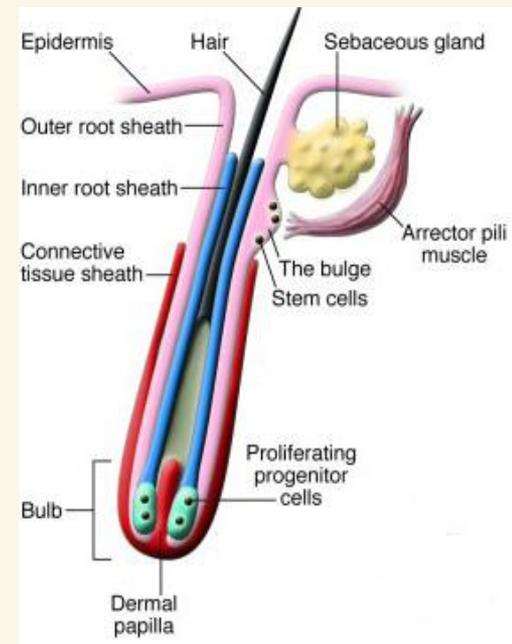
- AGA is a genetic disorder and the most common cause of hair loss<sup>1</sup>
- Experienced by 70% of men and 40% of women at some point in their lives<sup>1</sup>; affects ~50 million men and ~30 million women in the US<sup>2</sup>
- Affected individuals highly motivated to seek treatment<sup>1</sup>
- Potential benefits of topical JAK inhibitor in AGA:
  - ✓ New mechanism of action
  - ✓ Minimal systemic side effects
  - ✓ Non-hormonal
  - ✓ Novel option women with AGA



Male with AGA



Female with AGA

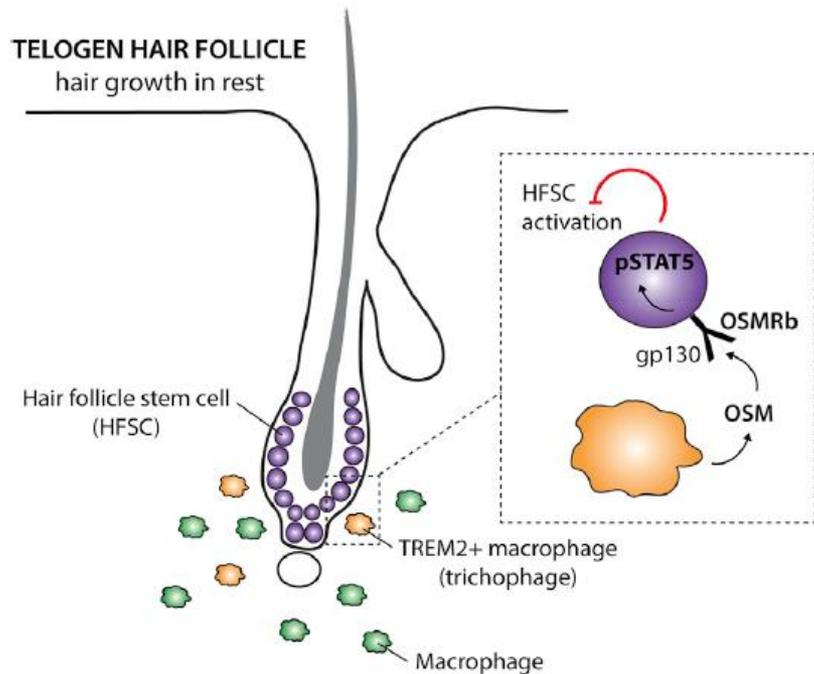


Cotsarelis, G. *J Clin Invest.* 2006;116(1):19-22.

<sup>1</sup> McElwee J., et al. Promising Therapies for Treating and/or Preventing Androgenic Alopecia. Medscape. 2012

<sup>2</sup> National Institute of Health Androgenetic Alopecia. <https://ghr.nlm.nih.gov/condition/androgenetic-alpecia#statistics>. Last accessed March 30, 2019.

# AGA – New Mechanism of Action Postulated



**Figure 1. Role of TREM2+ Macrophages in Skin**

Dermal TREM2+ macrophages, now termed "Trichophages," reside in close proximity to hair follicles. During telogen—the hair cycle phase when hair is not growing—trichophages produce the cytokine OSM that binds to OSM receptors on hair follicle stem cells (HFSCs). This triggers phosphorylation of STAT5 within HFSCs, impairing their activation, and therefore resulting in maintenance of telogen.

- Tissue-resident immune cells with potent sensing and effector functions are well-placed to fundamentally aid tissue homeostasis via crosstalk with stem cells.
- A dermis-resident TREM2+ macrophage subpopulation that promotes hair follicle stem cell quiescence via cytokine-mediated JAK-STAT signaling has been identified.
- pSTAT5 (the p indicates that STAT5 is in the ON position – ie: active, and then a red curved arrow blocks HFSC activation (this is telogen)
- The administration of a JAK inhibitor would turn the pSTAT5 to the OFF position, and then opens the red arrow and PROMOTES HFSC activation.

# AGA-201: Male and Female Subjects With Androgenetic Alopecia (AGA) Treated With ATI-502

## Open-Label Study\*1

### Eligibility

- AGA Diagnosis
- Males:  
Norwood-Hamilton Type III vertex, IV or V
- Females:  
Sinclair Grade 2, 3 or 4

**N=31**

**Treatment  
26 weeks**

**ATI-502 (0.46%) BID**

**Assessment  
(Baseline and Week 26)**

### Key Endpoints

#### Primary Endpoint

- Change in non-vellus Total Area Hair Count (TAHC) at week 26

#### Secondary Endpoints

- Investigator Global Assessment (IGA)
- Subject Self Assessment (SSA)

Safety & Tolerability

Efficacy and  
Safety  
12-month  
endpoint

ATI-502  
(0.46%) BID

**(Ongoing)**

\*3 US clinical sites

<sup>1</sup>ClinicalTrials.gov ID NCT03495817

# Summary of Efficacy and Safety

## Efficacy:

- ✓ TAHC (mean)
  - 8.6 hairs/cm<sup>2</sup> (15.3 females, 5.6 males) at 26 week
- ✓ IGA
  - 72.7% (16/22 with increased hair growth of +1 or greater)
- ✓ SSA
  - 81.8% (18/22 with increased hair growth of +1 or greater)

Grade	Description
-3	Greatly decreased hair growth
-2	Moderately decreased hair growth
-1	Slightly decreased hair growth
0	No change
+1	Slightly increased hair growth
+2	Moderately increased hair growth
+3	Greatly increased hair growth

## Safety:

- ✓ ATI-502 (0.46% concentration) was generally well-tolerated.
- ✓ No treatment-related serious adverse events (SAEs) reported in this study.
  - One subject had an unrelated SAE of breast cancer which led to withdrawal of study medication.
- ✓ One additional subject had an adverse event (AE) of alopecia assessed by the investigator as related to study medication, leading to discontinuation.
- ✓ Two subjects experienced treatment-related AEs, one with folliculitis and one with pruritus.
- ✓ AEs occurring in > 1 subject were vertigo, upper respiratory infection, neck pain, and alopecia.

# Subject 01-012 – 48 y/o Male

IGA	SSA	TAHC $\Delta$
+3	+3	+11



# Subject 03-005 – 42 y/o Male

IGA	SSA	TAHC $\Delta$
+1	+2	+24



Baseline

Week 26



Baseline

Week 26

# Subject 01-029 – 31 y/o Female

IGA	SSA	TAHC $\Delta$
+1	+2	+15

Baseline



Week 26



# Subject 02-002 – 41 y/o Female

IGA	SSA	TAHC $\Delta$
+2	+1	+18

**Baseline**



**Week 26**



# 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-501 & ATI-502 (COM) in dermatology
  - US Natural expiry dates 2030-2034 + potential applicable PTE for the treatment of AA
  - 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 6 issued U.S. patents and 1 pending application directed to methods of treating AA, AGA or hair loss disorders by administering ruxolitinib, deuterated ruxolitinib, baricitinib, decernotinib, topical tofacitinib or monotherapy tofacitinib.
  - This portfolio also includes an issued patent in Europe for tofacitinib or decernotinib for use in treating hair loss disorders and a pending European application for ruxolitinib or baricitinib to treat hair loss disorders, 3 issued patents in Japan to ruxolitinib, baricitinib, tofacitinib (topically or as monotherapy) and a pending Japanese application, and 1 issued patent in South Korea to methods of treating hair loss disorders using JAK 1 and/or JAK 2 inhibitors and 2 pending applications in South Korea to methods of treating hair loss disorders using JAK3 inhibitors.
  - Natural expiry in US 2031; naturally expiry in EU, JP, KR 2031-2033

# ATI-450 (MK2 Inhibitor)

(Investigational Drug Candidate)



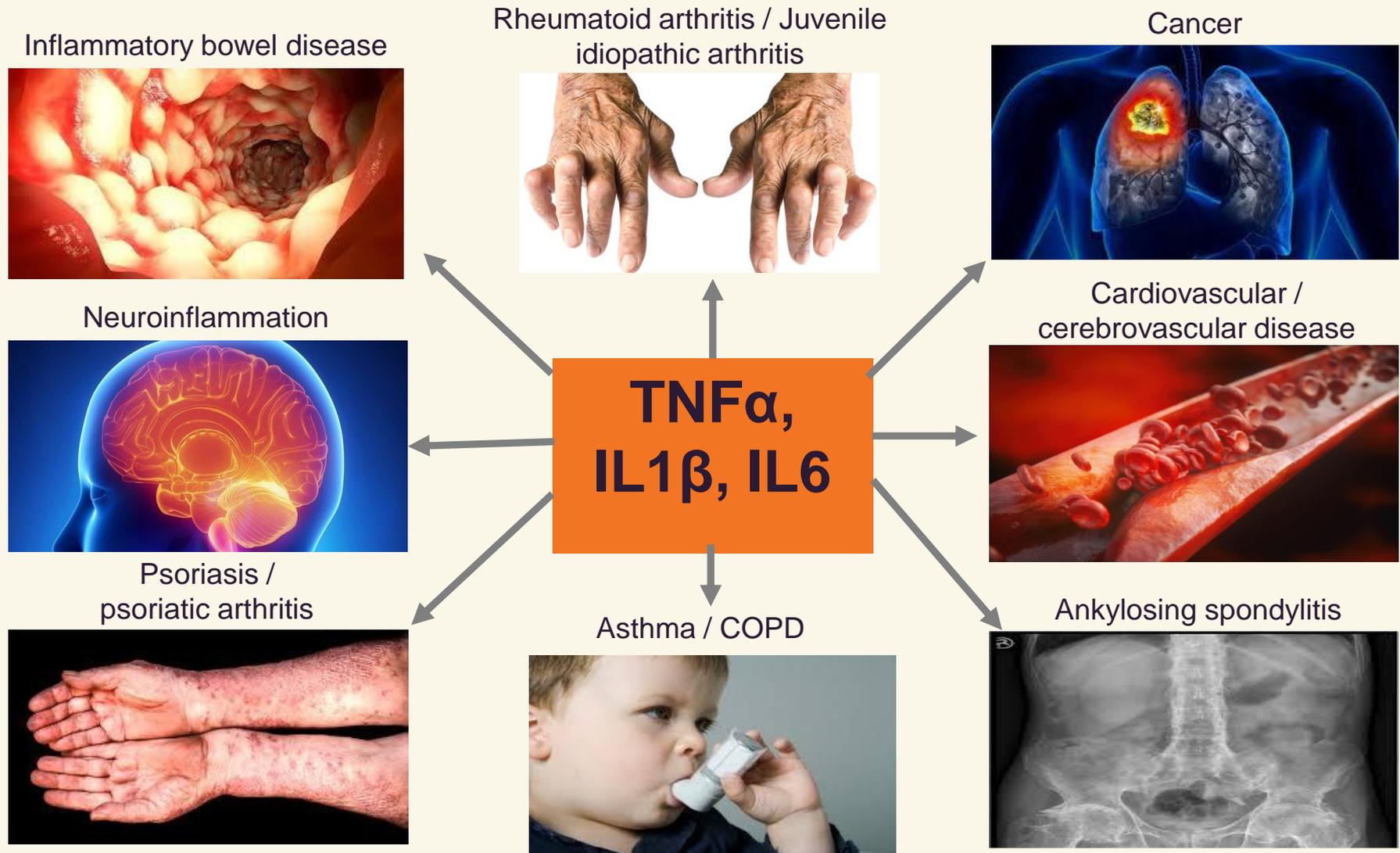
# MK2 Pathway Inhibitor (MK2 PI) ATI-450

- ATI-450
  - Pharmacologically unique MOA
  - MK2 pathway inhibitors target the production and activity of key inflammatory cytokines including TNF $\alpha$ , IL-1 $\alpha$ , IL-1 $\beta$  and IL-6
  - Inhibits the cytokine targets of established biologics:
    - *Anti-TNFs: Humira<sup>®</sup>, Enbrel<sup>®</sup>, Remicade<sup>®</sup>*
      - RA, psoriasis, psoriatic arthritis, IBD, ankylosing spondylitis
    - *Anti-IL1s: Kineret<sup>®</sup>, Ilaris<sup>®</sup>, Arcalyst<sup>®</sup>*
      - CAPS, Still's disease, SJIA, cardiovascular disease
    - *Anti-IL6: Kevzara<sup>®</sup>, Actemra<sup>®</sup>*
      - RA, Castleman's disease
- Aclaris is developing MK2 pathway inhibitors for chronic inflammatory disease and autoimmune disease
  - IND for treatment of RA allowed in May 2019
  - Plan to initiate a Single Ascending Dose / Multiple Ascending Dose Phase 1 trial in approximately 80 patients in the second half of 2019
  - If the Phase 1 trial is successful, plan to advance ATI-450 into Phase 2 trials in patients with RA and an additional inflammatory indication

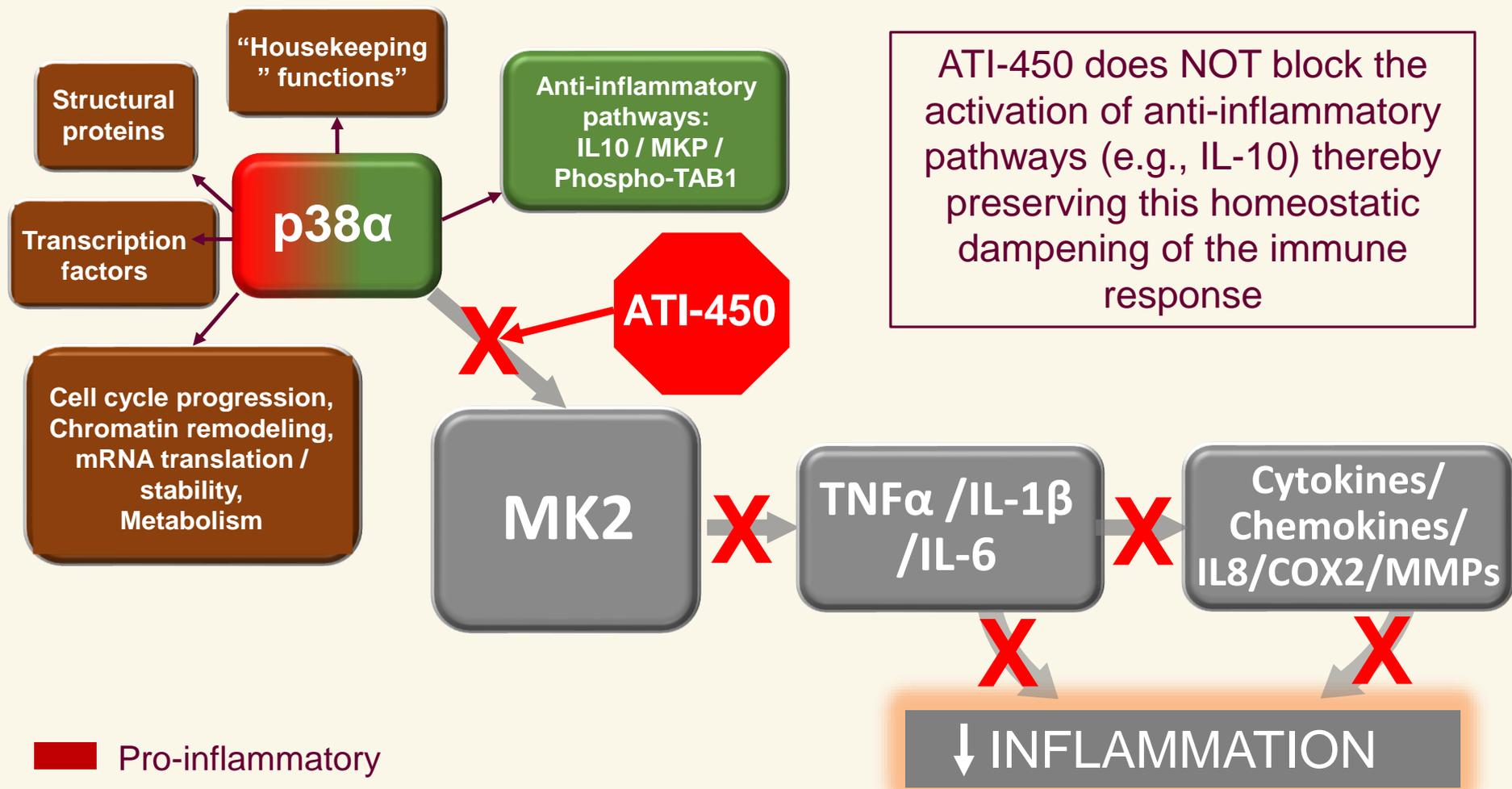
MK2 = mitogen-activated protein kinase-activated protein kinase 2 (MAPKAPK2)

RA = rheumatoid arthritis; IBD = inflammatory bowel disease; SJIA = systemic juvenile idiopathic arthritis

# MK2-driven cytokines are central to many diseases



# ATI-450 Inhibits the Expression of Key Inflammatory Cytokines: TNF $\alpha$ , IL-1 $\beta$ and IL-6



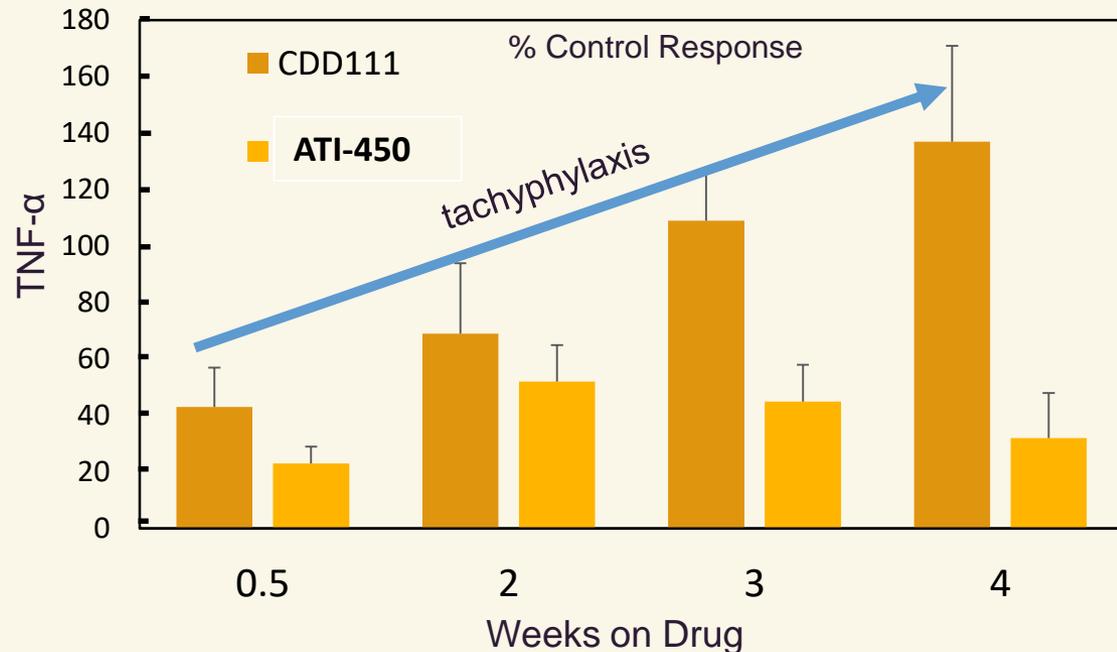
ATI-450 does NOT block the activation of anti-inflammatory pathways (e.g., IL-10) thereby preserving this homeostatic dampening of the immune response

- Pro-inflammatory
- Anti-inflammatory
- Housekeeping functions

# Mouse LPS-Induced TNF $\alpha$ Production

*ATI-450 demonstrated durable response (no tachyphylaxis)*

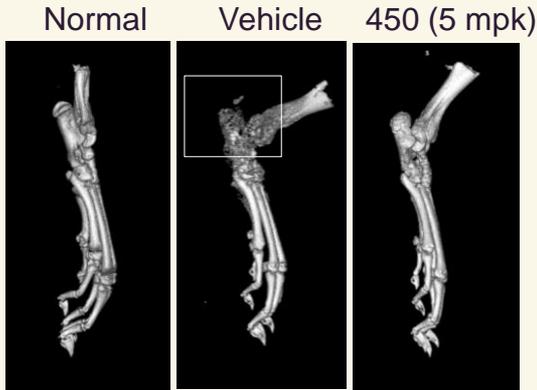
- Global p38 inhibitor CDD-111 lost inhibition over time
- **This investigational MK2 pathway inhibitor ATI-450 demonstrated durable responses in this mouse model (no tachyphylaxis)**



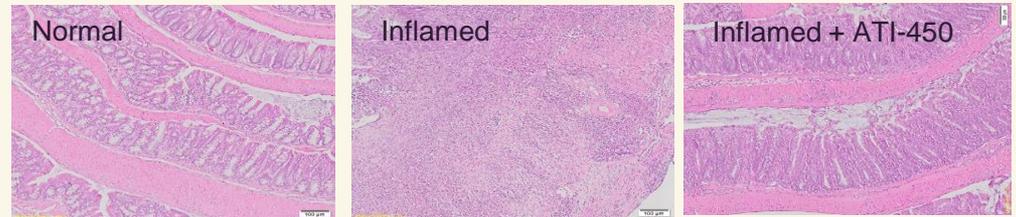
- Conventional p38 (CDD-111) and MK2PI (ATI-450) administered to mice in feed starting day 1 and continuing through day 28
- At the time point indicated, mice were LPS challenged and blood TNF $\alpha$  levels determined

# In vivo Results of MK2 Pathway Inhibitor ATI-450

## Joint Protection in Rat Arthritis Model<sup>1</sup>

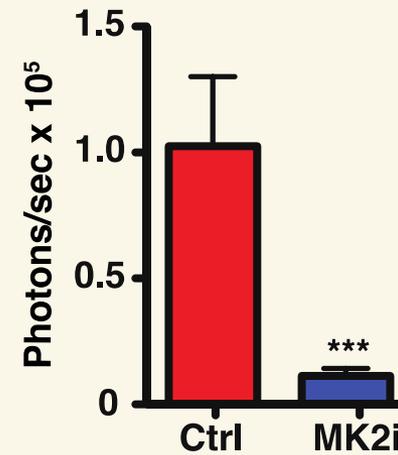


## Blockade of Gut Inflammatory Infiltrate in Murine Adoptive Transfer Ulcerative Colitis Model<sup>3</sup>

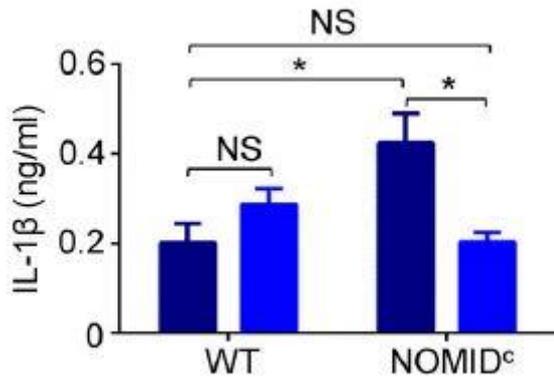


## Reduction in Breast Cancer Bone Metastasis in Mice<sup>2</sup>

### Bone Metastasis



## Cytokine Modulation in Orphan Autoinflammatory Disease (CAPS)<sup>1</sup>

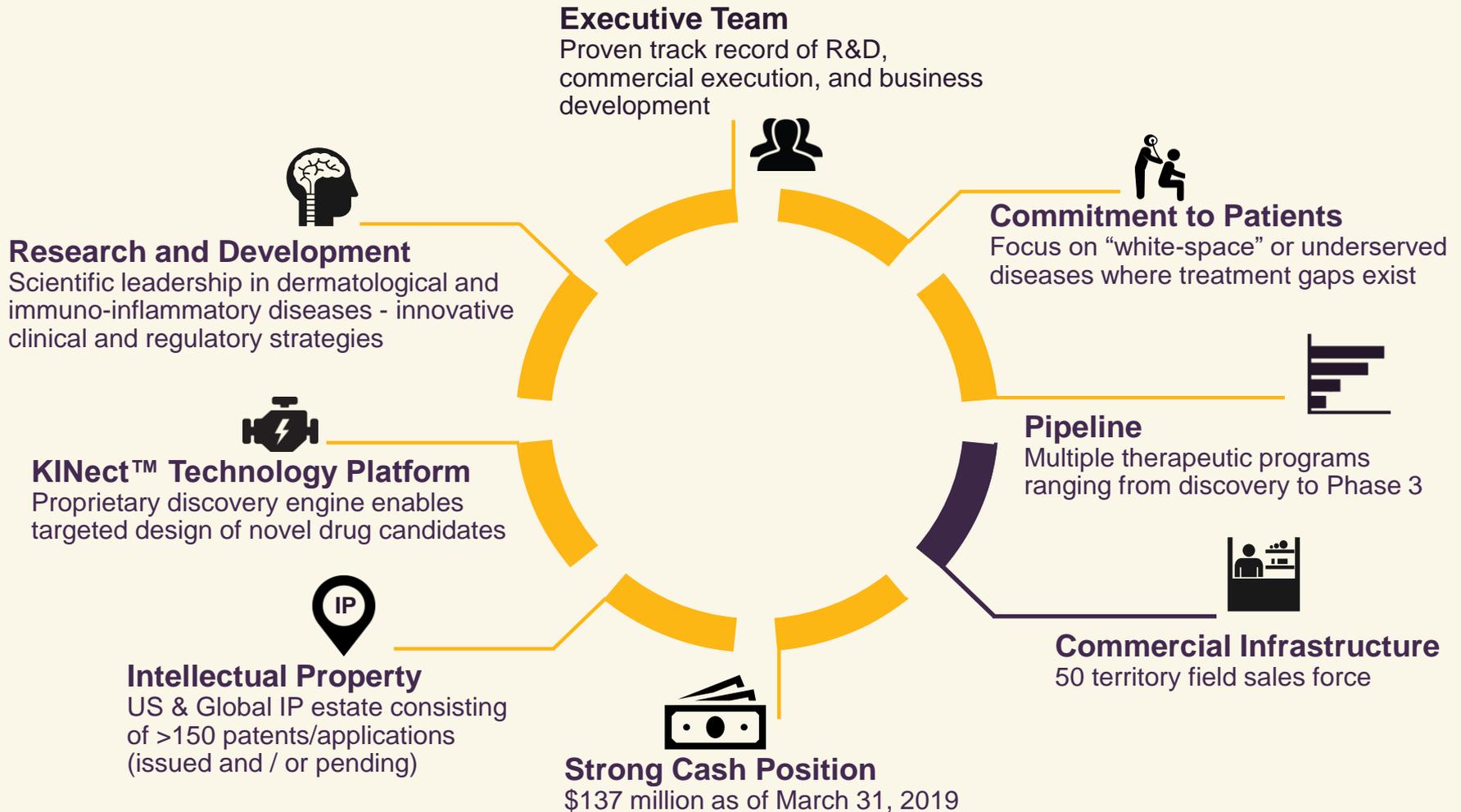


<sup>1</sup> Wang C, et al. *J Exp Med*. 2019;215(5):1315-1325.

<sup>2</sup> Murali B, et al. *Cancer Res*. 2019;78(19):5618-5630.

<sup>3</sup> Data on File. Aclaris Therapeutics, Inc.

# Fully Integrated Biopharmaceutical Company



# Milestone

2019

2020

Q1

Q2

Q3

Q4

Q1

Q2

Q3

Q4

## A-101 45% Common Warts

Phase 3 Data

Submit NDA

## ATI-501/ATI-502 (Oral/Topical JAK Inhibitor)

ATI-501 - Phase 2 AT/AU Dose Range Data

ATI-501 - AT/AU End of Phase 2 FDA mtg

ATI-502 - Phase 2 Patchy AA Dose Range Data

ATI-502 – Initiate Phase 3 Patchy AA Trial<sup>1</sup>

ATI-502 - Phase 2 Open-label Vitiligo Data<sup>2</sup>

ATI-502 - Phase 2 Open-label AGA Data<sup>3</sup>

ATI-502 - Initiate Phase 2 AGA Trial

ATI-502 - Phase 2 Open-label Atopic Dermatitis Data

## Inflammation / Immunology

ATI-450 (MK2 Inhibitor) - Initiate Phase 1 Trial

ATI-450 (MK2 Inhibitor) - Phase 1 Data

ATI-1777 (Soft JAK) – Submit IND

ATI-1777 (Soft JAK) - Initiate Phase 1/2 Trials

<sup>1</sup> If the results from the AA-201 trial are positive, our next steps may include holding an end of Phase 2 meeting with the FDA, and initiating a Phase 3 trial of ATI-502 as a topical treatment for AA in the first half of 2020.

<sup>2</sup> VITI-201: 6-month data interim expected mid-2019; 12-month data expected fourth quarter of 2019

<sup>3</sup> AGA-201: 6-month data expected second quarter of 2019; 12-month data expected fourth quarter of 2019

THANK YOU

