1,081,082 Shares



This prospectus supplement updates and should be read in conjunction with the prospectus dated June 28, 2016 (the "Prospectus") relating to the resale or other disposition, from time to time, by the selling stockholders identified in the Prospectus under the caption "Selling Stockholders," of up to 1,081,082 shares of our common stock, par value \$0.00001 per share. We are not selling any shares of our common stock under the Prospectus and will not receive any proceeds from the sale or other disposition of shares by the selling stockholders. The selling stockholders will bear all commissions and discounts, if any, attributable to the sale or other disposition of the shares. We will bear all costs, expenses and fees in connection with the registration of the shares. To the extent that there is any conflict between the information contained herein and the information contained in the Prospectus, the information contained herein supersedes and replaces such information.

Current Report

This prospectus supplement incorporates into our Prospectus the information contained in our attached current report on Form 8-K that we filed with the Securities and Exchange Commission on September 13, 2016 (the "Form 8-K"). The Form 8-K, as filed, is set forth below.

The information contained in this Prospectus Supplement No. 4 supplements and supersedes, in relevant part, the information contained in the Prospectus, as amended and supplemented to date. This Prospectus Supplement No. 4 is incorporated by reference into, and should be read in conjunction with, the Prospectus, as amended and supplemented to date, and is not complete without, and may not be delivered or utilized except in connection with, the Prospectus, as amended and supplemented to date.

The Prospectus, together with Prospectus Supplement No. 1, Prospectus Supplement No. 2, Prospectus Supplement No. 3 and this Prospectus Supplement No. 4 constitutes the prospectus required to be delivered by Section 5(b) of the Securities Act of 1933, as amended, with respect to offers and sales of the securities as set forth in the Prospectus, as amended and supplemented. All references in the Prospectus to "this prospectus" are amended to read "this prospectus (as supplemented and amended to date)."

Our common stock is traded on the NASDAQ Global Select Market under the symbol "ACRS." The last reported sale price of our common stock on September 12, 2016 was \$23.24 per share. You are urged to obtain current market quotations for the common stock.

We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings. Please see "Prospectus Summary—Implications of Being an Emerging Growth Company."

Investing in our common stock is highly speculative and involves a significant degree of risk. See "Risk Factors" beginning on page 5 of the Prospectus and the Risk Factors identified in our Annual Report for the year ended December 31, 2015 and in our Quarterly Report for the quarter ended June 30, 2016 for a discussion of information that should be considered before making a decision to purchase our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is September 13, 2016.

UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 13, 2016

ACLARIS THERAPEUTICS, INC. (Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation)

001-37581 (Commission File No.)

46-0571712 (IRS Employer Identification No.)

101 Lindenwood Drive, Suite 400

Malvern, PA 19355

(Address of principal executive offices and zip code) Registrant's telephone number, including area code: **(484) 324-7933**

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

□ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

□ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01 Other Events.

On September 13 and 14, 2016, members of management of Aclaris Therapeutics, Inc., or the Company, will hold meetings to review, among other things, the Company's product candidate pipeline and clinical development. In addition, on September 14, 2016, Neal Walker, the President and Chief Executive Officer of the Company, will present at the Morgan Stanley 2016 Global Healthcare Conference on, among other things, the Company's product candidate pipeline and clinical development. A copy of the presentation that will accompany the meetings and which is being presented at the Morgan Stanley conference is available on the Company's website at <u>www.aclaristx.com</u>, and is filed as Exhibit 99.1 to this Current Report on Form 8-K, the contents of which are incorporated herein by reference. A second presentation regarding the Company's wart disease program is also available on the Company's website at <u>www.aclaristx.com</u>, and is filed as Exhibit 99.1 to this Current Report on Form 8-K, the contents of which are incorporated herein by reference. A second presentation regarding the Company's wart disease program is also available on the Company's website at <u>www.aclaristx.com</u>, and is filed as Exhibit 99.2 to this Current Report on Form 8-K, the contents of which are incorporated herein by reference. The information contained in this Current Report on Form 8-K speaks only as the date hereof. While the Company may elect to update the information in this Current Report on Form 8-K in the future, the Company disclaims any obligation to do so except to the extent required by applicable law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Aclaris Therapeutics Corporate Overview Presentation.
99.2	Aclaris Therapeutics Wart Disease Presentation.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Aclaris Therapeutics, Inc.

Date: September 13, 2016

By: /s/ Frank Ruffo

Frank Ruffo Chief Financial Officer



Company Overview

Dr. Neal Walker President and CEO

September 2016

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This presentation contains forward-looking statements, including statements regarding the treatment and market opportunity for SK, common warts, alopecia areata, androgenetic alopecia, vitiligo, and the future operations of Aclaris. These statements involve substantial known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this presentation represent our views as of the date of this presentation. For further information regarding these risks, uncertainties and other factors you should read Aclaris' Annual Report on Form 10-K for the year ended December 31, 2015, Aclaris' Quarterly Report on Form 10-Q for the quarter ended June 30, 2016 and Aclaris' other filings it makes with the Securities and Exchange Commission from time to time. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.

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.





The Aclaris Opportunity

MANAGEMENT TEAM EXPERTISE IN DERMATOLOGY

- Founded and sold several companies
- Directly relevant experience in Dermatology
- Board-certified dermatologists as CEO and CSO
- Developed and commercialized multiple products

DRUG DEVELOPMENT PIPELINE

A-101: Proprietary formulation of high concentration H₂O₂

- Seborrheic Keratosis
 - Phase 3 Data 4Q 2016
- Common Warts
 - Phase 2 Data 3Q 2016

ATI-50001/ATI-50002/ATI-50003: JAK 3 and 1/3 Inhibitors

- Alopecia Areata
- Vitiligo
- Androgenetic Alopecia (AGA)

ATTRACTIVE DERMATOLOGY MARKETS

- Time and capital efficient
- Highly concentrated prescriber base
- Large unmet market segments with no FDAapproved drugs
- Growing market for cash pay aesthetic and medical dermatology products

ACLARIS

Build a Fully Integrated Dermatology Company

Our Drug Candidates

Exclusive, Worldwide Right to Commercialize A-101, A-102, ATI-50001, ATI-50002, and ATI-50003.

	RESEARCH	PRE-CLINICAL	PHASE I	PHASE II	PHASE III
A-101*					
Seborrheic Keratosis (topical)					
Common Warts (topical)					
ATI-50001					
Alopecia Areata (oral)					
ATI-50002					
Alopecia Areata (topical,oral)					
ATI-50001, ATI-50002					
Vitiligo (topical)					
ATI-50003					
Androgenetic Alopecia (topical)					

* Also developing A-102 topical gel as a lifecycle management opportunity for A-101



Seborrheic Keratosis (SK) Background



Untreated SK



Before Treatment 3 Months Post Cryosurgery

September 2016

- SK is one of most common diagnoses made by dermatologists
 - >83 million people with the disease in the U.S.
 - 18.5 million patient visits to dermatologists
 - 8.3 million procedures to remove SKs annually
 - \$1.2 billion historic costs of treatments for SK
- Patients seek diagnosis and treatment
 - Fear of skin cancer
 - Concern about appearance
 - Discomfort from itching and inflammation
- Current options for SK removal: cryosurgery, curettage, electrodessication or excision

Limitations of current removal options:

- Dyspigmentation (hypo or hyper)
- Scarring
- Pain
- Surgical invasive
- Treatment of numerous SK is impractical



Potential to Be First FDA-approved Drug for SK

A-101 is appealing concept for SK treatment

- Topical, non-invasive
- Minimal discomfort; no need for anesthesia
- Reduced risk of pigmentary changes and scarring
- Ability to treat larger numbers of lesions
- Ability to hand off to ancillary staff

Background

- Developed a proprietary formulation of 40.0% H₂O₂
- Conducted formal dose-ranging studies
- MOA: drives apoptotic and necrotic cell death



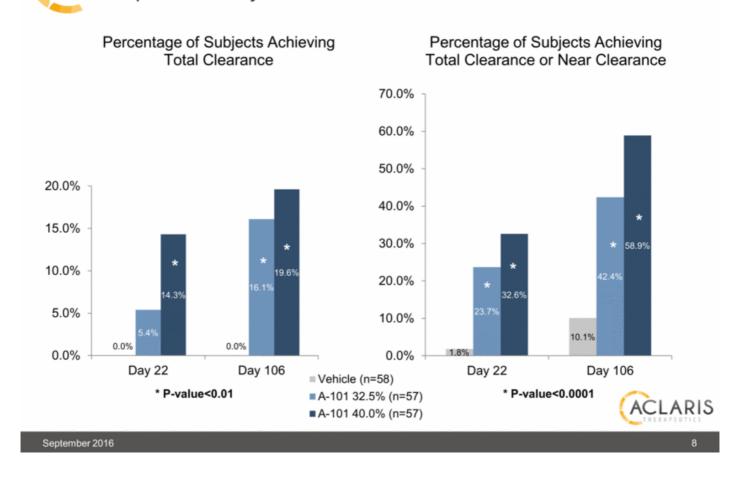
Inventor's Proof of Concept (with his initial formulation)



Summary of Completed Phase 2 Trials for SK

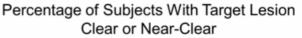
Trial	SK Lesion Area	Date Completed	Trial Design	Trial Outcome
SEBK-201 (n=35) Phase 2	Trunk (Back)	June 2014	 Single center, intra-subject Four lesions treated A-101 concentrations: 25.0%, 32.5%, 40.0% 1 or 2 applications Duration: 78 days 	 Efficacy: 32.4% clear; 67.7% clear or near clear with 40% concentration Favorable safety profile
SEBK–202 (n=172) Phase 2	Trunk and Extremities	December 2014	 Multicenter, parallel group Four lesions treated A-101 concentrations: 32.5%, 40.0% 1 or 2 applications Duration: 106 days 	 Efficacy: Demonstrated statistically significant clearance of all 4 lesions in top dose group (Phase 3 primary end point) Favorable safety profile
SEBK–203 (n=119) Phase 2	Face	March 2015	 Multicenter, parallel group One lesion treated A-101 concentrations: 32.5%, 40.0% 1 or 2 applications Duration: 106 days 	 Efficacy: Statistically significant clearance Favorable safety profile
				ACLARI

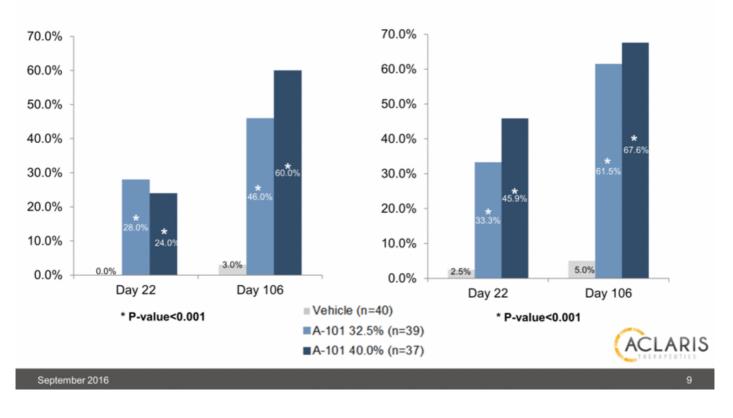
A-101 Phase 2 Trunk/Extremities Study: PLA Responder Analysis

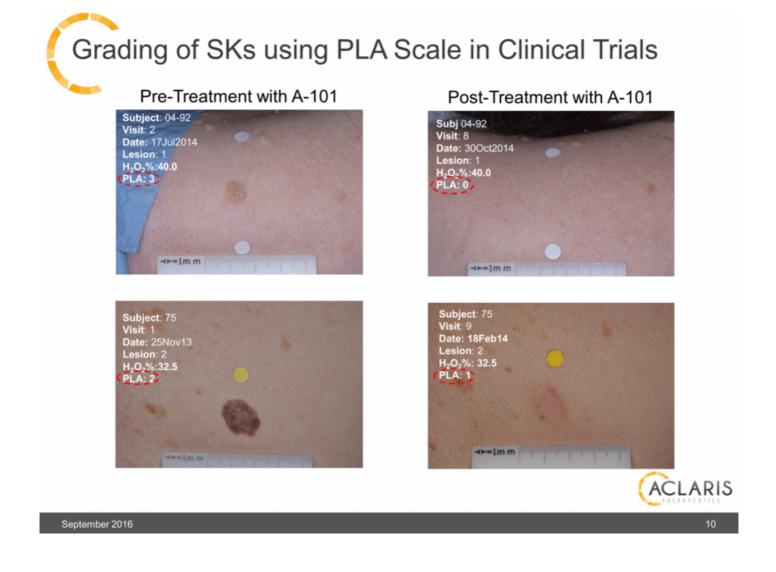




Percentage of Subjects With Target Lesion Clear







A-101 Next Steps: Phase 3 Overview

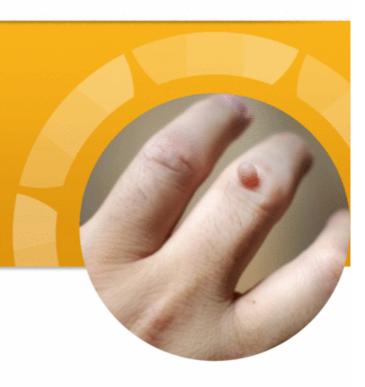
- A-101 40.0% is being used for Phase 3 clinical testing
- Initiated Phase 3 program January 2016
 - Pivotal trials (SEBK-301/302): Two identical Phase 3 trials
 - 4 lesions treated in total with at least one on face and one on trunk or extremities
 - Primary endpoint: Proportion of subjects with clear on PLA scale
 - 3 month drug-free follow-up
 - Open-label (SEBK-303): 4 SK lesions
 - Up to four applications
- Phase 3 Data 4Q 2016
- Plan to submit NDA 1Q 2017



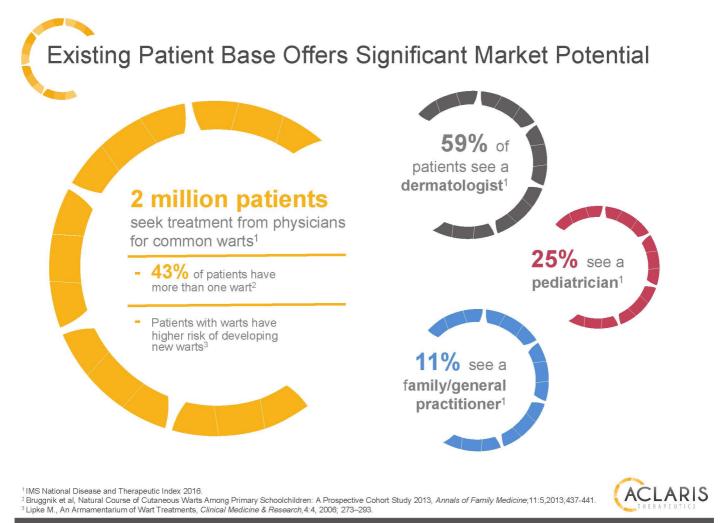
A-101 Commercialization Strategy

Buy and Bill Model	 Cash pay, minimally invasive procedure Lower cost relative to other aesthetic treatments (Botox[®], Fillers, Laser treatments)
Concentrated Prescriber Base	 5,000 dermatologists in US, accounting for over 70% of procedures performed Concentrated call point allows for high reach and frequency
Disease Awareness	Disease state awareness initiativesKOL engagement, conference presentations and publications
Commercial Launch	 50-60 person specialty sales team focused on high tier targets Comprehensive promotional campaign to include peer-influence programs
Patient Engagement	 Campaigns focused on driving awareness and furthering interest in treatment options
	ACLA











Trial	Common Wart Area	Topline Data	Trial Objective and Design	Trial Outcome
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:

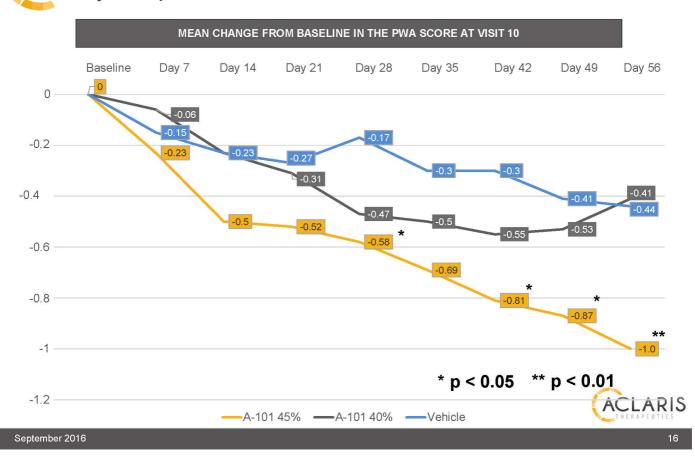
Mean change from baseline in the Physician's Wart Assessment (PWA) score at Visit 10 using a analysis of covariance

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.

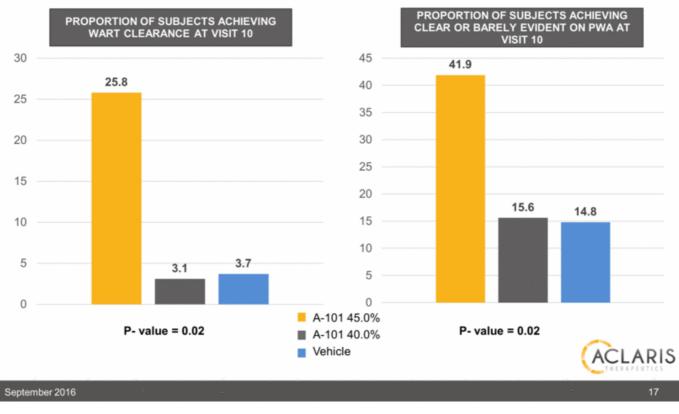


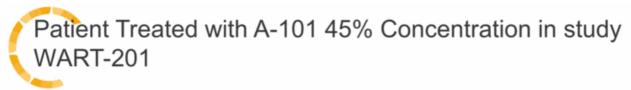
Both Statistical and Clinical Significance Achieved on Primary Endpoint with A-101 45% Concentration



Statistical Significance Achieved on Secondary Endpoints in Clearance of Common Warts with A-101 45% Concentration

Responder Analysis





Pre-Treatment with A-101



Visit 2 (PLA 3)

Post-Treatment with A-101



Visit 10 (PLA 0)



Skin Reactions Similar to Vehicle at Visit 10; Favorable Safety Profile



Based on Results, A-101 45% Concentration Considered for Further Development as Treatment for Common Warts

45% Concentration of A-101 Observed to be Safe and Effective

Statistical Significance	 Achieved both statistical and clinical significance on the primary endpoint Achieved statistical significance in complete clearance of the warts
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 commercial dosage form for common warts Develop as RX drug for patient to use at home
September 2016	

ATI-50001/ATI-50002 Candidates for Alopecia Areata





Alopecia Areata (AA) Background



AA - Patchy



Alopecia Universalis

September 2016

- AA is an autoimmune condition, characterized by patchy, nonscarring hair loss on the scalp and body
- Large unmet need: >6.6 million people in the U.S. have had or will develop AA at some point in their lives
 - 2/3 of affected individuals ≤30 years old at disease onset
 - 25-50% of patients have persistent patchy AA
 - 14%-25% of patients progress to totalis or universalis
- Current off label treatments include topical steroids, steroid injections, and minoxidil
- Recent translational research work by Dr. Angela Christiano
 - Furthered genetic understanding of disease
 - Identified JAK inhibitors as a potential treatment for AA

Potential to be First FDA-Approved Drug for AA



ATI-50001/ATI-50002: JAK Inhibitors in Alopecia Areata

- Lead asset: Selective JAK 1/3 inhibitor from Rigel
 - Exclusive, worldwide license and development collaboration
 - Oral and topical rights
 - Known mechanism of action and biological response in humans
 - Promoted hair regrowth in mouse model of AA
- Drug Candidates:
 - ATI-50001 for oral administration in Alopecia Totalis and Alopecia Universalis
 - ATI-50002 for topical administration in Patchy Alopecia Areata
- Development Strategy
 - Planned submission of IND: 2H 2016
 - Initiation of clinical trial: 1H 2017



Business Development Transactions

- Vixen (Columbia University IP) and Key Organics/JAKPharm
 - Broadens our IP estate
 - Methods of use covering JAK inhibitors for the treatment of:
 - Alopecia Areata
 - Androgenetic alopecia (female and male pattern hair loss)
 - Additional hair loss disorders
 - Next generation JAK inhibitors
 - Covalently bound highly selective JAK3 inhibitors



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Additional Potential Indications

- Androgenic alopecia (male and female pattern hair loss)
 - ٠ AGA is the most common cause of hair loss and is experienced by 70% of men and 40% of women at some point in their lives1
 - . In 2012, 35 million men and 21 million women suffered hair loss²
 - Topical JAK inhibitor

Vitiligo .

- Vitiligo impacts 1% to 2% of the overall global population irrespective of sex, race, or age³
- Disease onset occurs in about one-half of sufferers between the ages of 10 and 303
- Oral and topical JAK inhibitor

Cassiopea. Androgenic Alopecia.
 Bergeson, L. The Truth About Hair Loss and Baldness Cures. 11.08.2014.
 Fitzpatrick T., et al. Vitiligo Facts. American Vitiligo Research Foundation Inc.

September 2016



Male with AGA



Female with AGA







Milestone		20	16			20	17	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
A-101 SK								
Phase 3 Trials Initiated								
Phase 3 Data								
Submit NDA								
Submit MAA								
A-101 Common Warts								
Phase 2 Data								
ATI-50001/ATI-50002 Alopecia	Areata							
Submit IND								
Commence POC trial								
							A	CLAR



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Verruca Vulgaris (Common Warts) Market Opportunity

September 2016

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Trial	Common Wart Area	Topline Data	Trial Objective and Design	Trial Outcome
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:

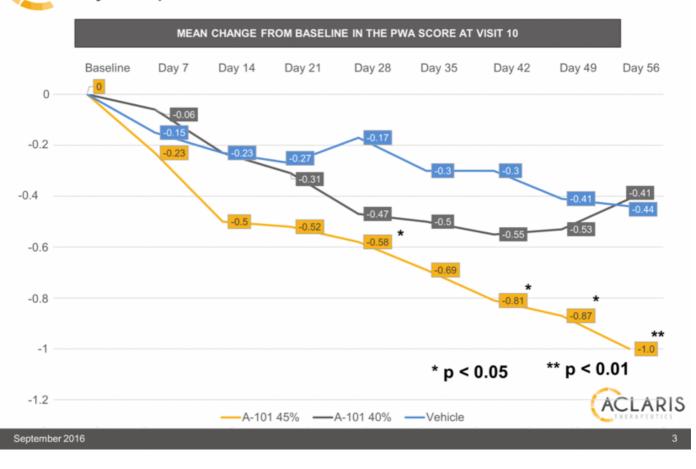
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Secondary Endpoints:

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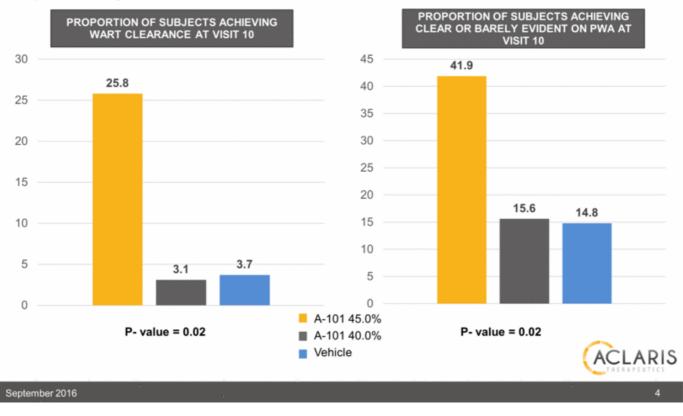


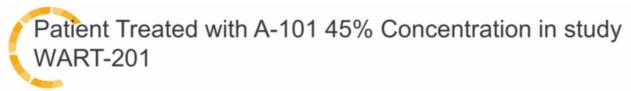
Both Statistical and Clinical Significance Achieved on Primary Endpoint with A-101 45% Concentration



Statistical Significance Achieved on Secondary Endpoints in Clearance of Common Warts with A-101 45% Concentration

Responder Analysis





Pre-Treatment with A-101



Visit 2 (PLA 3)

Post-Treatment with A-101



Visit 10 (PLA 0)

ACLARIS

Skin Reactions Similar to Vehicle at Visit 10; Favorable Safety Profile



Based on Results, A-101 45% Concentration Considered for Further Development as Treatment for Common Warts

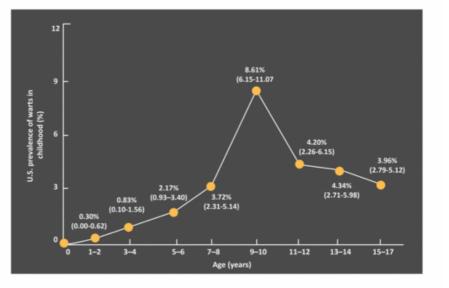
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	CACLARIS

Verruca Vulgaris (Common Warts): Common Skin Disease

ABOUT COMMON WARTS:

- Etiology keratinocytes infected by human papillomavirus (HPV); manifests as common warts, plantar warts or genital warts
- Virus spreads via direct contact or contact with environment
- U.S. population-based prevalence estimates in adults are lacking¹
- Children have increased risk due to immature immunologic response and frequent skin-to-skin contact with peers
 - U.S. prevalence of warts in children reported at 3.3%¹
 - In the U.S., in children ages 9-10, the estimated prevalence of warts. is 8.6%



¹ Silverberg et al, The US Prevalence of Common Warts in Childhood: A Population-Based Study, Journal of Investigative Dermatology; 2013; 133, 2788–2790.





- 50% of patients report discomfort¹
- 39% of patients say warts impact social/leisure activities¹ ٠
- Perceived social stigma,² possibly due to contagious nature ٠
- Warts can persist for years
 - In children, up to 2/3 of warts may resolve within two years³ ٠
 - ٠ Warts that do not clear within a year are unlikely to do so without treatment⁴
- OTC topical treatments containing salicylic acid are first-line and most common therapy¹
 - Promote exfoliation; stimulate host immunity ٠
 - Slow to work; require frequent application for up to 12 weeks² ٠
 - ٠ Marginally effective; 1.6 times more likely to clear treated warts than placebo4
- Two million patients seek treatment from HCP annually⁵

- ¹ Lipke M., An Armanmentanum or wart freatments, *Caincar Medicine & Research*, 44, 2006; 213–293.
 ² Mulhem et al, Treatment of Nongenital Cutaneous Warts, *American Family Physician*; 84:3, 2011; 288-293.
 ³ Bruggnik et al, Cryotherapy with liquid nitrogen versus topical salicytic acid application for cutaneous warts in primary care: randomized controlled trial, *Canadian Medical Association Journal*; 182:15, 2010; 1624-1630.
 ⁴ Kwok et al, Topical treatments for cutaneous warts (Review), *Cochrane Database of Systematic Reviews*, 9, 2012; Art. No.: CD001781.
- ⁵ IMS National Disease and Therapeutic Index 2016. 6 Patient interview



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

Treatment Guidelines for Common Warts



Lipke M., An Armamentarium of Wart Treatments, *Clinical Medicine & Research*,4:4, 2006; 273–293.
 ² IMS National Disease and Therapeutic Index 2016.

10

Significant Unmet Need Exists

COMMON WART TREATMENTS CURRENTLY USED BY PHYSICIANS...

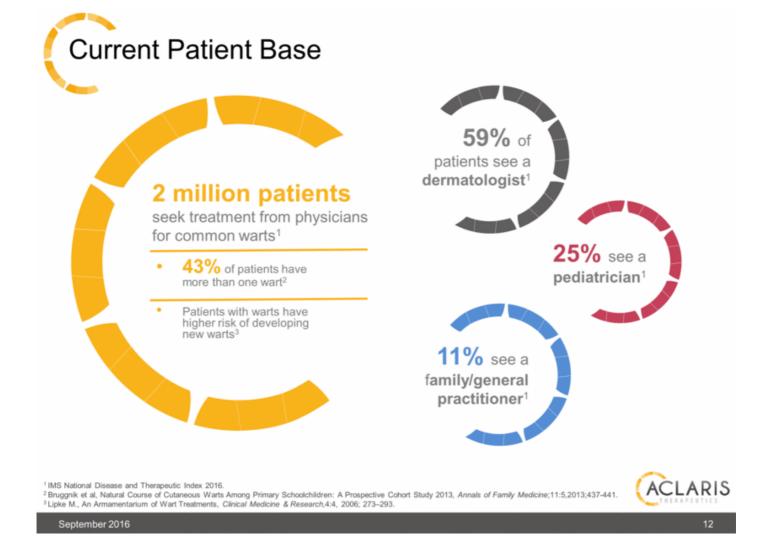
- About 45% of patients treated by a physician • receive cryosurgery
- Other in-office treatments (e.g., surgery, cautery, ٠ intralesional bleomycin injections)
- Off-label uses of Rx drugs (e.g., imiquimod) ٠
- Over-the-counter treatments (e.g., salicylic acid) ٠

- May be painful; challenge to treat children
- May cause scarring
- May cause dyspigmentation (hypo or hyper)
 Recurrence rate is high
- Lack of rigorous clinical studies
- Slow to work

- ¹ IMS National Disease and Therapeutic Index 2016.
 ² Lipke M., An Armamentarium of Wart Treatments, *Clinical Medicine & Research*,4:4, 2006; 273–293.
- ³ Stering et al, British Association of Dermatologists' guidelines for the management of cutaneous warts 2014, *British Journal of Dermatology*, 171, 2014; 696-712.
 ⁴ Kwok et al, Topical treatments for cutaneous warts (Review), *Cochrane Database of Systematic Reviews*, 9, 2012; Art. No.: CD001781.
 ⁵ Mulhem et al, Treatment of Nongenital Cutaneous Warts, *American Family Physician*; 84:3, 2011; 288-293











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