

EMPOWERING PATIENTS THROUGH  
**REVELATIONARY**  
SCIENCE

**THWART-1 and THWART-2 Phase 3 Data**

A-101 45% Topical Solution (An Investigational Drug  
Candidate for the Potential Treatment of Verruca Vulgaris  
(Common Warts))

October 24, 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 the development of Aclaris' drug candidates, including A-101 45% Topical Solution. 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 and in commercialization of products, 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, Aclaris' Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, 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 press release 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.

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# A-101 45% Topical Solution for the Treatment of Common Warts

- Benign cutaneous lesions caused by human papillomavirus infection of keratinocytes<sup>1-3</sup>
- Viral warts - one of the most common conditions seen by dermatologists<sup>4</sup>
- Estimated US prevalence of 5.8%<sup>5</sup>
- No FDA-approved prescription drug product for the treatment of common warts
- A-101 is a proprietary, stabilized, high-concentration hydrogen peroxide topical solution (45%)



1. Bacelieri R, Johnson SM. *Am Fam Physician*. 2005;72:647-52.

2. Al About AM, Nigam PK. *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2018.

3. Sterling JC, et al. *Br J Dermatol*. 2014;171:696-712.

4. Wilmer, Erin N., et al, *Cutis*. 2014; 94:285-292.

5. Kwong, PC, Berman, B , Wang, S, Prevalence of Common Warts in the United States: Findings From General Population and Physician-Focused Surveys, presented at Annual Fall Clinical Dermatology Conference Oct 17-20, 2019.

# Burden of Common Warts

## Estimated US Prevalence of 5.8%<sup>1</sup>

Internet Health Survey of 20,056 Respondents

N=1168 reported common warts currently or within the preceding month

Audience <sup>a</sup>	Total Numbers of Respondents	Respondents With Common Warts <sup>b</sup>	Estimated Prevalence Rate
Children	4967	409	8.2%
Adults	15,089	759	5.0%
Total	20,056	1168	5.8%

<sup>a</sup> Adult participants selected responses for children in their household with common warts.

<sup>b</sup> Counts of respondents after the reduction factor step of the methodology was applied.

## US Market Estimate ~19 million patients<sup>1</sup>

Patients with warts have a **higher risk** of developing new warts<sup>3</sup>

## Patients with common warts who seek professional treatment...<sup>2</sup>



**45%** see a family/general practitioner



**29%** see a dermatologist  
(31% referred by another HCP)

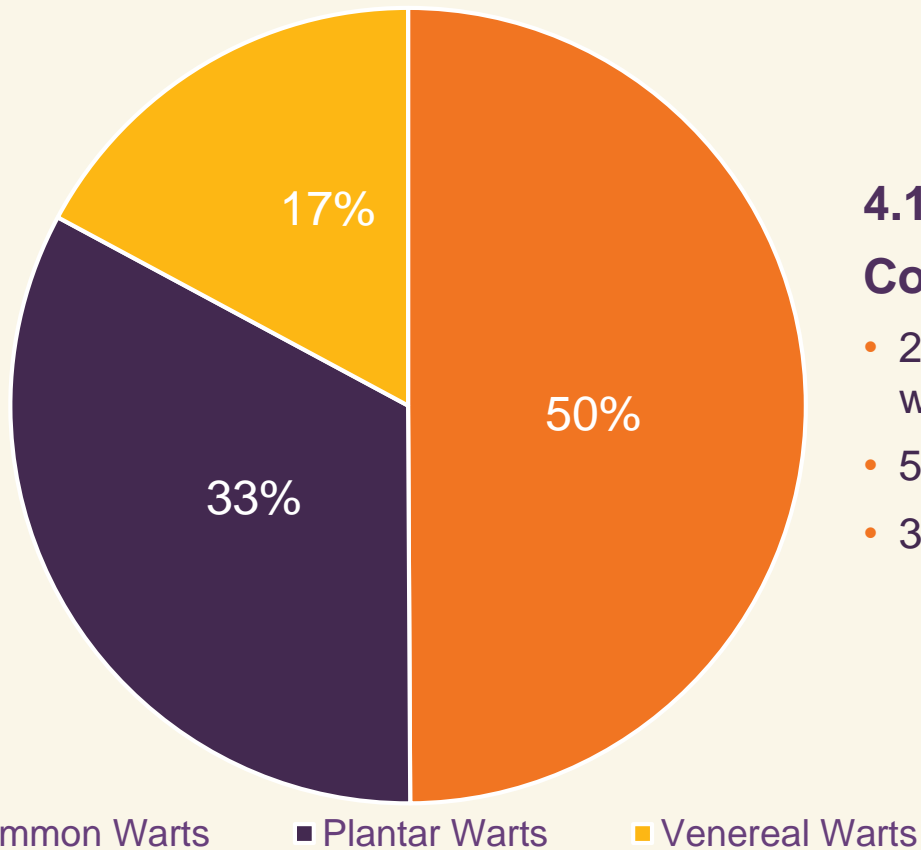
<sup>1</sup>Kwong, PC, Berman, B, Wang, S, Prevalence of Common Warts in the United States: Findings From General Population and Physician-Focused Surveys, presented at Annual Fall Clinical Dermatology Conference Oct 17-20, 2019.

<sup>2</sup>Data on file.

<sup>3</sup>Lipke M. Clin Med & Res 2006;4(4):273–293.

# Wart Market: Patient Visits by Wart Type

## Patient Visits for Warts



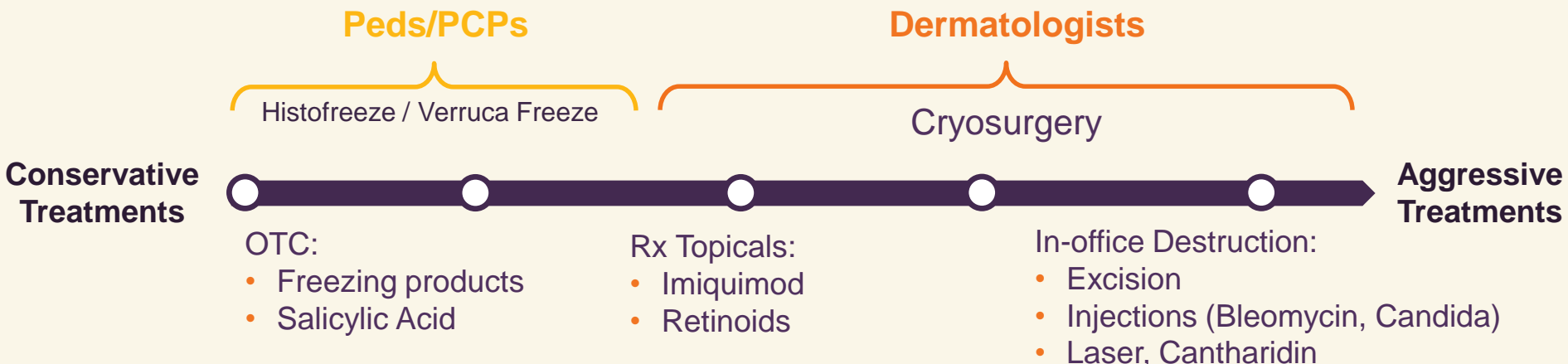
## 4.1MM Patient Visits for Warts<sup>1</sup>

### Common Warts:

- 2-2.5MM patient visits for common warts<sup>1</sup>
- 50% of all patient visits for warts<sup>1</sup>
- 3x more patient visits than genital warts<sup>1</sup>

<sup>1</sup> IMS National Disease and Therapeutic Index 2016.

# 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

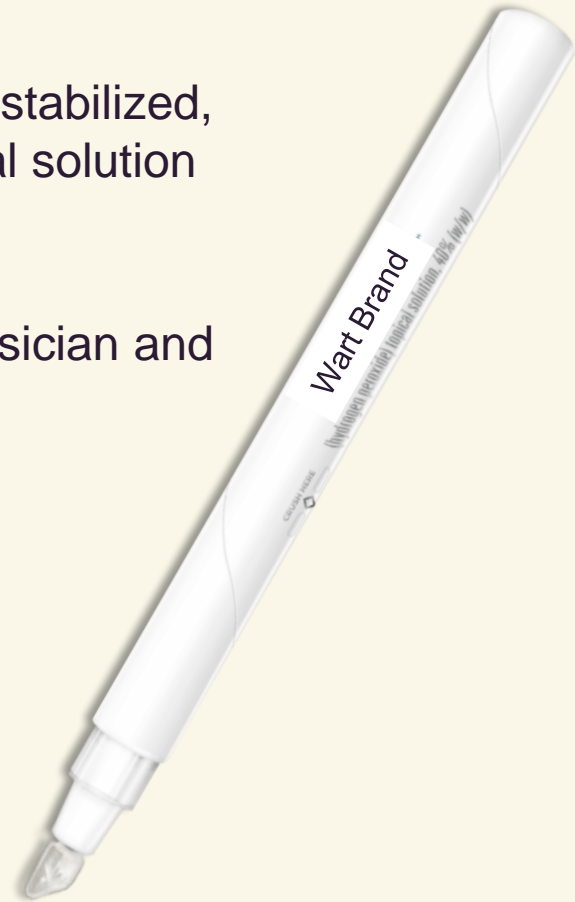
## Dermatologists:

- 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
- Standard of Care includes multiple treatment modalities
- Opportunity to position A-101 45% as Rx treatment with convenience of home use

# A-101 45% Topical Solution & Proprietary Applicator

- ✓ A-101 45% Topical Solution is a proprietary, stabilized, high-concentration hydrogen peroxide topical solution (45%)
- ✓ Treatment designed to be prescribed by physician and applied at home
  - Handheld and disposable
  - No refrigeration required
  - Retail pharmacy distribution channel



# THWART-1 & THWART-2

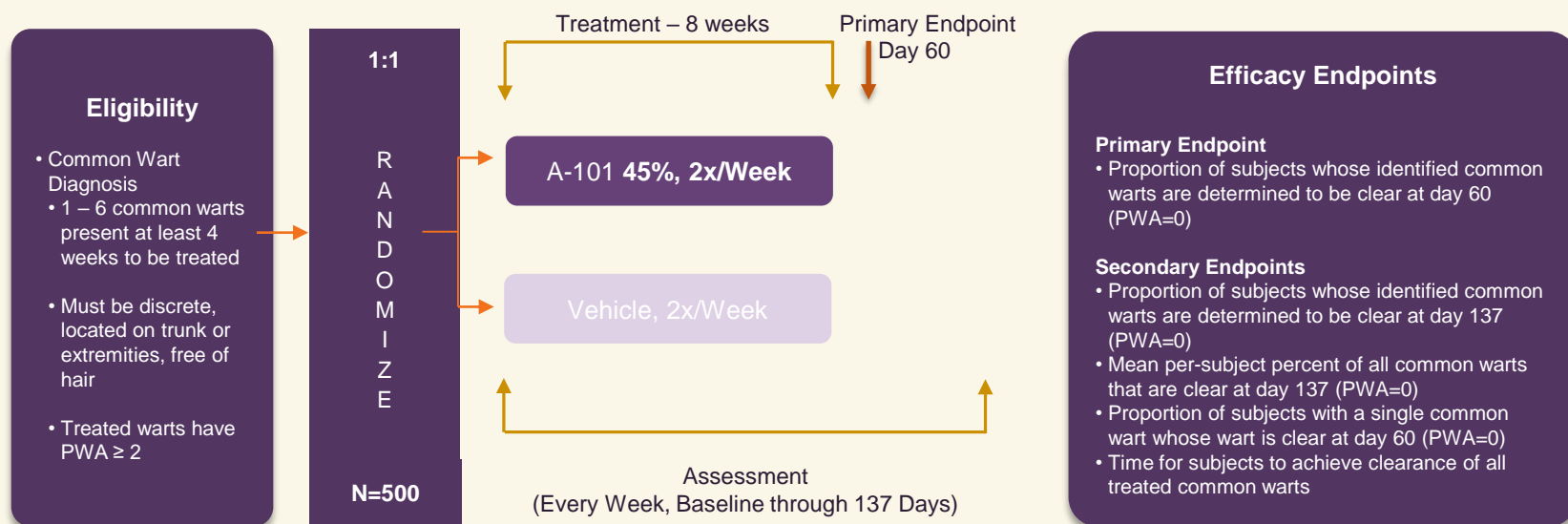




# Pivotal Phase 3 Clinical Trials Design THWART-1 and THWART-2

## A-101 45% Topical Solution vs Vehicle in Subjects With Common Warts

### Randomized, Double-blind, Vehicle-controlled Multicenter Studies



# Hierarchical Testing of Efficacy Endpoints

Hierarchy	Endpoint Description
Primary Endpoint	Proportion of subjects whose identified common warts are determined to be clear at day 60 (PWA=0)
1st Secondary Endpoint	Proportion of subjects whose identified common warts are determined to be clear at day 137 (PWA=0)
2nd Secondary Endpoint	Mean per-subject percent of all common warts that are clear at day 137 (PWA=0)
3rd Secondary Endpoint	Proportion of subjects with a single common wart whose wart is clear at day 60 (PWA=0)
4th Secondary Endpoint	Time for subjects to achieve clearance of all treated common warts

Pre-defined fixed-sequence step down method; testing stopped if an endpoint is non-significant

# Subject Disposition

## THWART-1

## THWART-2

Enrolled

N=581

N=551

Randomized

N=503

N=502

Allocation

A-101  
45% BIW  
N=254

Vehicle  
BIW  
N=249

A-101  
45% BIW  
N=251

Vehicle  
BIW  
N=251

Completed

N=237  
(93.3%)

N=210  
(84.3%)

N= 224  
(89.2%)

N=220  
(87.6%)

Discontinued  
Reasons

N=17 (6.7%)  
AE 0  
Loss to Follow-Up 12 (4.7%)  
Withdrew Consent 4 (1.6%)  
Other 1 (0.4%)

N=39 (15.7%)  
AE 0  
Loss to Follow-Up 21 (8.4%)  
Withdrew Consent 17 (6.8%)  
Other 1 (0.4%)

N=27 (10.8%)  
AE 0  
Loss to Follow-Up 16 (6.4%)  
Withdrew Consent 9 (3.6%)  
Other 2 (0.8%)

N=31 (12.4%)  
AE 0  
Loss to Follow-Up 12 (4.8%)  
Withdrew Consent 17 (6.8%)  
Other 2 (0.8%)

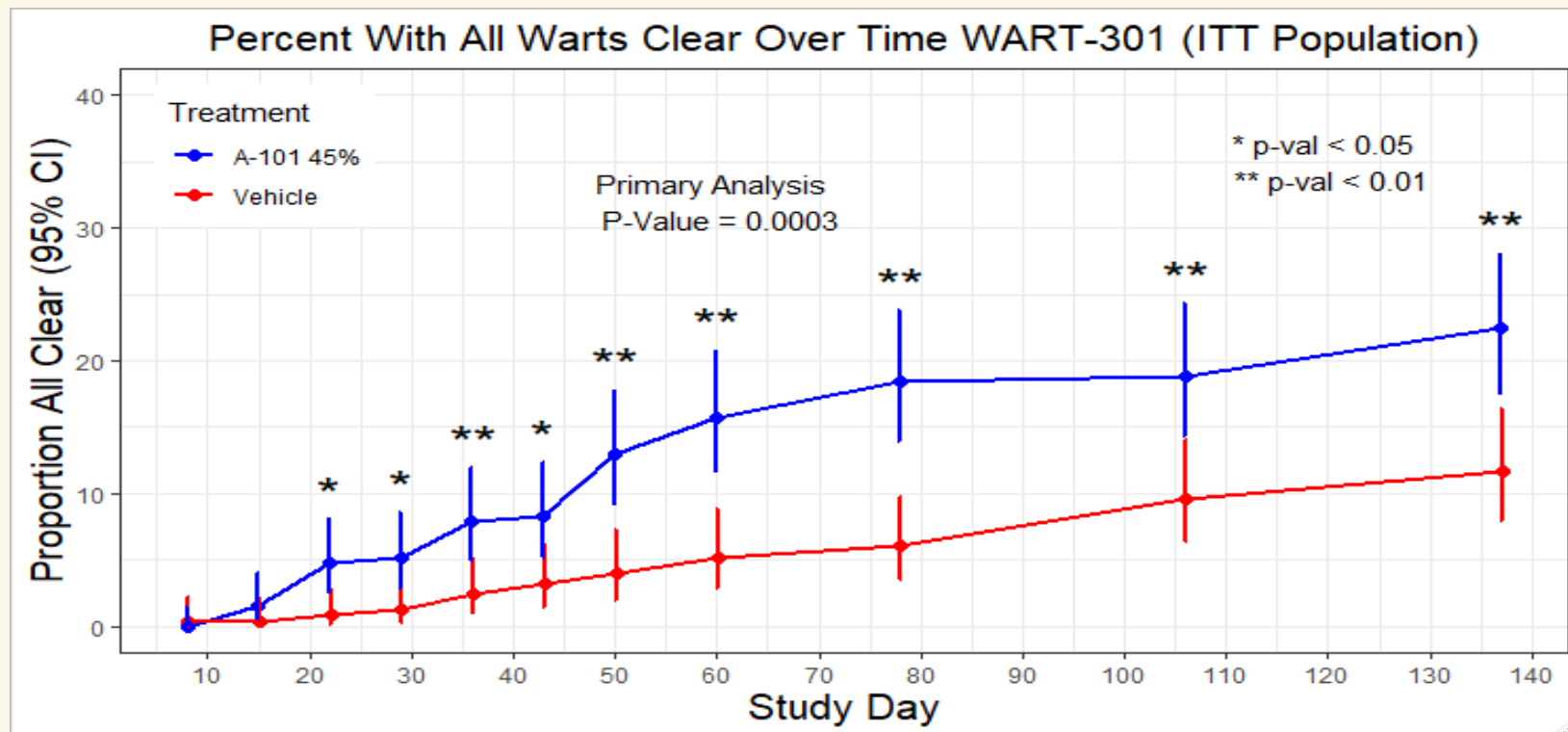
# Demographics

	THWART-1		THWART-2	
	A-101 45% N=254	Vehicle N=249	A-101 45% N=251	Vehicle N=251
Age Mean (SD)	31.0 (18.21)	29.4 (18.3)	31.1 (17.8)	31.7 (17.33)
Sex, N(%)				
Sex Male	112 (44.1%)	112 (45.0%)	104 (41.4%)	111 (44.2%)
Sex Female	142 (55.9%)	137 (55.0%)	147 (58.6%)	140 (55.8%)
Race, N(%)				
White	238 (93.7%)	236 (94.8%)	228 (90.8%)	230 (91.6%)
African American	4 (1.6%)	4 (1.6%)	13 (5.2%)	13 (5.2%)
Asian	8 (3.1%)	4 (1.6%)	5 (2.0%)	2 (0.8%)
Native Hawaiian or Pacific Islander	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
American Indian	2 (0.8%)	0	1 (0.4%)	0
Alaskan Native	0	0	0	0
Other	1 (0.4%)	4 (1.6%)	2 (0.8%)	6 (2.4%)

# Demographics

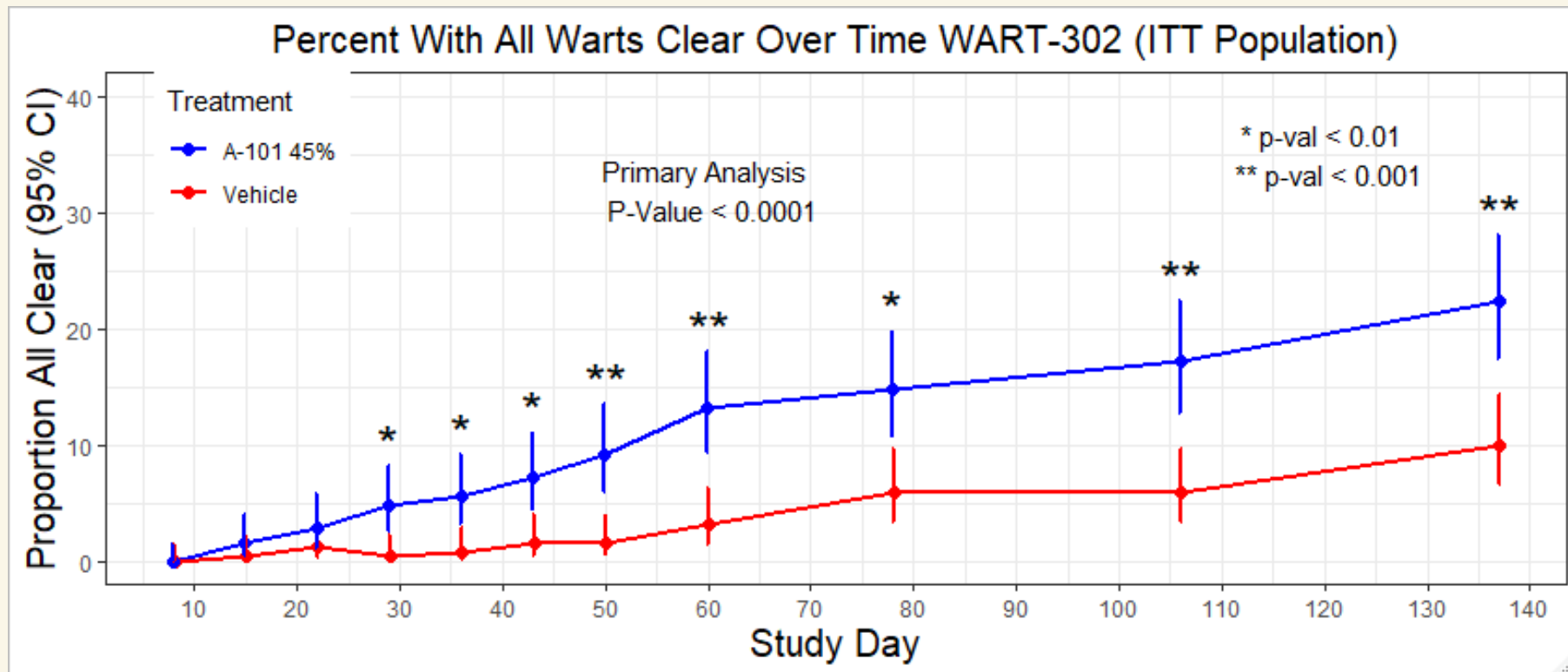
	THWART-1		THWART-2	
	A-101 45% N=254	Vehicle N=249	A-101 45% N=251	Vehicle N=251
Prior Treatment of any Treated wart, N(%)				
Yes	124 (48.8%)	118 (47.4%)	114 (45.4%)	112 (44.6%)
No	130 (51.2%)	131 (52.6%)	137 (54.6%)	139 (55.4%)
Total warts treated, N(%)				
1	162 (63.8%)	141 (56.6%)	126 (50.2%)	142 (56.6%)
2	37 (14.6%)	49 (19.7%)	68 (27.1%)	49 (19.5%)
3	28 (11.0%)	22 (8.8%)	22 (8.8%)	18 (7.2%)
>3	27 (10.6%)	37 (14.9%)	35 (13.9%)	42 (16.7%)
4	10 (3.9%)	15 (6.0%)	13 (5.2%)	14 (5.6%)
5	5 (2.0%)	9 (3.6%)	10 (4.0%)	10 (4.0%)
6	12 (4.7%)	13 (5.2%)	12 (4.8%)	18 (7.2%)

# THWART-1: Primary Endpoint & 1<sup>st</sup> Secondary Efficacy Endpoint: Percent Clearance of all Treated Warts at Day 60 and at Day 137



- Primary endpoint (complete clearance at Day 60): 15.7% A-101 45% vs 5.2% vehicle ( $p=0.0003$ )
- First secondary efficacy endpoint (complete clearance at Day 137): 22.4% A-101 45% vs 11.6% vehicle ( $p=0.0024$ )

# THWART-2: Primary Endpoint & 1<sup>st</sup> Secondary Efficacy Endpoint: Percent Clearance of all Treated Warts at Day 60 and at Day 137



- Primary endpoint (complete clearance at Day 60): 13.1% A-101 45% vs 3.2% vehicle (p<.0001)
- First secondary efficacy endpoint (complete clearance at Day 137): 22.3% A-101 45% vs 10.0% vehicle (p<.0001)

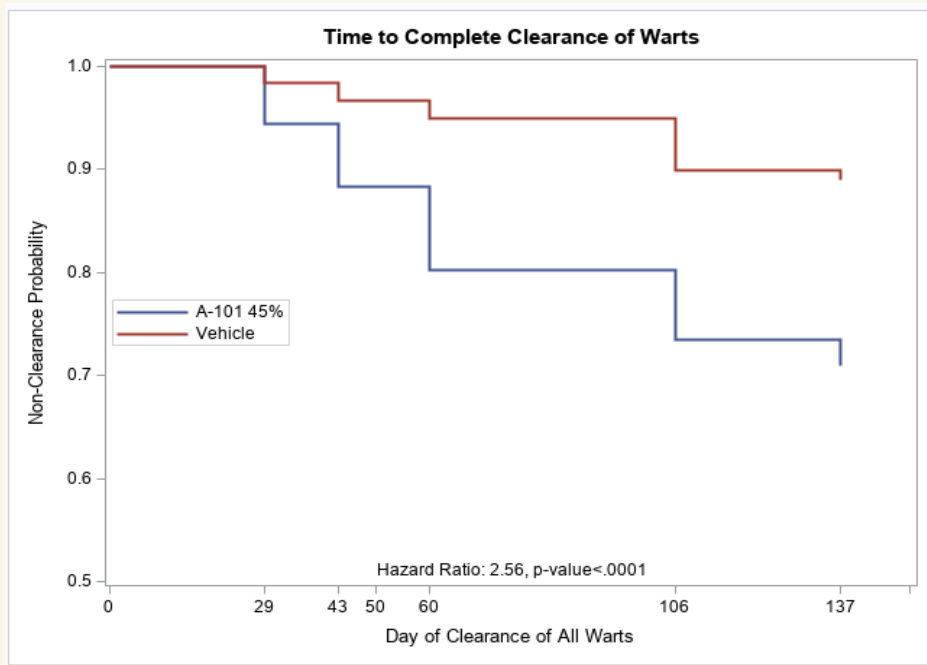
# Summary of Primary & Secondary Endpoints

	<b>PRIMARY</b> Proportion of subjects whose identified common warts are determined to be clear at day 60 (PWA=0) (%)	<b>SECONDARY</b> Proportion of subjects whose identified common warts are determined to be clear at day 137 (PWA=0) (%)	<b>SECONDARY</b> Mean per-subject percent of all common warts that are clear at day 137 (PWA=0) (%)	<b>SECONDARY</b> Proportion of subjects with a single common wart whose wart is clear at day 60 (PWA=0) (%)	<b>SECONDARY</b> Time for subjects to achieve clearance of all treated common warts. 25th percentile (Days)
<b>THWART-1</b>					
A-101 45%	15.7%	22.4%	28.6%	20.4%	84
VEHICLE	5.2%	11.6%	14.5%	7.1%	147
p-value	0.0003	0.0024	<0.0001	0.0009	<0.0001
<b>THWART-2</b>					
A-101 45%	13.1%	22.3%	27.7%	15.1%	113
VEHICLE	3.2%	10%	12.2%	2.8%	169
p-value	<0.0001	0.0001	<0.0001	0.0006	<0.0001



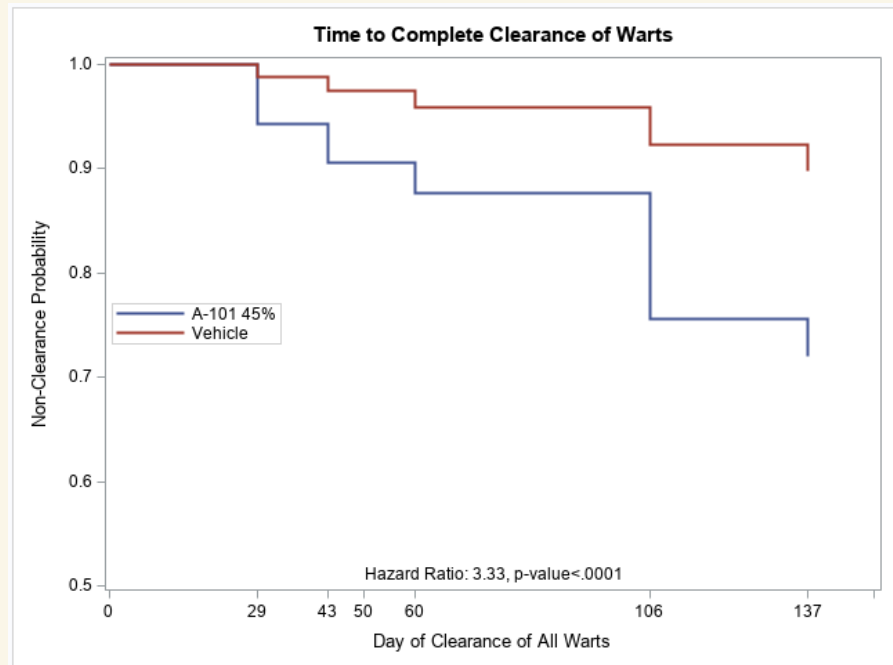
# Time to Complete Clearance of All Treated Common Warts

## THWART-1



(p<.0001) met with a Hazard Ratio of 2.56

## THWART-2



(p<.0001) met with a Hazard Ratio of 3.33

# Efficacy Results of Wart Treatments

*There are no head-to-head comparisons between A-101 45% and other treatments*

- THWART-1: Complete Clearance of All Warts at V10 (Day 60) Risk Ratio **2.8275 [1.5578, 5.1323]**
- THWART-2: Complete Clearance of All Warts at V10 (Day 60) Risk Ratio **4.4007 [1.9987, 9.6893]**

Meta-analysis of other treatments, Studies Ranged from 6 weeks to 6 months<sup>1</sup>

## Comparison 1. Topical salicylic acid (SA/LA) vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cure rate all studies all sites	6	486	Risk Ratio (M-H, Random, 95% CI)	1.56 [1.20, 2.03]

## Comparison 2. Cryotherapy vs placebo/no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cure rate all studies all sites	3	227	Risk Ratio (M-H, Random, 95% CI)	1.45 [0.65, 3.23]

1 Kwok CS, Gibbs S, Bennett C, Holland R, Abbott R. 2012. Topical treatments for cutaneous warts. *Cochrane Database Syst Rev*. CD001781

# Safety Results: Overall Summary of Adverse Events

	THWART-1		THWART-2	
	A-101 45% N=254	Vehicle N=249	A-101 45% N=251	Vehicle N=251
Number of Treatment-emergent Adverse Events (TEAEs) Reported	733	111	1622	107
Number of Subjects with TEAEs <sup>1</sup>	153 (60.2%)	67 (26.9%)	154 (61.4%)	61 (24.3%)
Number of Subjects with TESAEs <sup>1</sup>	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
Number of Subjects Discontinued Study Treatment Due to AEs	1 (0.4%)	0	0	0
Number of Subjects Discontinued Study Treatment Due to SAE	0	0	0	0
Number of Subjects Discontinued Study Due to AE	0	0	0	0
Number of Subjects Discontinued Study Due to SAE	0	0	0	0
Number of Subjects with Related AE	134 (52.8%)	15 (6.0%)	134 (53.4%)	22 (8.8%)
Number of Subjects with Related SAE	0	0	0	0

<sup>1</sup> Subjects who had more than one adverse event or serious adverse event were only counted once.

# Treatment-Related Adverse Events (> 1% in A-101 45% group)

	THWART-1		THWART-2	
	A-101 45% N= 254	Vehicle N= 249	A-101 45% N=251	Vehicle N=251
<b>Any Adverse Events</b>	134 (52.8%)	15 (6.0%)	134 (53.4%)	22 (8.8%)
<b>General disorders and administration site conditions</b>	133 (52.4%)	15 (6.0%)	134 (53.4%)	21 (8.4%)
Application site discoloration	1 (0.4%)	0	4 (1.6%)	1 (0.4%)
Application site erosion	16 (6.3%)	2 (0.8%)	13 (5.2%)	2 (0.8%)
Application site erythema	43 (16.9%)	4 (1.6%)	26 (10.4%)	9 (3.6%)
Application site irritation	3 (1.2%)	0	5 (2.0%)	0
Application site edema	10 (3.9%)	0	10 (4.0%)	5 (2.0%)
Application site pain	80 (31.5%)	5 (2.0%)	107 (42.6%)	5 (2.0%)
Application site pallor	3 (1.2%)	0	44 (17.5%)	0
Application site paresthesia	0	1 (0.4%)	3 (1.2%)	3 (1.2%)
Application site pruritus	26 (10.2%)	5 (2.0%)	23 (9.2%)	2 (0.8%)
Application site reaction	3 (1.2%)	0	0	0
Application site scab	50 (19.7%)	1 (0.4%)	20 (8.0%)	0
Application site vesicles	3 (1.2%)	0	1 (0.4%)	0

# THWART-1: Treatment-related Adverse Events by Severity

	A-101 45% (N=254), n (%)			
MedDRA SOC	Severity			
Preferred term	Mild	Moderate	Severe	Total
<b>Any Adverse Event</b>	<b>88 (34.6%)</b>	<b>44 (17.3%)</b>	<b>2 (0.8%)</b>	<b>134 (52.8%)</b>
<b>General disorders and administration site conditions</b>	87 (34.25%)	44 (17.3%)	2 (0.8%)	133 (52.4%)
Application site discoloration	0	1 (0.4%)	0	1 (0.4%)
Application site dryness	2 (0.8%)	0	0	2 (0.8%)
Application site dysesthesia	1 (0.4%)	0	0	1 (0.4%)
Application site erosion	16 (6.3%)	0	0	16 (6.3%)
Application site erythema	33 (12.9%)	10 (3.9%)	0	43 (16.9%)
Application site fissure	2 (0.8%)	0	0	2 (0.8%)
Application site irritation	3 (1.2%)	0	0	3 (1.2%)
Application site edema	9 (3.5%)	1 (0.4%)	0	10 (3.9%)
Application site pain	57 (22.4%)	22 (8.7%)	1 (0.4%)	80 (31.5%)
Application site pallor	3 (1.2%)	0	0	3 (1.2%)
Application site pruritus	21 (8.3%)	5 (1.9%)	0	26 (10.2%)
Application site reaction	3 (1.2%)	0	0	3 (1.2%)
Application site scab	32 (12.6%)	18 (7.1%)	0	50 (19.7%)
Application site ulcer	2 (0.8%)	0	0	2 (0.8%)
Application site vesicles	2 (0.8%)	0	1 (0.4%)	3 (1.2%)
<b>Skin and subcutaneous tissue disorders</b>	4 (1.8%)	0	0	4 (1.8%)
Erythema	1 (0.4%)	0	0	1 (0.4%)
Nail dystrophy	1 (0.4%)	0	0	1 (0.4%)
Onycholysis	1 (0.4%)	0	0	1 (0.4%)
Skin exfoliation	1 (0.4%)	0	0	1 (0.4%)

# THWART-2: Treatment-related Adverse Events by Severity

	A-101 45% (N=251), n (%)			
MedDRA SOC	Severity			
Preferred term	Mild	Moderate	Severe	Total
<b>Any Adverse Event</b>	<b>108 (43.0%)</b>	<b>21 (8.4%)</b>	<b>5 (2.0%)</b>	<b>134 (53.4%)</b>
<b>General disorders and administration site conditions</b>	108 (43.0%)	21 (8.4%)	5 (2.0%)	134 (53.4%)
Application site dermatitis	2 (0.8%)	0	0	2 (0.8%)
Application site discolouration	2 (0.8%)	2 (0.8%)	0	4 (1.6%)
Application site dryness	2 (0.8%)	0	0	2 (0.8%)
Application site erosion	11 (4.4%)	2 (0.8%)	0	13 (5.2%)
Application site erythema	23 (9.2%)	3 (1.2%)	0	26 (10.4%)
Application site haemorrhage	1 (0.4%)	0	0	1 (0.4%)
Application site hypoaesthesia	1 (0.4%)	0	0	1 (0.4%)
Application site irritation	5 (2.0%)	0	0	5 (2.0%)
Application site oedema	8 (3.2%)	2 (0.8%)	0	10 (4.0%)
Application site pain	92 (36.7%)	14 (5.6%)	1 (0.4%)	107 (42.6%)
Application site pallor	37 (14.7%)	3 (1.2%)	4 (1.6%)	44 (17.5%)
Application site paraesthesia	3 (1.2%)	0	0	3 (1.2%)
Application site pruritus	21 (8.4%)	2 (0.8%)	0	23 (9.2%)
Application site scab	14 (5.6%)	6 (2.4%)	0	20 (8.0%)
Application site swelling	1 (0.4%)	0	0	1 (0.4%)
Application site ulcer	1 (0.4%)	0	0	1 (0.4%)
Application site vesicles	1 (0.4%)	0	0	1 (0.4%)
Feeling cold	1 (0.4%)	0	0	1 (0.4%)
Pain	1 (0.4%)	0	0	1 (0.4%)
<b>Nervous system disorders</b>	1 (0.4%)	0	0	1 (0.4%)
Burning sensation	1 (0.4%)	0	0	1 (0.4%)
<b>Skin and subcutaneous tissue disorders</b>	1 (0.4%)	0	0	1 (0.4%)
Nail discoloration	1 (0.4%)	0	0	1 (0.4%)

# Treatment Emergent Serious Adverse Events

<b>THWART-1</b>	<b>A-101 45% N=254</b>	<b>Vehicle N=249</b>
Any Treatment Emergent Serious Adverse Events	1 (0.4%)	1 (0.4%)
Injury, poisoning, and procedural complications	1 (0.4%)	0
Animal bite	1 (0.4%)	0
Psychiatric disorders	0	1 (0.4%)
Suicide attempt	0	1 (0.4%)
<b>THWART-2</b>	<b>A-101 45% N=251</b>	<b>Vehicle N=251</b>
Any Treatment Emergent Serious Adverse Events	1 (0.4%)	1 (0.4%)
Gastrointestinal disorders	1 (0.4%)	0
Intestinal obstruction	1 (0.4%)	0
Renal and urinary disorders	0	1 (0.4%)
Stag horn calculus	0	1 (0.4%)

# THWART-1 & THWART-2 Summary

- A-101 45% met the primary endpoint and all secondary efficacy endpoints in THWART-1 & THWART-2
- AE profile:
  - ✓ the majority of AEs were application site reactions
    - application site AEs were predominantly mild or moderate
  - ✓ no treatment-related SAEs were observed in the trials
  - ✓ one AE led to treatment discontinuation (no trial discontinuations due to AE)
  - ✓ the most common AEs occurring in more than 5% of subjects in the A-101 45% group were application site pain, scabbing, erythema, pruritus, pallor and erosion
- A-101 45% has potential to be the first FDA approved prescription medicine for the treatment of common warts



THANK YOU

