

Results From Phase II Study of Nitric Oxide-Releasing SB206 Once Daily Administration Show Favorable Efficacy and Safety in Genital Warts

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ORANGE COUNTY CONVENTION CENTER

DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Stephen K. Tyring, MD, PhD

F056: Results From Phase II Study of Nitric Oxide-Releasing SB206 Once Daily Administration Show Favorable Efficacy and Safety in Genital Warts

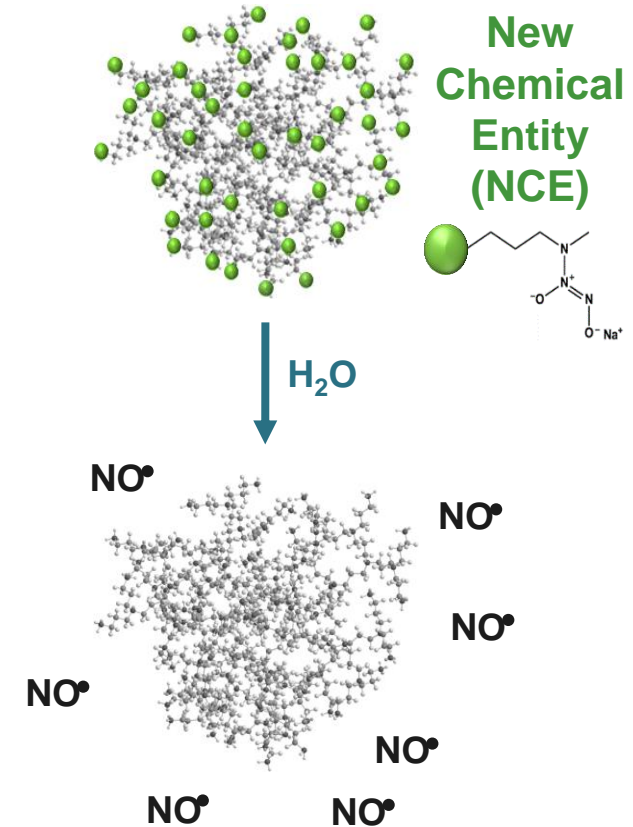
DISCLOSURES

Novan, Inc Investigator (grants)

SB206 – an Investigational, Nitric Oxide-releasing Topical Gel for Genital Warts

- SB206 contains NVN1000¹, a macromolecule that releases nitric oxide, an endogenous anti-viral agent.
- In non-clinical studies,^{2,3} NVN1000 and similar compounds have shown:
 - Dose-dependent inhibition of HPV-18 replication with selective targeting of E6 and E7 protein expression.
 - Dose-responsive inhibition of wart formation in a CRPV* animal model.
- SB206 may offer a novel mechanism of action for the treatment of genital warts.

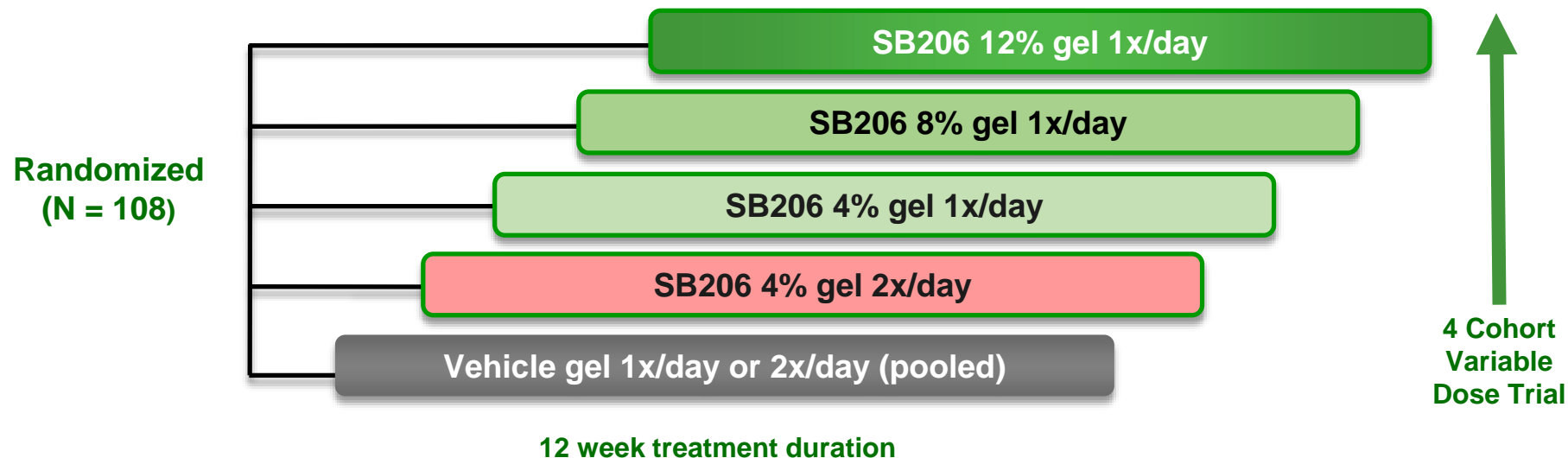
*CRPV – Cottontail Rabbit Papilloma Virus



1. Shin JH, Schoenfisch MH. *Chemistry of Materials* (2008); 20(1):239-249
2. McHale KA. et al. Abstract 536. *Journal of Investigative Dermatology*. 2016:v136(5):S95
3. Banerjee SN, et al. Antiviral Effects of Nitric Oxide-Releasing Drug Candidates in Suppressing Productive Infection of HPV-18 in an Organotypic Epithelial Raft Culture Model System. International Papillomavirus Conference 2017 in South Africa February 28th-March 3rd.

Phase 2 SB206 Study Design

- Randomized, double-blind, vehicle-controlled, variable dose trial assessing tolerability, safety and efficacy of NVN1000 gel* and vehicle gel (3:1 randomization) in subjects with external genital and perianal warts.
- An independent DSMB+ reviewed the safety/tolerability data for each cohort after 12 subjects completed a week 2 visit prior to dose escalation.



*NVN1000 gel was co-administered topically with a buffered hydrogel, each supplied in 15-gram aluminum tubes, to result in the final SB206 doses as dispensed.

+ DSMB - Data Safety Monitoring Board.

Major Inclusion/Exclusion Criteria

Inclusion Criteria

- ⦿ Non-immunocompromised, Male or Female, 18-50 years old.
- ⦿ 2-20 external genital warts/perianal warts with a maximum total wart surface area <1% BSA.

Exclusion Criteria

- ⦿ Received treatment for EGW/PAW during the 28 days prior to baseline.
- ⦿ Any recent history of other genital infections or other genital diseases.
- ⦿ Active HSV infection of the genitals or frequent recurrences.
- ⦿ History of neoplasia within 5 years or current neoplasia.

Endpoints

Primary Endpoint:

- ⦿ Proportion of patients at week 12 completely clear of baseline warts.

Secondary Endpoints:

- ⦿ Proportion of patients at week 12 completely clear of total warts.
- ⦿ Proportion of patients at week 12 with a partial response.
- ⦿ Efficacy by gender.

Phase 2 Patient Demographics and Disposition

	Vehicle gel QD/BID (n = 27)	SB206 4% gel BID (n = 12)	SB206 4% gel QD (n = 24)	SB206 8% gel QD (n = 14)	SB206 12% gel QD (n = 30)
Gender, n (%)					
Male	19 (70.4%)	6 (50.0%)	16 (66.7%)	12 (85.7%)	23 (76.7%)
Female	8 (29.6%)	6 (50.0%)	8 (33.3%)	2 (14.3%)	7 (23.3%)
Age, years					
Mean	32.1	36.8	33.3	32.5	33.6
Min to max	21-48	24-47	19-45	22-43	19-48
Baseline wart count					
Mean (SD)	7.71 (6.75)	9.3 (5.93)	7.5 (5.05)	5.1 (2.6)	7.2 (5.58)
Completed study, n (%)					
Yes	20 (74.1%)	8 (61.5%)	19 (79.2%)	9 (64.3%)	23 (76.7%)
No	7 (25.9%)	5 (38.5%)	5 (20.8%)	5 (35.7%)	7 (23.3%)
Reason for discontinuation, n (%)					
Adverse event	0 (0.0%)	3 (25.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
Lost to follow-up	6 (22.2%)	1 (8.3%)	4 (16.7%)	2 (14.3%)	4 (13.3%)
Physician decision	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
Withdrawal by subject	1 (3.7%)	0 (0.0%)	1 (4.2%)	3 (21.4%)	1 (3.3%)

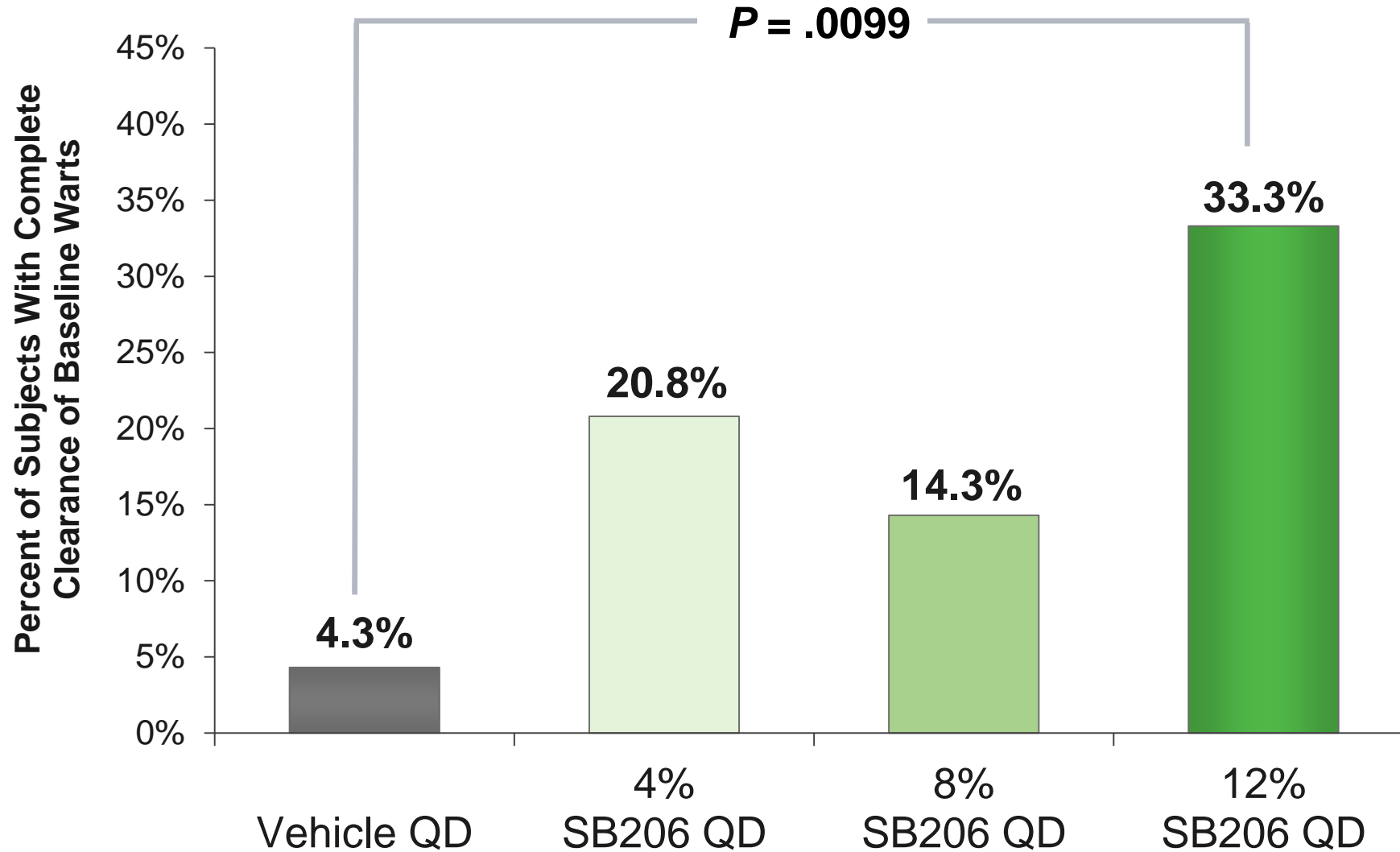
Study Results

- Two subjects in Cohort 1, randomized to SB206 4% twice daily or Vehicle were discontinued at week 2 due to prespecified tolerability criteria.
- Results for Cohort 1:

	Vehicle (n=4)	SB206 (n=13)
Randomized	4	13
Completed	4	8
Discontinued due to AE	0	3
Clearance of BL warts	2 (50%)	2 (16.7%)

- Subsequent cohorts were dosed with SB206 or Vehicle once daily.

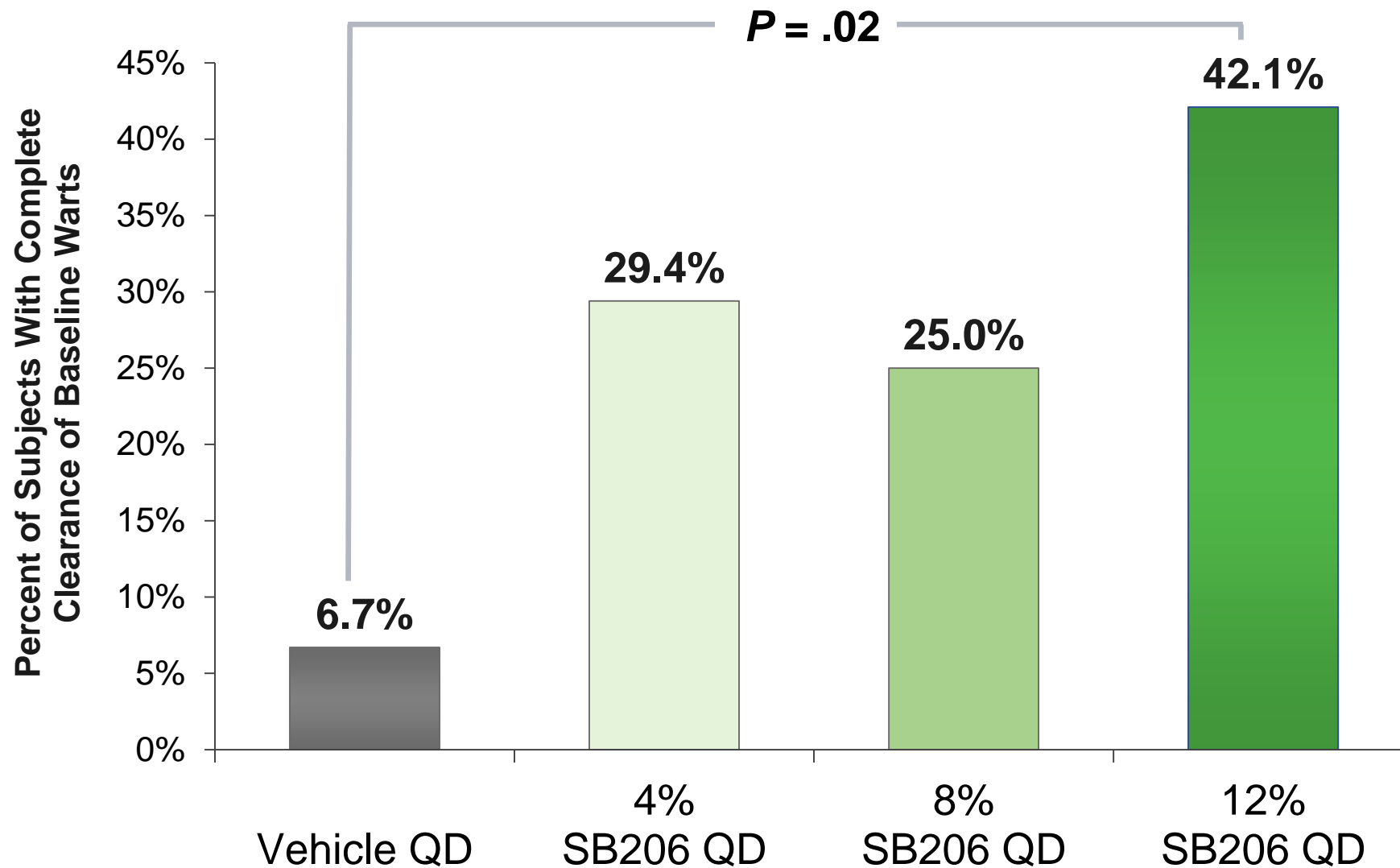
Primary Endpoint (ITT, QD treatment) Complete Clearance of Baseline Warts at Week 12



ITT, intent to treat.

Data on File. Clinical Study Report NI-WA201. Novan, Inc.

Primary Endpoint (PP, QD treatment) Complete Clearance of Baseline Warts



PP, per protocol.

Data on File. Clinical Study Report NI-WA201. Novan, Inc.

Secondary Endpoints

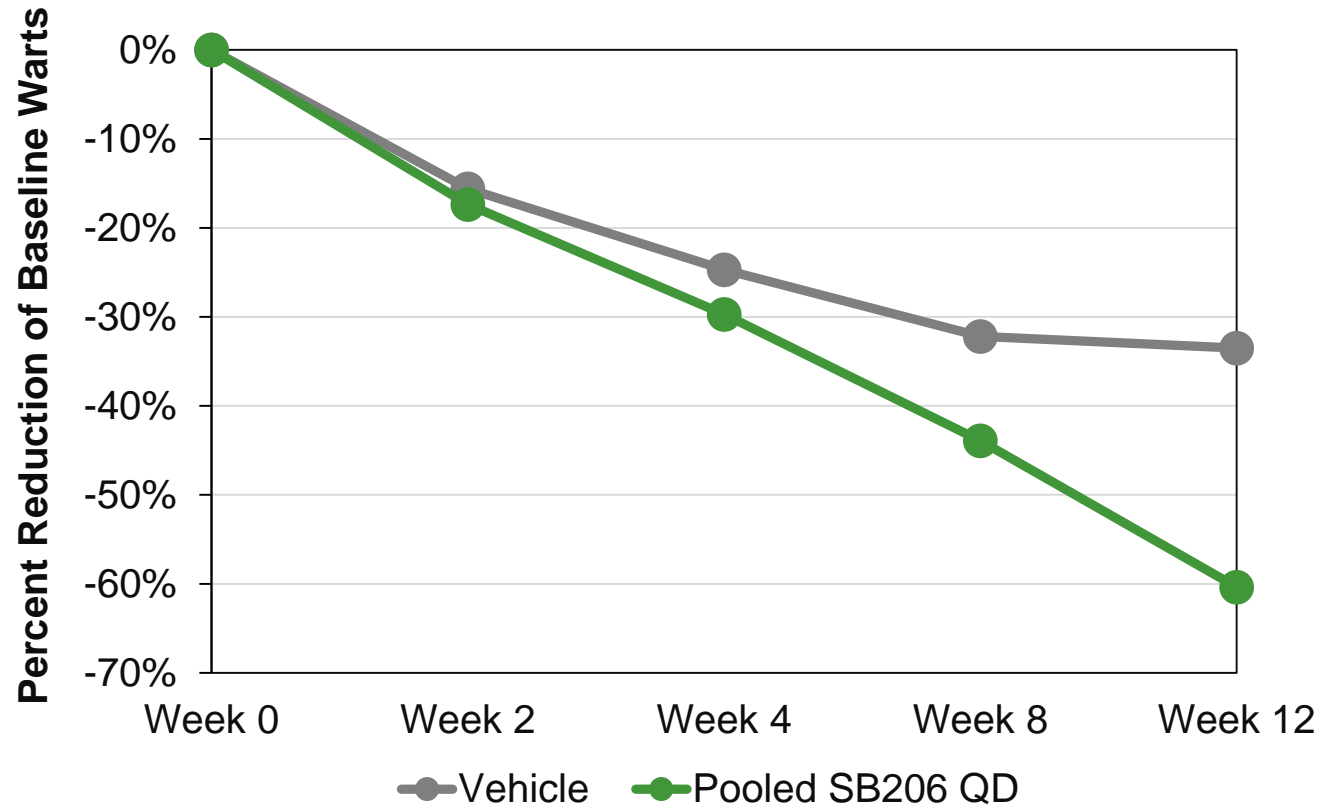
- ⦿ The proportion of subjects (ITT) with complete clearance of total EGW/PAW* was significantly higher in SB206 12% once daily treatment group (9/30 or 30%) vs Vehicle (1/17 or 6%) ($p < 0.02$).
- ⦿ A higher percentage of subjects (PP) treated with SB206 had complete or partial clearance of baseline warts after 12 weeks of treatment:
 - 8/15 or 53% on QD Vehicle.
 - 32/40 or 80% on pooled QD active.
- ⦿ In subjects (ITT) treated with SB206 once daily, 25% of males and 23% of female achieved complete clearance of baseline warts versus 6% of males and none of the females treated with vehicle by week 12.

*Endpoint used by FDA for approval of therapies for external and perianal genital warts.

PP - per protocol; ITT – Intent to Treat.

Data on File. Clinical Study Report NI-WA201. Novan, Inc.

Secondary Endpoints (PP, QD treatment) Percent Reduction of Baseline Warts



- Subjects treated with SB206 once daily had 60% reduction in baseline wart counts by week 12 (pooled QD active vs vehicle).

PP, per protocol.

Data on File. Clinical Study Report NI-WA201 (Table 14.2.9.2). Novan, Inc.

Most Frequent Adverse Events

	Vehicle gel QD/BID (n = 27)	SB206 4% gel BID (n = 12)	SB206 4% gel QD (n = 23)	SB206 8% gel QD (n = 14)	SB206 12% gel QD (n = 30)
General Disorders and Administration-Site Conditions	1 (4.2%)	6 (50.0%)	6 (26.1%)	1 (7.1%)	5 (16.7%)
Burn	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erosion	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	2 (6.7%)
Erythema	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	2 (6.7%)
Exfoliation	0 (0.0%)	0 (0.0%)	3 (13.0%)	0 (0.0%)	0 (0.0%)
Pain	0 (0.0%)	3 (25.0%)	1 (4.3%)	0 (0.0%)	2 (6.7%)
Pruritus	0 (0.0%)	1 (8.3%)	5 (21.7%)	0 (0.0%)	0 (0.0%)
Rash	0 (0.0%)	1 (8.3%)	1 (4.3%)	0 (0.0%)	0 (0.0%)
Reaction	1 (4.2%)	2 (16.7%)	1 (4.3%)	0 (0.0%)	0 (0.0%)
Ulcer	0 (0.0%)	1 (8.3%)	0 (0.0%)	1 (7.1%)	0 (0.0%)

1 of 30 subjects in the SB206 12% once daily treatment group discontinued due to an adverse event.

Summary

- ⊙ SB206 is an investigational, nitric oxide–releasing topical gel with a novel mechanism of action in development for the treatment of genital/perianal warts.
- ⊙ In a phase 2 study,¹ treatment with SB206 12% once daily to external genital or perianal warts in adults:
 - led to a statistically significant difference from vehicle in clearance of both baseline and total warts at week 12 ($p < 0.05$).
 - appeared to be safe and well tolerated with a low rate (16.7%) of application site adverse events and low discontinuation rate (3%).