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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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Stephen K. Tyring, MD, PhD

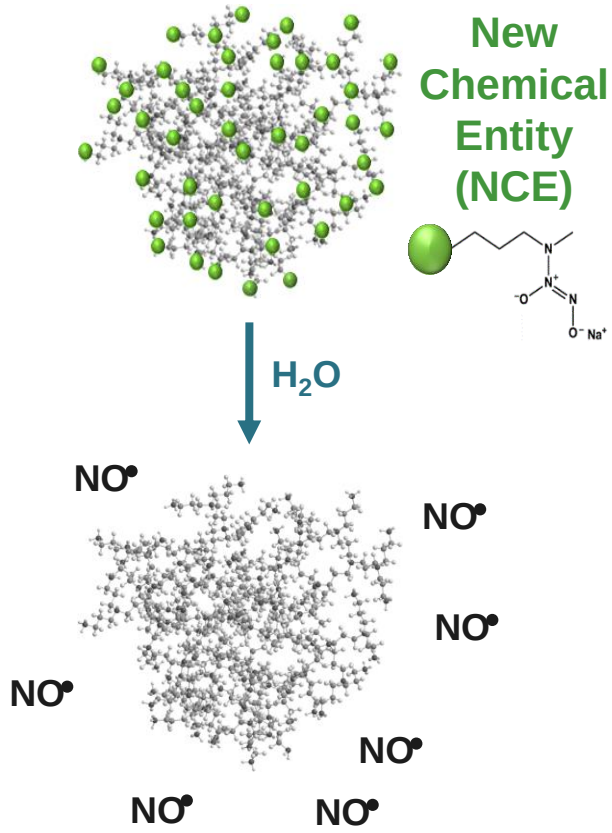
F056: Results From Phase II Study of Nitric Oxide-Releasing SB206 Once Daily Administration Show Favorable Efficacy and Safety in Genital Warts

DISCLOSURES

Novan, Inc Investigator (grants)

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

- SB206 contains NVN1000[1], 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.

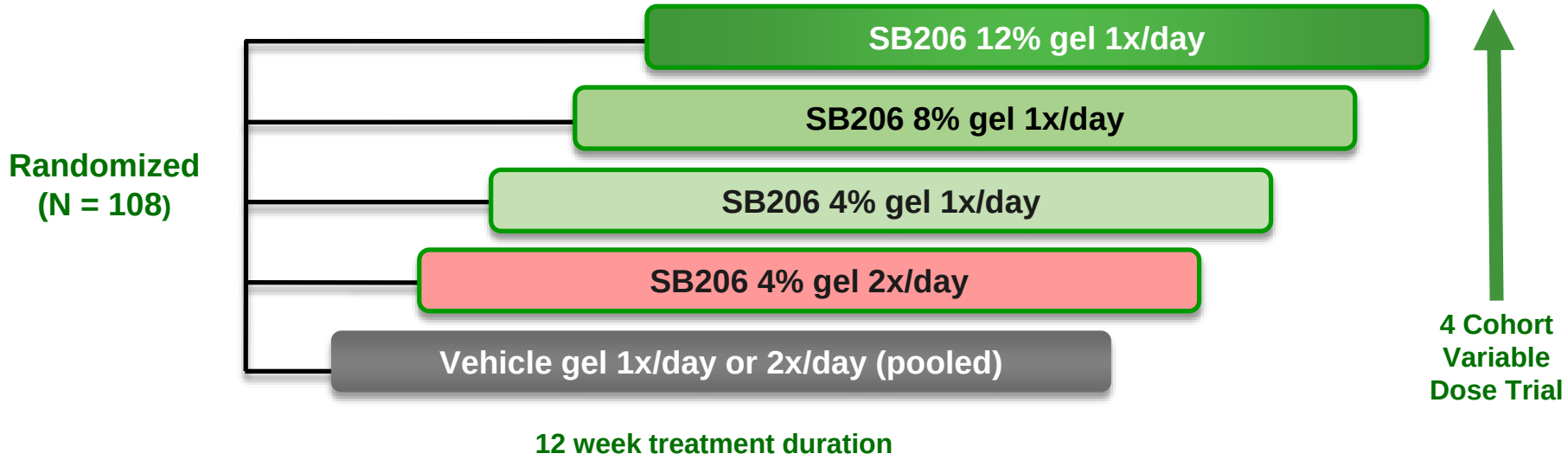


*CRPV – Cottontail Rabbit Papilloma Virus

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.

1. ClinicalTrials.gov identifier: NCT02462187 2. Data on File. Clinical Study Report NI-WA201. Novan, Inc.

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.

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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.

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

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%)

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

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.

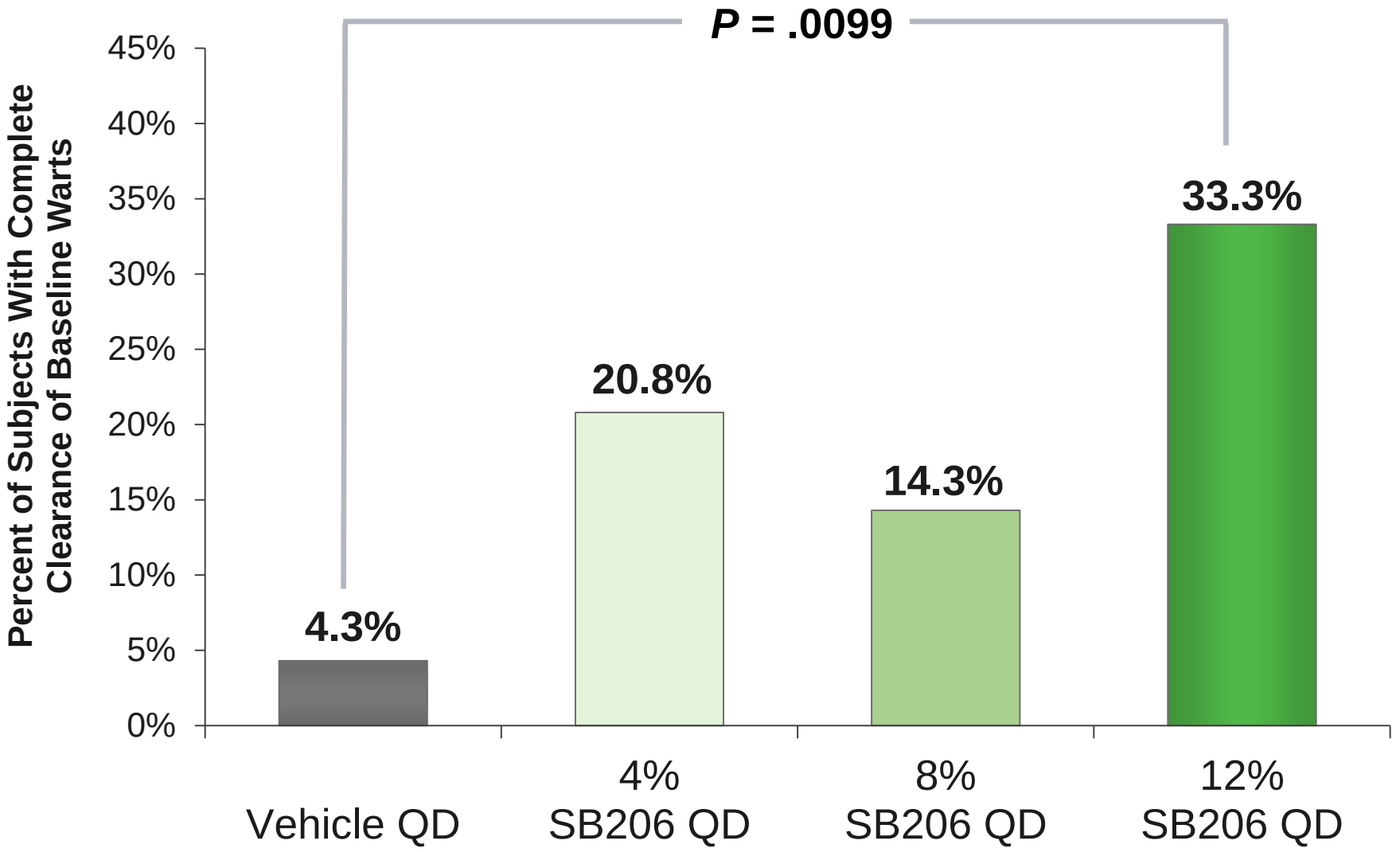
- Results for Cohort 1:

	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.

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

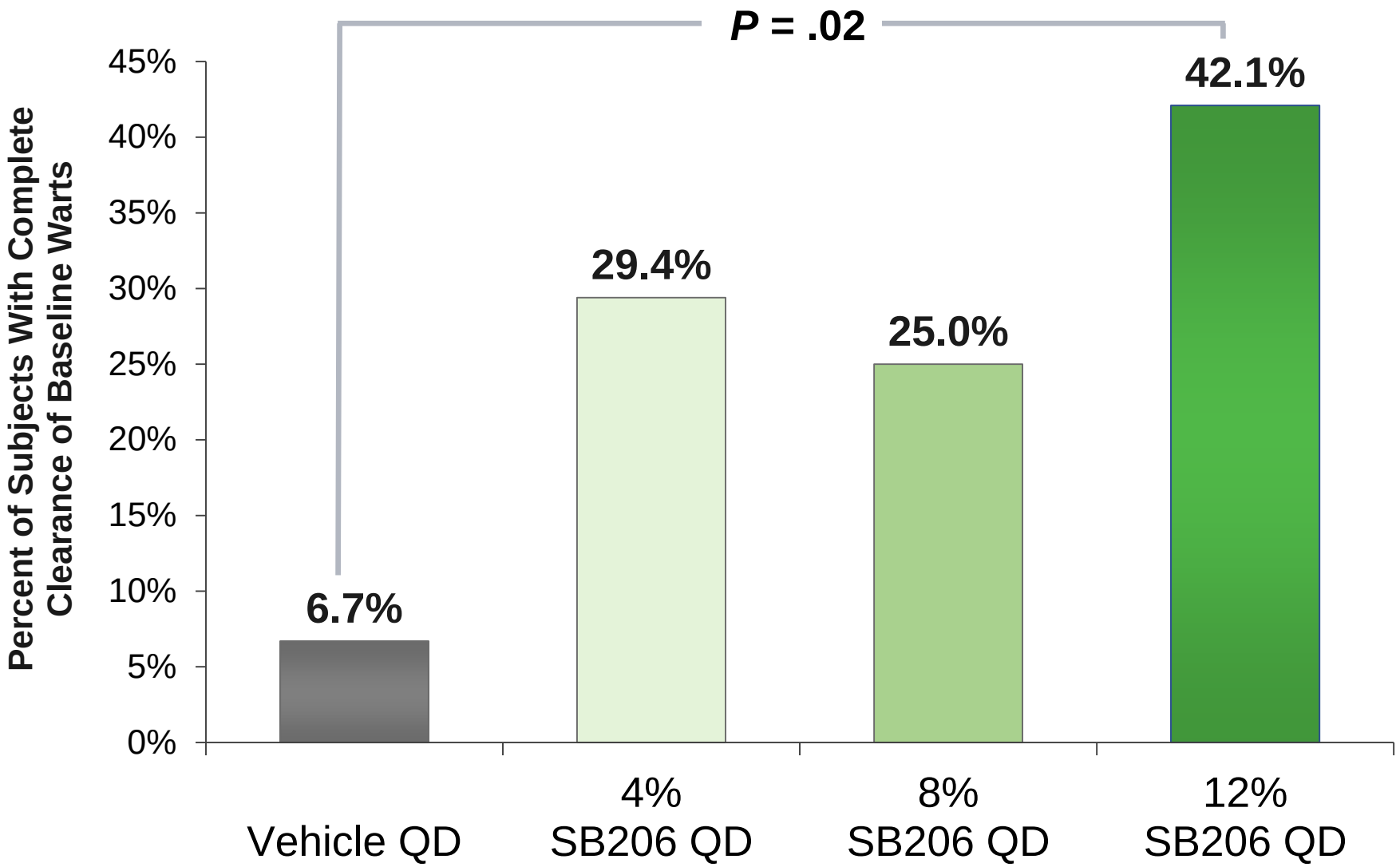
Primary Endpoint (ITT, QD treatment)
Complete Clearance of Baseline Warts at Week 12



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.

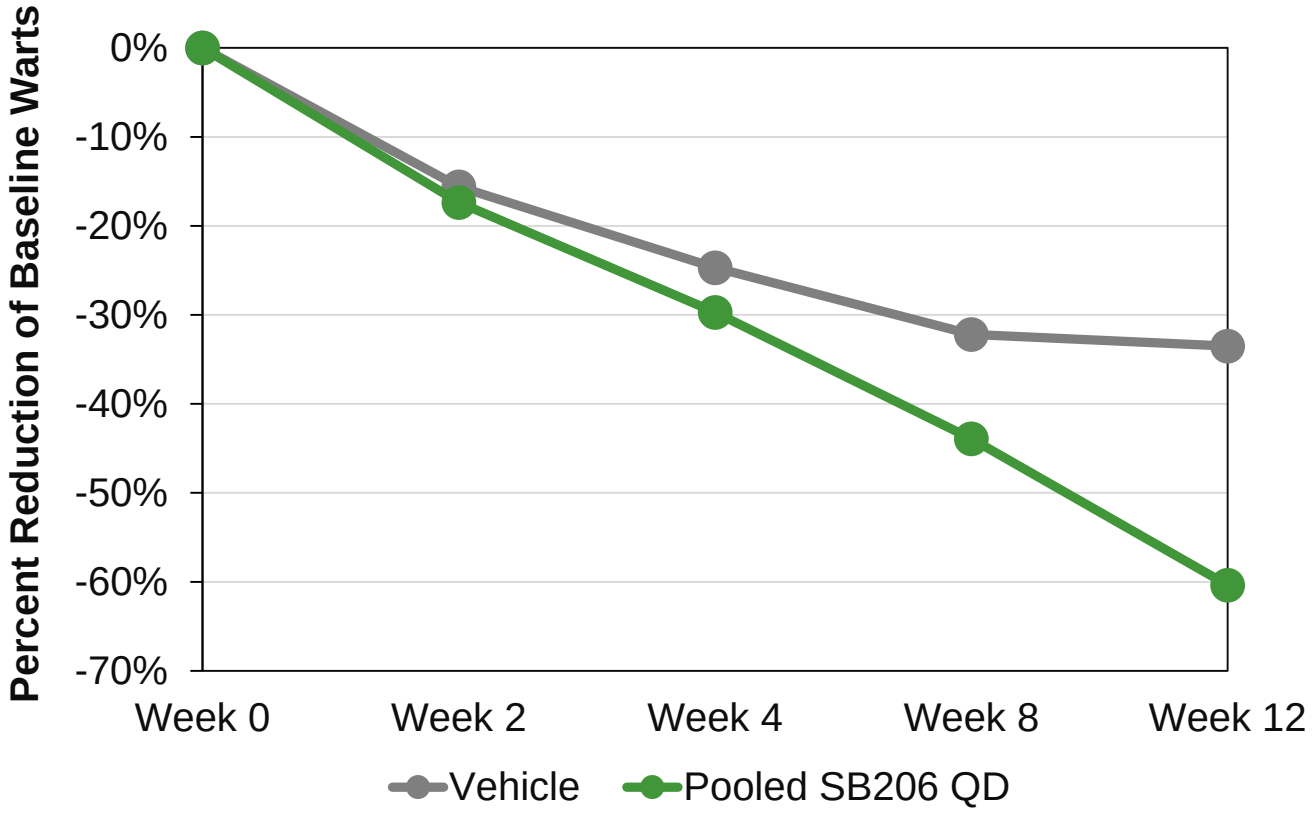
- In subjects (ITT) treated with SB206 once daily, 25% of males and 23% of female achieved complete clearance of baseline warts versus 6% of males and none of the females treated with vehicle by week 12.

*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.

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

Summary

- SB206 is a 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%).

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