Rapid Improvement with BPX-01 Minocycline Topical Gel in the Treatment of Moderate-to-Severe Inflammatory Acne Vulgaris: a Randomized, Double-Blind, Vehicle-Controlled Study

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Introduction

Acne affects up to 50 million Americans annually.[1] It can be caused by sebaceous gland hyperactivity, abnormal keratinocyte desquamation, and bacteria-related local inflammatory changes.[2,3] Comedones and inflammatory papules, pustules and nodules are sites of proliferation for *Propionibacterium acnes* bacteria.

The study medication: **BPX-01** topical minocycline gel

Strong Safety Profile
- Low dose: 1% and 2% minocycline
- Minimizes side effects
- Low systemic exposure

Strong Efficacy
- Stabilizes & solubilizes minocycline
- Delivered directly to pilosebaceous unit
- Targeted penetration

Positive Patient Experience
- Rapidly absorbing
- Non-staining
- Non-oily
- Non-fluorescing
- Very high patient satisfaction in clinical trials

BPX-01 is the first completely solubilized minocycline gel for topical use. It is intended for the treatment of non-nodular, moderate-to-severe inflammatory acne vulgaris in patients nine years of age and older. Its preliminary safety and efficacy profile have been demonstrated in extensive preclinical testing and a phase 2a study:

Primary Endpoint Achieved: Reduction in *P. acnes* colonies

RESULTS

	Change from Baseline at 4 weeks	
	Mean (Log_{10})	Percentage
BPX-01 Minocycline (n=17)	-1.04	-90.9%
Vehicle (n=7)	-0.46	-65.3%

Favorable Secondary and Safety Endpoints
- No drug-related adverse events
- No detectable plasma minocycline
- No cutaneous toxicity
- 100% patient satisfaction

Methods

This phase 2b study was intended to describe the safety and efficacy of topical minocycline in the treatment of inflammatory acne vulgaris.

STUDY DESIGN
- Randomized, double-blind, vehicle-controlled, dose-ranging study in 226 patients with moderate-to-severe acne
- 12-week study evaluating 3 arms: BPX-01 1% , BPX-01 2%, vehicle
- Conducted at 15 U.S. sites
- Patients ages 9 to 40, IGA* of 3 or 4, 20-60 non-nodular inflammatory lesions

ENDPOINTS

Primary Endpoint: Absolute mean change in number of inflammatory lesions from baseline at week 12

Secondary Endpoint: Proportion of subjects with at least a two-grade reduction in IGA* to clear or almost clear (0 or 1) at week 12

EXPLORATORY/ SAFETY
- Minocycline plasma concentrations
- Safety – adverse events
- Cutaneous tolerance
- Patient satisfaction
- Non-inflammatory lesion reduction

* Investigator Global Assessment; based on scale of 0 (clear) to 4 (severe)

Results: Rapid and Effective

Rapid Rate of Improvement in BPX-01 2% Arm: Key Takeaways

- > 25% reduction in lesions at week 2 with both doses
  - A 25% improvement is considered meaningful to patients
  - Reaching a 25% improvement within 2 weeks may lead to patient compliance and satisfaction with treatment
- 43.3% reduction in lesions at week 4 with 2% dose
- 58.5% reduction in lesions at week 12 with 2% dose

Week 2 >25% | Week 4 43% | Week 12 59%

Reduction in Inflammatory Lesions

	BPX-01 1%	BPX-01 2%	Vehicle
Subjects per arm	73	72	74
Absolute mean change in inflammatory lesions at week 12	- 15.5	- 15.4	- 11.2
p-value	0.0543	0.0352	
Percent reduction in inflammatory lesions	54.4%	58.5%	43.8%
p-value	0.0765	0.0256	

15%

- **Primary endpoint:** Absolute mean change in number of inflammatory lesions from baseline at week 12
- The above analysis reflects the intent to treat (ITT) population of 219

Clear Trend in IGA Reduction for 2% Treatment Arm

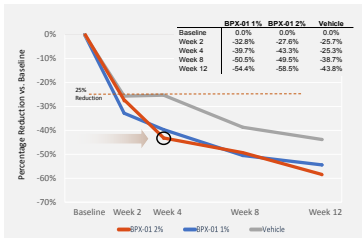
	BPX-01 1%	BPX-01 2%	Vehicle
Subjects per arm	73	72	74
Proportion with ≥ two-grade reduction and clear or almost clear	20.5%	25.0%	17.6%
p-value (vs vehicle)	>0.9999	0.5445	

7.4%

- **Secondary Endpoint*:** 25% of subjects in the 2% arm demonstrated at least a two-grade reduction in IGA to clear or almost clear (0 or 1)
- 7.4% separation between 2% dose and vehicle informs sample size for confirmatory phase 3 trials

* Study was not powered for this endpoint

Demonstrated Rapid Lesion Reduction

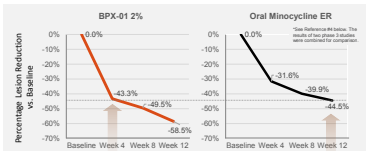


	BPX-01 1%	BPX-01 2%	Vehicle
Baseline	0.0%	0.0%	0.0%
Week 2	-32.8%	-27.6%	-25.7%
Week 4	-39.7%	-43.3%	-25.3%
Week 8	-50.5%	-49.5%	-38.7%
Week 12	-54.4%	-58.5%	-43.8%

Adverse Events

- Treatment-related adverse events occurred in 0.4% of subjects
- Generally safe and well tolerated in this study
- No serious treatment-related adverse events
- No photosensitivity or post-inflammation hyperpigmentation was reported
- No staining and/or skin discoloration was reported

Onset of Benefit: BPX-01 vs. Oral Minocycline ER



- Not conducted as a head-to-head trial. While recognizing that these trial data cannot be directly compared, BPX-01 may demonstrate a more rapid rate of improvement when compared to clinical data available for oral ER minocycline.*
- BPX-01 may demonstrate a greater percentage of reduction in inflammatory lesions at all time points.

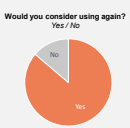
Safety Endpoint: Systemic Exposure

	BPX-01 1%	BPX-01 2%	Vehicle
Baseline	BLOQ	BLOQ	BLOQ
Week 4	BLOQ	BLOQ	BLOQ
Week 12	BLOQ	BLOQ*	BLOQ

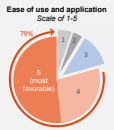
*One subject measured 42 ng/ml at 12 weeks; no AEs BLOQ=Below Limit of Quantification (10 ng/mL)

- Minocycline was undetectable in the plasma of 99.5% of subjects.
- Further support for no anticipated systemic side effects
- Highly sensitive assay with LLoQ for minocycline of 10 ng/mL in plasma

Positive Patient Experience: BPX-01 2% Shows Potential for High Patient Compliance



86% of subjects would use BPX-01 2% again



79% of subjects thought BPX-01 2% was easy to use and apply

A reduction of 25% in the number of inflammatory lesions is considered clinically important and is recognized by patients as an indicator of an effective treatment. Because this milestone was reached within two weeks of treatment with BPX-01, it has the potential to result in optimal treatment compliance and improved patient satisfaction. The rapid rate of improvement (43% after four weeks) outpaced that observed in a separate clinical trial with oral minocycline for acne in which improvement exceeding 40% required 12 weeks of treatment,[4] with much lower systemic exposure.

Additionally, BPX-01 2% resulted in 58.5% reduction in lesions with consistent trends toward improvement in IGA, PGI, and satisfaction scores. The medication was well tolerated with good safety profile and was largely undetectable in blood plasma, hence no systemic side effects are anticipated.

In conclusion,

BPX-01 2% minocycline topical gel resulted in rapid improvement and better outcomes than vehicle control in the treatment of moderate-to-severe non-nodular inflammatory acne vulgaris.

This treatment may provide an effective new option with a favorable safety profile and potential for high patient compliance.

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This work was sponsored by BioPharmX; all investigators were active participants in the trial. BPX-01 is limited by federal or US law to investigational use only.