

January 2019

# Corporate Overview

# Forward-Looking Statements

This presentation includes forward-looking statements that reflect our current views with respect to, among other things, our plans to develop and commercialize our product candidates, including our interpretation of preclinical and clinical studies and the success and timing of our product development activities and clinical trials, our intention to advance the development of SB206 for molluscum, which is subject to our ability to obtain additional financing or enter into strategic relationships to enable such development, the future prospects of our business and financial condition and our needs for additional financing. These forward-looking statements are included throughout this presentation. We have used the words “anticipate,” “assume,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “future,” “will,” “seek,” “foreseeable”, “targeted” and similar terms and phrases to identify forward-looking statements in this presentation. The forward-looking statements contained in this presentation are based on management’s current expectations and are subject to substantial risks, uncertainty and changes in circumstances. Actual results may differ materially from these expectations due to risks and uncertainties including, but not limited to: risks and uncertainties in the clinical development process, including, among others, length, expense, ability to enroll patients, reliance on third parties, and that results of earlier research and preclinical or clinical trials may not be predictive of results, conclusions or interpretations of later research or trials; risks related to the regulatory approval process, which is lengthy, time-consuming and inherently unpredictable; our ability to obtain substantial additional funding for the further advancement and development of our product candidates; our ability to identify and enter into strategic relationships for the further development and potential commercialization of our product candidates; and other risks and uncertainties described in our annual report filed with the SEC on Form 10-K for the twelve months ended Dec. 31, 2017, and in any subsequent filings with the SEC. Any forward-looking statement made by us in this presentation speaks only as of the date of this presentation. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by any applicable securities laws.

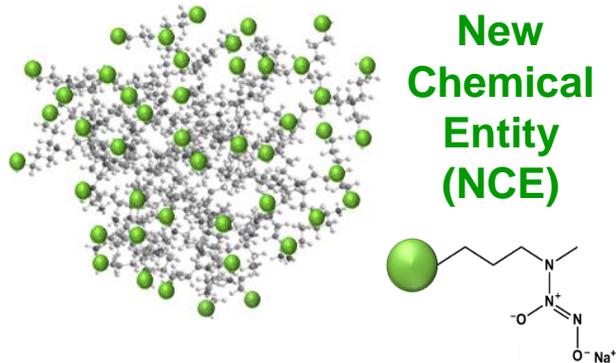
# Core Technology Platform Based on Nitric Oxide

- **Naturally produced nitric oxide has diverse biological activity within the body**
  - Immunology (bacterial, viral and inflammatory responses)
  - Cardiology/pulmonology (vasodilation/hemostasis, anti-coagulation, and respiration)
  - Neurology (neurotransmitter)
- **Physiological effects are controlled by the dose of nitric oxide**
  - Depending on dose and release kinetics, nitric oxide has positive or negative effects on the human body (e.g. anti- or pro-inflammatory)
  - Necessary to tune nitric oxide dose over time (e.g. release rates) to selectively target therapeutic indications and maximize desired effects
  - Our bodies naturally manage the complexity via multiple nitric oxide-donors/carriers to help ensure nitric oxide is in the right place at the right time
- **Robustly studied in the literature**
  - In general, the role and mechanisms of nitric oxide have been well researched
  - Prior to Novan, nitric oxide therapies have been limited by the ability to store and deliver tunable amounts of nitric oxide

# Novan's Nitric Oxide Technology Platform

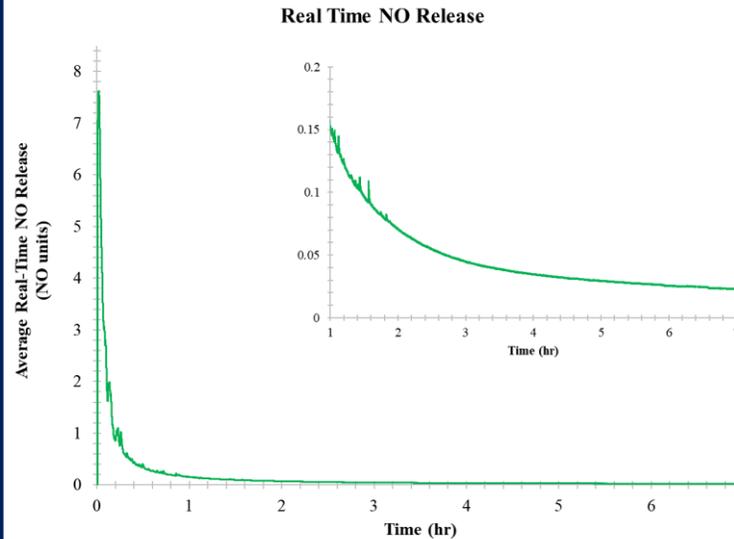
*First macromolecular platform to achieve stable, tunable and druggable delivery of nitric oxide:*

## Stable



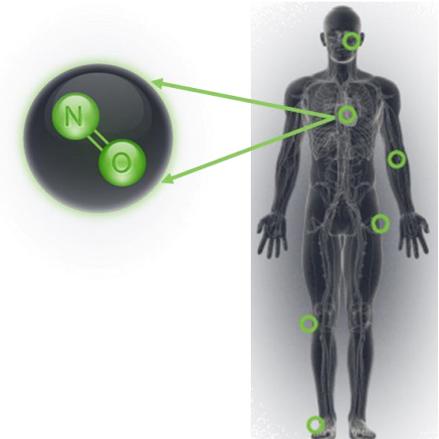
Novan has created a proprietary platform enabling development of NCEs with sustained delivery of nitric oxide

## Tunable



Proprietary formulations, targeted to each indication, enable tunable dosing

## Druggable



Multiple drug candidates with unique nitric oxide delivery and proven target engagement

# Experienced Leadership Team

Alignment of significant scientific and drug development expertise to Novan's short, intermediate and longer-term opportunities

**Robert A. Ingram**  
*Executive Chairman*



**G. Kelly Martin**  
*Chief Executive Officer*



**Paula Brown Stafford**  
*President and Chief Operating Officer*



**Carri Geer, PhD**  
*SVP, Chief Technology Officer*



**Elizabeth Messersmith, PhD**  
*SVP, Chief Development Officer*



**Jeff Hunter**  
*EVP, Chief Business Officer*



**Andrew Novak**  
*VP, Chief Accounting Officer*



**Tomoko Maeda-Chubachi, MD**  
*VP, Medical Dermatology*



# Clinical Progress Made Since Q4 of 2017

**Oct-17**: SB414  
(Psoriasis) Ph 1b  
Trial Initiation

**Dec-17**: SB414  
(Atopic Dermatitis)  
Ph 1b Trial Initiation

**Jan-18**: SB206  
(Molluscum) Ph 2  
Trial Initiation

**Q2-18**: SB204  
(Acne) Type C  
Meeting with FDA

**Aug-18**: SB414  
(Psoriasis & Atopic Dermatitis)  
Ph 1b Clinical Results

**Sep-18**: SB204  
(Acne) FDA Clarity

**Nov-18**: SB206  
(Molluscum) Ph 2  
Preliminary Top Line  
Results

**Dec-18**: SB206  
(Molluscum) Ph 2 Full  
Top Line Results

4Q 2017

2018

# Focused Dermatology Development Pipeline

Product Candidates	Indication	Preclinical	Phase 1	Phase 2	Phase 3
SB204	Acne Vulgaris				
SB206	Molluscum				
SB414	Atopic Dermatitis				

- **Acne Vulgaris (Multifactorial<sup>1</sup>):** Successful in 1 of 2 Phase 3 pivotal trials
- **Molluscum (Antiviral):** Positive Phase 2 results with upcoming end-of-Phase 2 meeting
- **Atopic Dermatitis (Anti-Inflammatory):** Phase 1b results support progression into Phase 2

# Corporate Progress Made Over the Past 12 Months

**Jan-18**: Closing of \$38.0M Financing

**Feb-18**: Formation of Science & Technology Committee, chaired by Dr. Eugene Sun

**Oct-18**: Extension of Nitric Oxide Dermatology Partnership with Sato in Japan

**Oct-18**: Strategic Alliance with Orion Provides Extension of Technical Production Capacity

**Oct-18**: Formation of a Dedicated Women's Health Business Unit and Collaboration with Health Decisions

**Jan-19**: Strengthens and Aligns Management Team, GI Diseases Added as Field of Focus

2018

Q1 2019

# Value Creation Opportunities Over the Past 12 Months

- **Sato/Japan amendment to include SB206: EGW and molluscum<sup>1</sup>**
  - ~\$11M of upfront non-dilutive cash inflows; payable in installments through 3Q 2019
  - Further potential milestone and royalty payments
- **Multiple geographic business development discussions ongoing**
- **Women's Health business unit established; HPV academic research collaboration with University of Alabama-Birmingham and clinical research collaboration with Health Decisions<sup>2</sup>**
- **Expansion of technical production capacity with Orion/Finland enables business leveragability<sup>3</sup>**
- **Addition of gastrointestinal (GI) diseases as a therapeutic focus area as part of overall science and business strategy**

# Nitric Oxide Platform Expansion: Women's Health & Gastroenterology

## Women's Health

- Novan's nitric oxide technology has demonstrated the ability to inhibit HPV amplification and replication in nonclinical models
- Targeting high-risk HPV infections and associated cancers affecting women
- Clinical research collaboration established with Health Decisions, a specialist women's health CRO
- Existing multi-year research collaboration with University of Alabama-Birmingham extended
- Pipeline:
  - Previously announced Phase 2 data for the treatment of external genital warts (EGW) provide a specific late stage clinical asset that targets HPV-associated diseases
  - IND enabling preclinical studies ongoing targeting high-risk HPV

## Gastroenterology

- Inherent connection between the multi-factorial pathologies of GI diseases and the demonstrable anti-microbial, anti-viral and anti-inflammatory properties of Novan's nitric oxide technology
- Nitric oxide produced in the gastrointestinal (GI) tract regulates many of its functions<sup>1-3</sup>
- Nitric oxide supplied from nitric oxide donors are protective against gastric damage in a dose-dependent manner<sup>1-3</sup>
- NO-releasing variants of NSAIDs (nonsteroidal anti-inflammatory drugs) have enhanced therapeutic benefit versus NSAID alone<sup>2,3</sup>

*"The future of this field with respect to drug development will require patented molecules that will release the gaseous mediator at a rate appropriate for promoting health, and at the specific locations where the effects of the mediator are most needed"<sup>3</sup>*

# Molluscum Contagiosum Overview

**Molluscum is a contagious skin infection caused by the molluscipoxvirus, a double-stranded DNA virus**



Small pink, red or pinkish colored, raised lesions (2 - 5 mm) with small dimple in center. Commonly occur in groups on face, neck, arms, legs, abdomen and genital area.

- **Prevalence of ~6 million in the US<sup>1,2</sup>**
  - ~1 million diagnosed annually
  - ~90% of patients below the age of 18
  
- **Typically present with 10-30 lesions, up to 100 in severe cases**
  - Avg. time to resolution is 13 months<sup>2</sup>
  
- **No FDA-approved treatments indicated for molluscum**

# Anti-Viral Mechanism of Action

- **Multiple publications show nitric oxide inhibits viral replication via S-nitrosylation in the following viruses:**
  - Human papillomavirus (HPV): double-stranded DNA virus
  - Herpes simplex virus (HSV): double-stranded DNA virus
  - Coxsackievirus: single-stranded RNA virus
  - Dengue virus: single-stranded RNA virus
- **Novan's nitric oxide technology has demonstrated the ability to inhibit HPV amplification and replication in nonclinical models, as well as efficacy in a Phase 2 clinical trial against external genital warts**
- **The inhibition of viral replication demonstrated in HPV is hypothesized to be translatable to other double stranded DNA virus families:**
  - Adenoviridae
  - Polymoviridae
  - Poxviridae (e.g. molluscipoxvirus, a double-stranded DNA virus)
- **Mechanism of action supported by *in vitro* data against vaccinia, a double-stranded DNA pox virus**
- **And now, Novan has demonstrated efficacy against the molluscipoxvirus in a Phase 2 clinical trial**

# Molluscum Contagiosum Current Treatment Landscape

	Description	Side-Effects/Limitations	Choice of 1 <sup>st</sup> Line Treatment <sup>1</sup>
Physical Therapies	<ul style="list-style-type: none"> <li>Curettage, cryotherapy, laser surgery</li> </ul>	<ul style="list-style-type: none"> <li>Pain, anxiety, burning, erythema, dyspigmentation</li> </ul>	29%
Cantharidin	<ul style="list-style-type: none"> <li>Applied with wooden end of cotton-tipped swab</li> <li>Compounding pharmacies</li> </ul>	<ul style="list-style-type: none"> <li>Blistering agent</li> <li>Erythema, pruritus</li> </ul>	20%

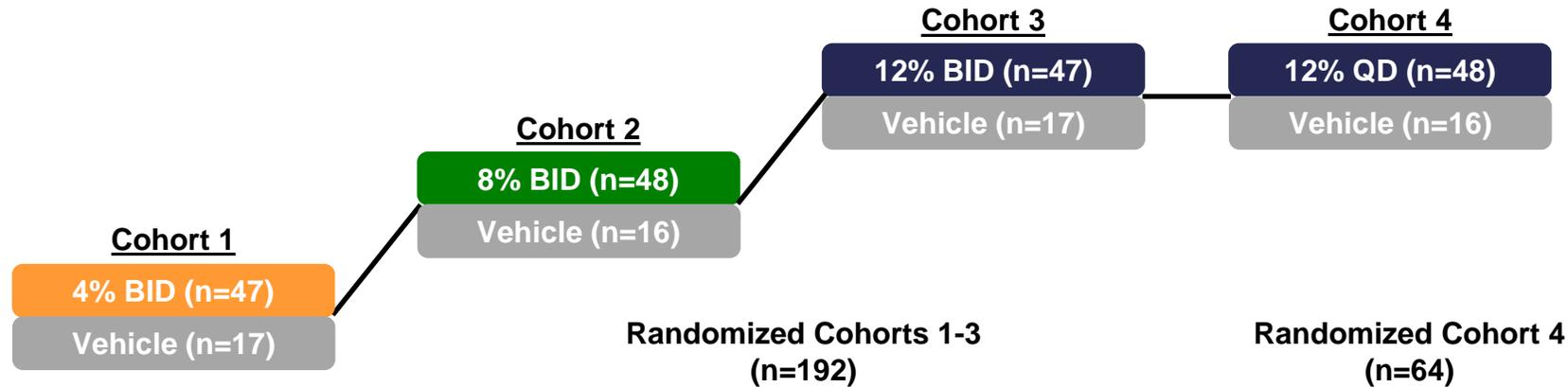
***Painful scraping, freezing, burning and blistering treatment options; no FDA approved Rx products creates significant unmet need in this childhood skin disease***

Off-Label Rx's	<ul style="list-style-type: none"> <li>Imiquimod</li> <li>Retinoids</li> </ul>	<ul style="list-style-type: none"> <li>Limited efficacy</li> <li>Erythema, burning, pruritus</li> </ul>	33%
OTC	<ul style="list-style-type: none"> <li>Home remedies</li> <li>ZymaDerm, salicylic acid</li> </ul>	<ul style="list-style-type: none"> <li>Unproven efficacy</li> <li>Some irritation</li> </ul>	15%

***>30% of patients are receiving Rx's with no molluscum indication or proven clinical efficacy***

# Phase 2 Study of SB206 in the Treatment of Molluscum

A Phase 2, multi-center, randomized, double-blind, vehicle-controlled, ascending dose study of SB206 in subjects with molluscum contagiosum



Primary Endpoint	Secondary Endpoints
<ul style="list-style-type: none"><li>Proportion of subjects achieving complete clearance of all molluscum contagiosum at week 12</li></ul>	<ul style="list-style-type: none"><li>Proportion of subjects achieving complete clearance of all molluscum contagiosum lesions at each visit</li><li>Proportion of subjects achieving <math>\geq 75\%</math> reduction from baseline in number of molluscum</li><li>Mean % change from baseline in number of molluscum contagiosum lesions at every visit</li><li>Time to complete clearance</li></ul>

# SB206 Phase 2 Disposition & Demographics

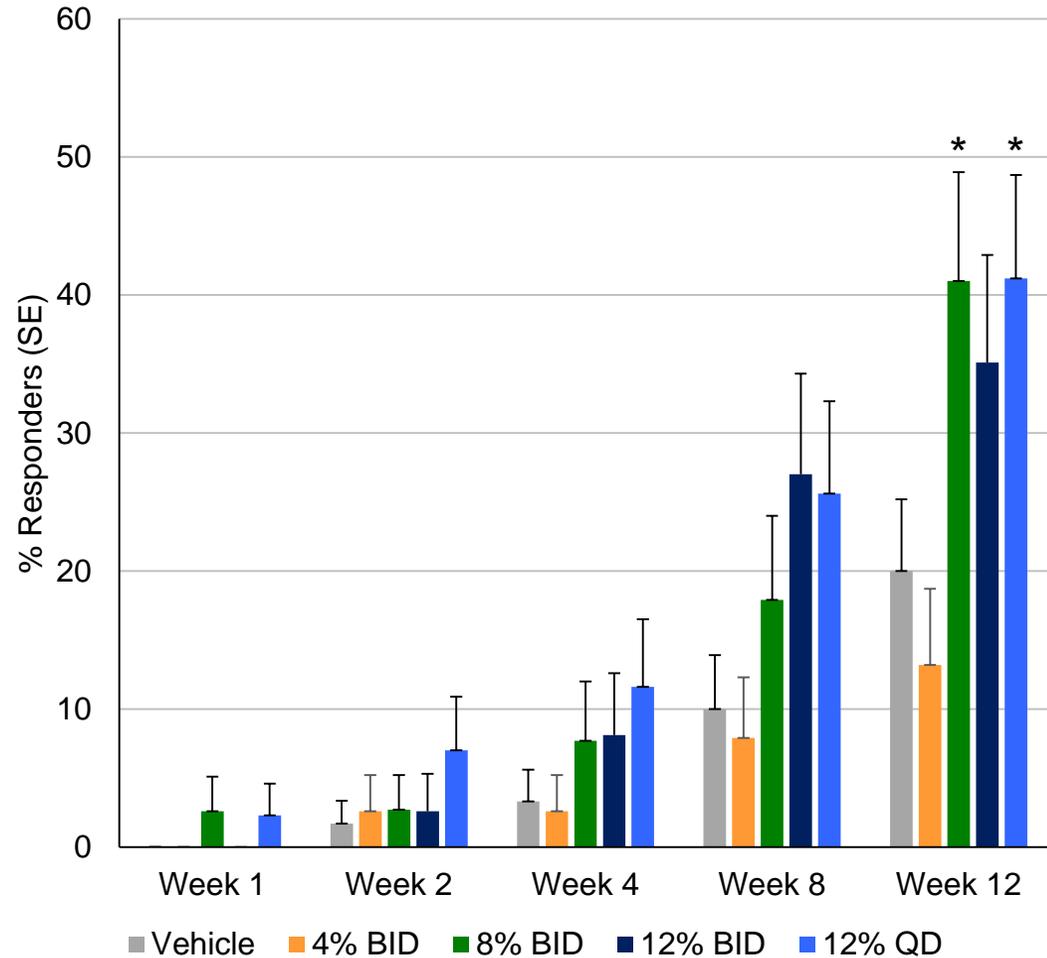
	Vehicle	All SB206	SB206 12% QD
Randomized, N <sup>1</sup>	66	190	48
Completed study visits and treatment	60 (90.9%)	156 (82.1%)	43 (89.6%)
Age, mean (range)	7.0 (2 - 16)	6.9 (2 – 62)	5.7 (2 - 11)
Baseline lesion count, mean	18.3	19.3	17.6

*Randomization was stratified by the following:*

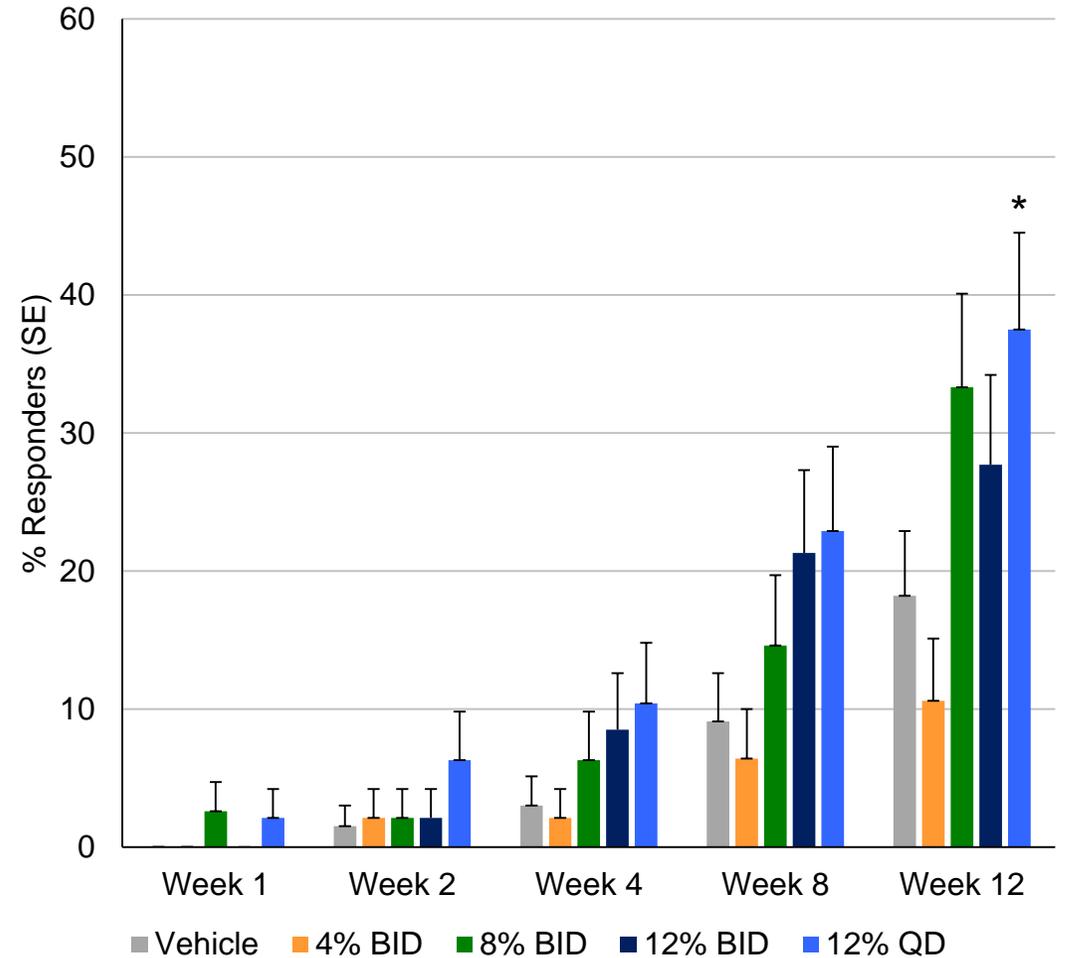
	Vehicle	All SB206	SB206 12% QD
Baseline lesion count = 3 to 18	41 (62.1%)	116 (61.4%)	33 (68.8%)
History of atopic dermatitis	11 (16.7%)	31 (16.3%)	10 (20.8%)

# SB206 Phase 2 Primary Endpoint: Complete Clearance of All Lesions

## mITT Population



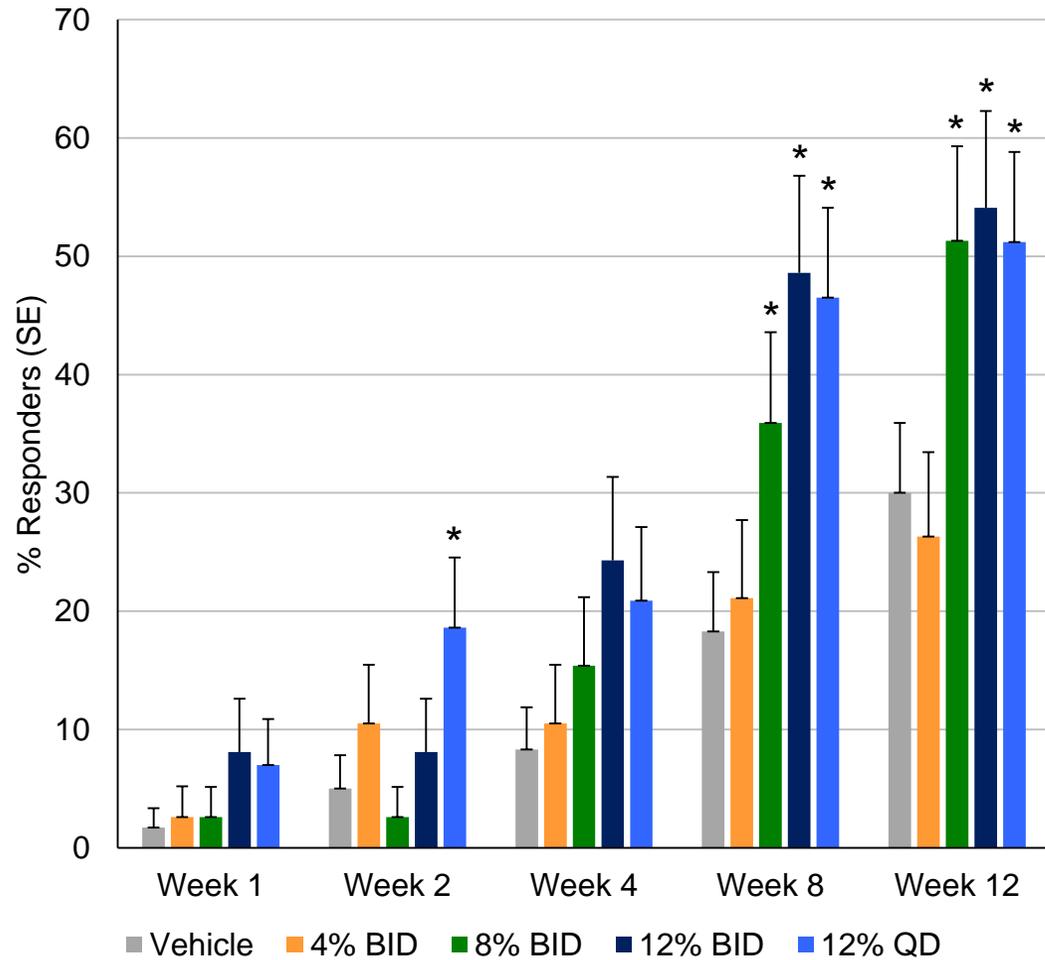
## ITT Population



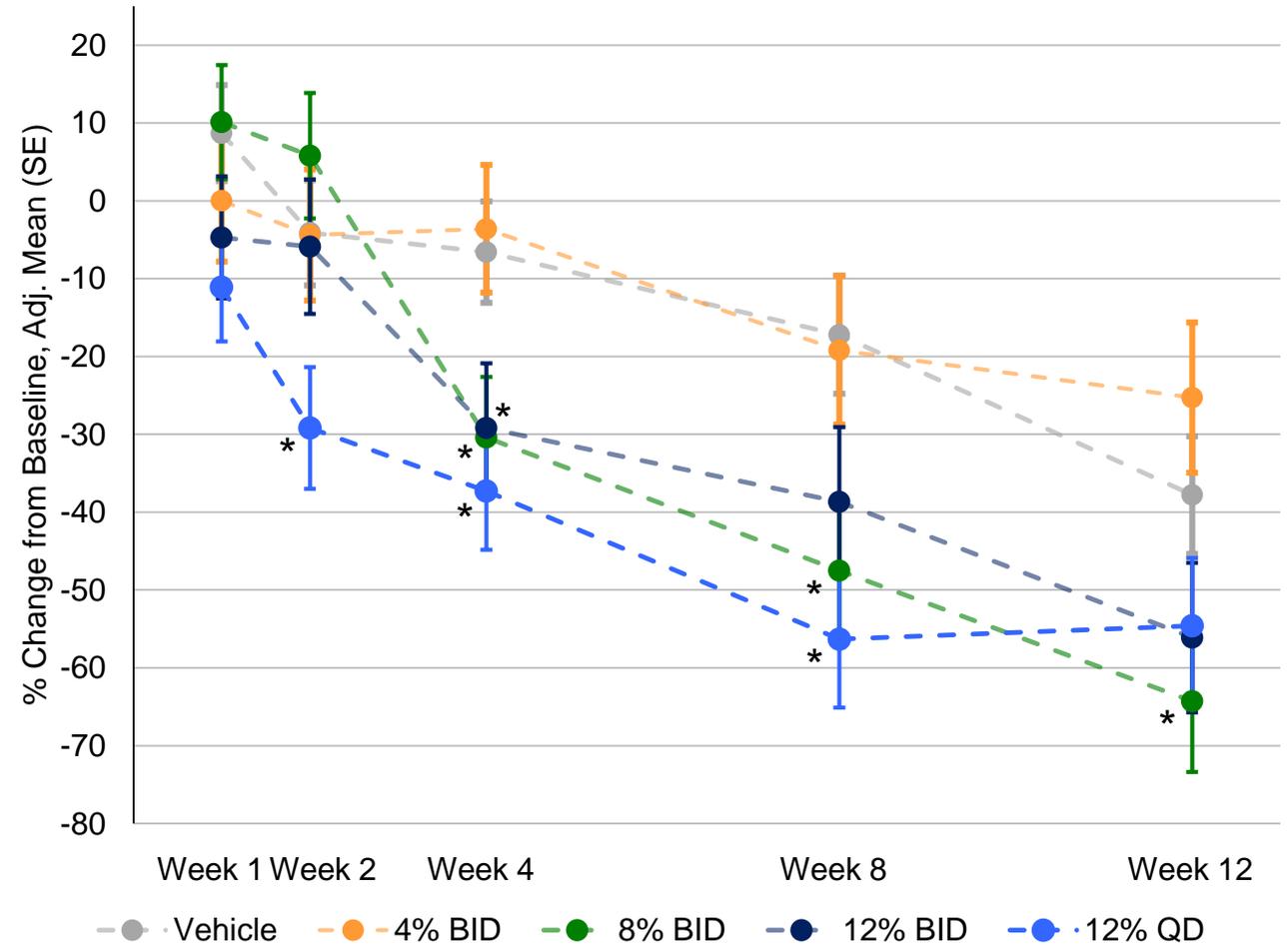
The Modified Intent-to-Treat Population (mITT) consists of all subjects who are randomized and completed the study treatment.  
 The Intent-to-Treat Population (ITT) consists of all subjects who are randomized.  
 \*p<0.05

# SB206 Phase 2 Secondary Endpoints

## Clearance of $\geq 75\%$ Lesions (mITT)



## Percent Change from Baseline Lesion Count (mITT)



# SB206 Phase 2 Safety and Tolerability (Safety Population)

	Vehicle (N=66)	All SB206 (N=188)	SB206 12% QD (N=47)
<b>Subjects who discontinued treatment due to adverse events (AEs)</b>	0	7 (3.7%)	0
<b>AEs leading to treatment discontinuation (subjects)</b>			
Application site reaction (pain, erythema)	0	6	0
Worsening molluscum	0	1	0
<b>Investigator assessment of irritation as defined by dryness, erythema and peeling at Week 12</b>	N = 60	N = 149	N = 41
Mild	10 (16.7%)	45 (30.2%)	10 (24.4%)
Moderate	2 (3.3%)	9 (6.0%)	2 (4.9%)
Severe	0	1 (0.7%)	0
Very severe	0	0	0
<b>Subject assessment of burning/stinging and itching at Week 12</b>	N = 60	N = 149	N = 41
Slight	15 (25.0%)	39 (26.2%)	7 (17.1%)
Mild	1 (1.7%)	15 (10.0%)	3 (7.3%)
Moderate	0	4 (2.7%)	1 (2.4%)
Strong / severe	0	0	0

## Summary of SB206 Phase 2 Top Line Results

- **Higher rates of complete clearance of all molluscum lesions at Week 12 for the three highest doses, 8% twice-daily, 12% twice-daily and 12% once-daily, more than double the rate observed in the vehicle group**
- **Statistically significant reductions in molluscum lesions as early as Week 2 with 12% once-daily**
- **Attractive safety and tolerability profile, a critical and highly appealing feature for a predominantly childhood disease**
- **No quantifiable levels of systemic exposure detected for SB206 12% twice or once-daily at Week 12**
- **SB206 as a once-daily, at-home, caregiver-applied topical therapy with a rapid treatment benefit, if approved, would satisfy an important patient-care need for the treatment of molluscum**

# SB206 for the Treatment of Molluscum Path Forward

- **Novan has requested an end-of-Phase 2 meeting with the FDA**
  - This meeting would enable Novan and the FDA to agree on a Phase 3 development plan for molluscum with SB206 12% once-daily as the active treatment arm
- **Following a successful end-of-Phase 2 meeting with the FDA, the Company plans to initiate a Phase 3 program of SB206 for molluscum in 1H 2019<sup>1</sup>**
- **Top line results from Phase 3 program possible by the end of 2019 or early in 2020**

## **SB204 as a Potential Treatment for Acne Vulgaris**

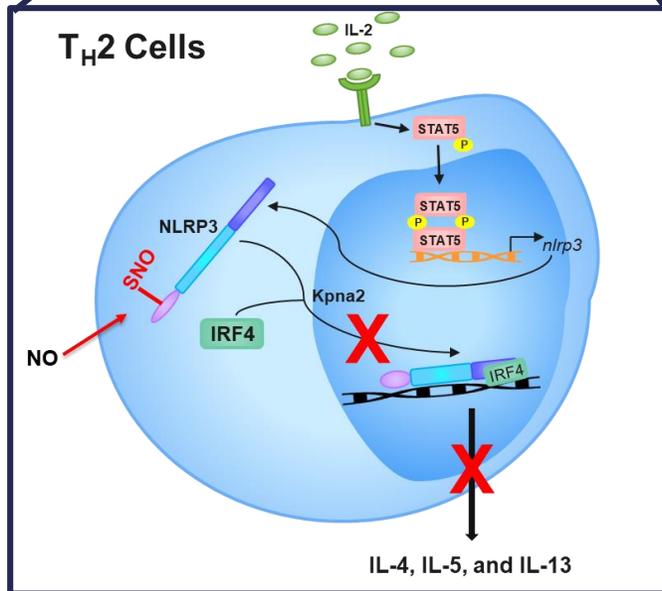
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- **In 2Q 2018, conducted a Type C meeting; focus was on the severe patient population**
- **In 3Q 2018, the FDA provided feedback in their minutes on two paths forward:**
  - One additional pivotal trial for moderate-to-severe acne patients, or
  - Additional preliminary trials for a severe-only patient population
- **We believe one additional pivotal Phase 3 trial in moderate-to-severe acne patients is most pragmatic path forward for Novan**
- **Recent positive Phase 3 acne clinical trial results from Cassiopea and Foamix, follow disappointing results from Dermira**

# Confirmatory SB204 Phase 3 Clinical Trial Optimizations

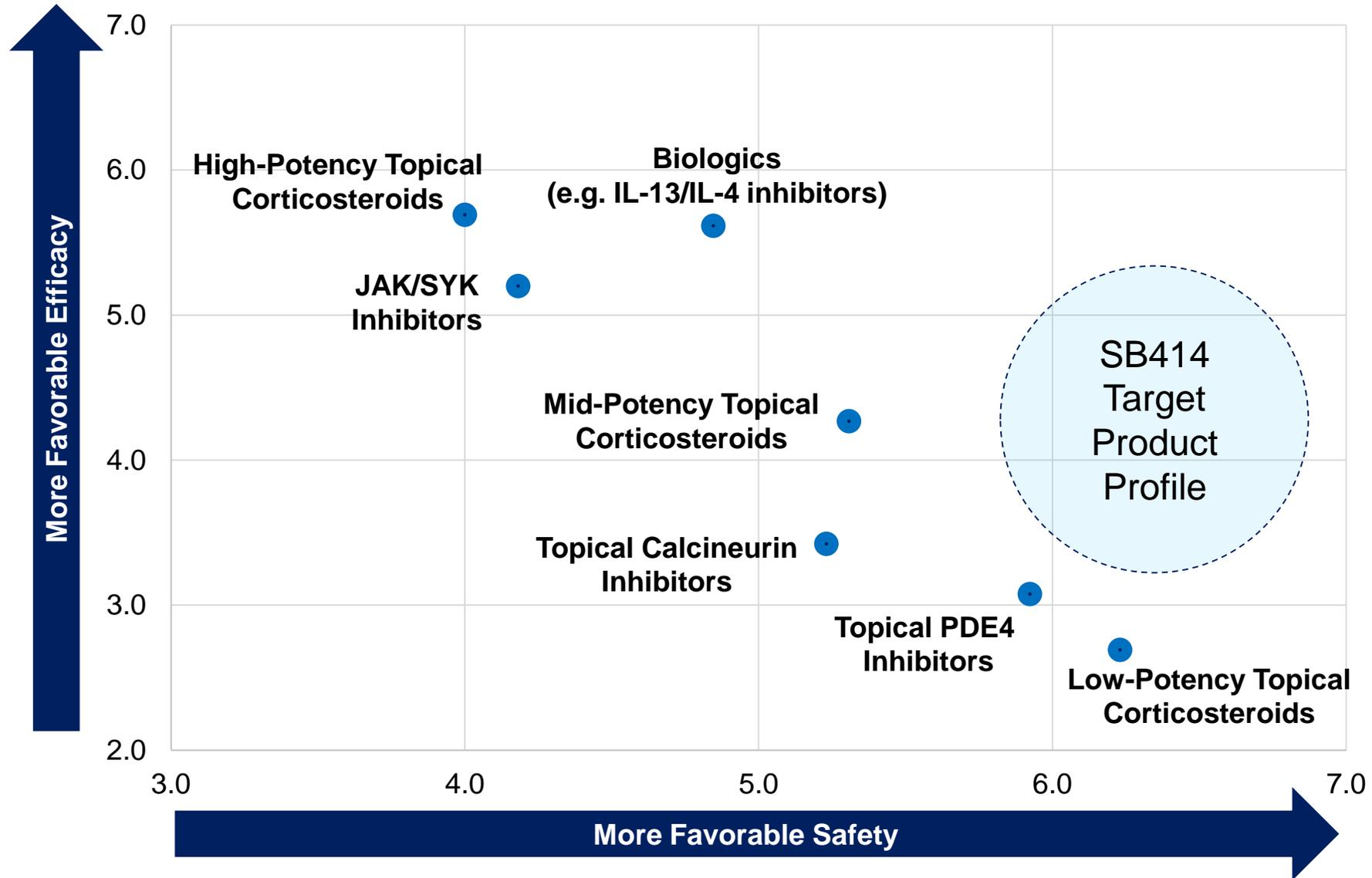
- **We have executed a business arrangement with a specialized-dermatology Contract Research Organization (CRO) for trial start-up activities**
  
- **Trial Optimizations:**
  - Increased patient density per clinical site relative to NI-AC301 or NI-AC302
  - Fewer sites relative to NI-AC301 or NI-AC302
  - Enrich patient selection – increase inflammatory lesion count at baseline relative to NI-AC301 or NI-AC302
  - Train IGA Assessors, before and during trial; ensure consistency in assessing IGA scores
  - Photograph patients' acne to support training and illustrate IGA scoring system

# Atopic Dermatitis Overview

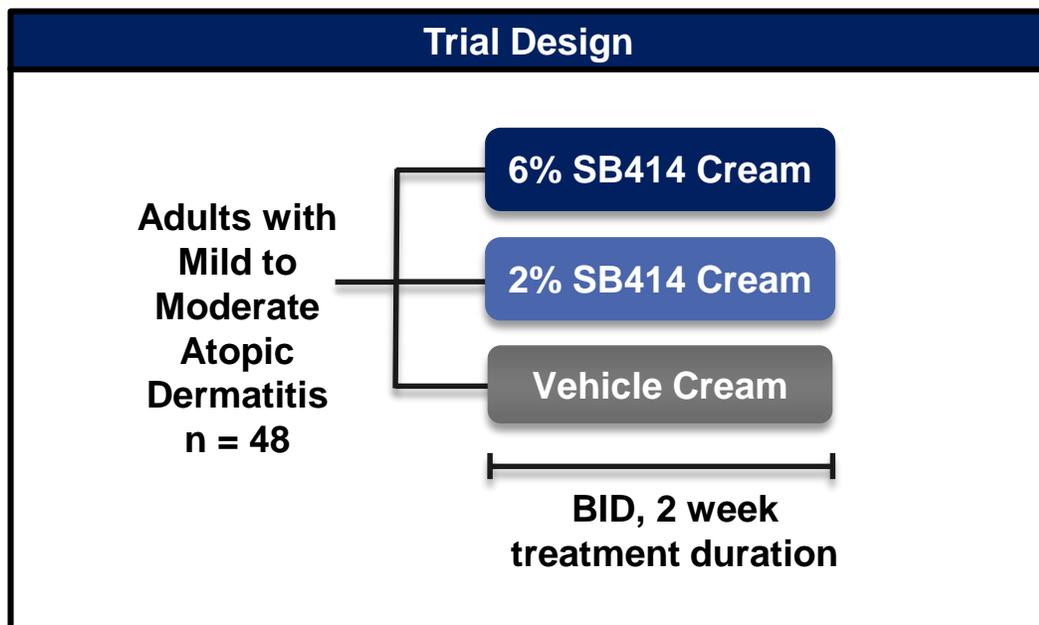


- ~22M Americans suffer from mild-to-moderate AD<sup>1</sup>
  - ~80% of disease burden
- Typically patients are treated first line with topical therapies
  - Corticosteroids, calcineurin inhibitors and PDE4 inhibitors
- Nitric oxide targets the NLRP3 inflammasome and has the ability to impact multiple mechanisms of the disease<sup>2</sup>

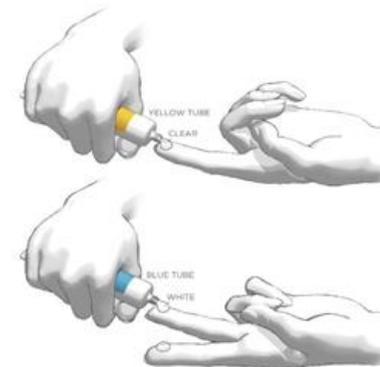
# Mean Perceived Efficacy/Safety of Atopic Dermatitis Treatments



# SB414 Phase 1b Trial Design for Atopic Dermatitis



pH Restoring Hydrogel



NVN1000 Ointment

## Randomized, double-blind, vehicle-controlled Phase 1b trial to assess:

- IL-4, IL-5, IL-13, and other key inflammatory cytokines
- Efficacy as measured by EASI (Eczema Area and Severity Index) score
- Efficacy as measured by Itch NRS – reported by subject on a 10-point numerical rating scale
- Safety and cutaneous tolerability (investigator and subject assessment)
- Systemic exposure via PK assessments of NVN1000 on Day 1 and Day 14

## **Self-emulsifying cream formulation upon admixture**



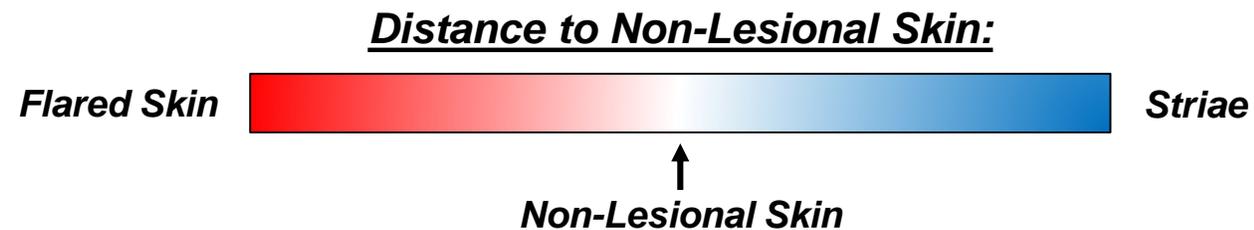
# SB414 Phase 1b Atopic Dermatitis Trial Results

	Vehicle (N=14)	SB414 2% (N=17)	SB414 6% (N=17)	
<b>Fold Change in Biomarkers over Vehicle at Wk 2</b>				
IL-4R	-	-2.5*	-1.7	<b>Confirmation of key biomarker downregulation</b>
IL-5	-	-7.1*	-4.2	
IL-13	-	-10.5*	-3.6	
IL-17A	-	-7.4*	-1.0	
IL-22	-	-7.5*	-1.8	
<b>Eczema Area and Severity Index (EASI) at Wk 2</b>				
Mean Change	-1.0	-1.2	-1.8	<b>Larger reductions in SB414 treated groups</b>
Median % Reduction	15.8%	28.6%	25.8%	
<b>Pruritus (Itch) Numeric Rating Scale (NRS) at Wk 2</b>				
≥ 3-point reduction (%)	43%	71%	59%	<b>Strong anti-pruritic effect</b>
≥ 4-point reduction (%)	29%	59%	41%	
<b>Treatment-Emergent Adverse Events (TEAE)</b>				
General Disorders and Administration Site Conditions (%)	2 (14.3%)	0 (0%)	2 (11.8%)	<b>Low TEAEs</b>

# Cross Study Comparison of Atopic Dermatitis Biomarkers

**SB414 2% reduced key atopic dermatitis biomarkers to near non-lesional levels in 2 weeks of treatment**

Biomarker	Inflamm. Pathway	Vehicle <sup>1</sup>	Pimecrolimus 1% <sup>2</sup>	Non-Lesional Skin	SB414 2% <sup>1</sup>	Betamethasone dipropionate 0.05% <sup>2</sup>
IL-4R	Th2	...	N/A	Non-Lesional Skin	...	N/A
IL-5		...	...		...	...
IL-13		...	...		...	...
IL-31		...	...		...	...
IL-22	Th22	...	...	Non-Lesional Skin	...	...
S100A7		...	...		...	...
S100A8		...	...		...	...
S100A9		...	...		...	...
S100A12	...	...	...	...	...	
IL-17A	Th17	...	...	Non-Lesional Skin	...	...
IL-17F		...	N/A		...	N/A



# Financial Update

- **Cash balance at September 30, 2018 was \$12.2 million**
- **Cash on hand along with the upfront payments expected from the Sato Amendment anticipated to provide a cash runway into late 2Q 2019**
- **Operating model adjustments from fixed infrastructure to variable activities and costs, including:**
  - Established strategic alliance with Orion Corporation in October 2018, enabling technology transfer and manufacture of our product candidates;
  - Realigned internal resources and reduced overall headcount in November 2018;
  - Evaluating current drug manufacturing capabilities and alternative structures that align with our operating strategy and the needs of current and potential future partners.
- **Focused on pursuing relevant financing alternatives, with a particular emphasis on non-dilutive options, to strengthen the Company's capital position and advance the business platform**
- **Established long-term performance-based bonus awards for all Tangible Stockholder Return Plan participants to align compensation incentives with interests of our shareholders**

# Previous 12 Months Objectives and Results

## Corporate

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- ✓ Further strengthened management team and board
- ✓ Execute on business development interest around platform and across geographies
- ✓ De-risk the platform in order to maximize shareholder value
- ✓ \$35M Capital raise in January 2018

## Clinical

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- ✓ Finalize SB204 (acne) business construct and clinical/regulatory pathway
- ✓ SB206 (molluscum) Phase 2 trial top line results and clinical path forward
- ✓ SB414 (psoriasis & atopic dermatitis) Phase 1b trial top line results and clinical path forward