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In Pursuit of a Targeted Non-Steroidal Topical Innovation in Psoriasis

Forward-Looking Statements

This presentation contains forward-looking statements. All statements other than descriptions of historical facts contained in this presentation, including statements regarding future operational and financial results and positions, business strategy, prospective products, potential market, commercial opportunity and market share, availability and potential sources of funding, clinical trial results, product approvals and regulatory pathways, research and development costs, timing (including but not limited to clinical development and regulatory timelines), strategies for completion and likelihood of success for our business activities, and plans for future operations, are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Such risks and uncertainties include, among others, those inherent in the preclinical and clinical development process and the regulatory approval process; the risks and uncertainties in commercialization and gaining market acceptance; the risks associated with protecting and defending our patents or other proprietary rights; the risk that our proprietary rights may be insufficient to protect our product candidates; the risk that we will be unable to obtain necessary capital when needed on acceptable terms or at all; competition from other products or procedures; our reliance on third-parties to conduct our clinical and non-clinical trials; and our reliance on single-source third-party suppliers to manufacture clinical, non-clinical and any future commercial supplies of our product candidates.

For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to our business in general, see our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission and any subsequent current and periodic reports. Except as required by applicable law, we assume no obligation to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

SNA-120: A Novel Phase 3 Drug for Psoriasis

- Topical non-steroidal drug which in trials has shown benefits on psoriasis and pruritus
- $1B+ global potential
- Moving rapidly to initiate Phase 3 pivotal trials, expected to start in 2H 2019
- Clinically and statistically significant efficacy on FDA psoriasis primary endpoint for topicals (IGA 2-grade composite[1]) in recent Phase 2b trial[2]
- Additional novel NCEs from Topical by Design™ Platform

1. IGA 2-grade composite = proportion of subjects achieving two-grade improvement from baseline and 'clear' or 'almost clear' in Investigator Global Assessment
2. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.

SNA-120: A Unique Clinical Profile

- Novel topical non-steroidal which has shown benefits in trials on psoriasis and pruritus and is moving into phase 3
- Data from 500+ patients, including two Phase 2 studies in psoriasis
- Clinically and statistically significant efficacy on IGA 2-grade composite and PASI 75[1]
- ~60% reduction on pruritus[2]
- Safety profile characterized as highly meaningful by polled physicians[3]
  - Optimal for sensitive areas
- Numerous potential product line extensions

1. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.
2. Statistically significant in itchy patients in Creabilis Phase 2b trial (Study CT327-2003); statistically significant from baseline, but not compared to Vehicle in Study SNA-120-201.
3. Data on file, Sienna Biopharmaceuticals, Inc.: poll of 75 Dermatologists and Primary Care Physicians.

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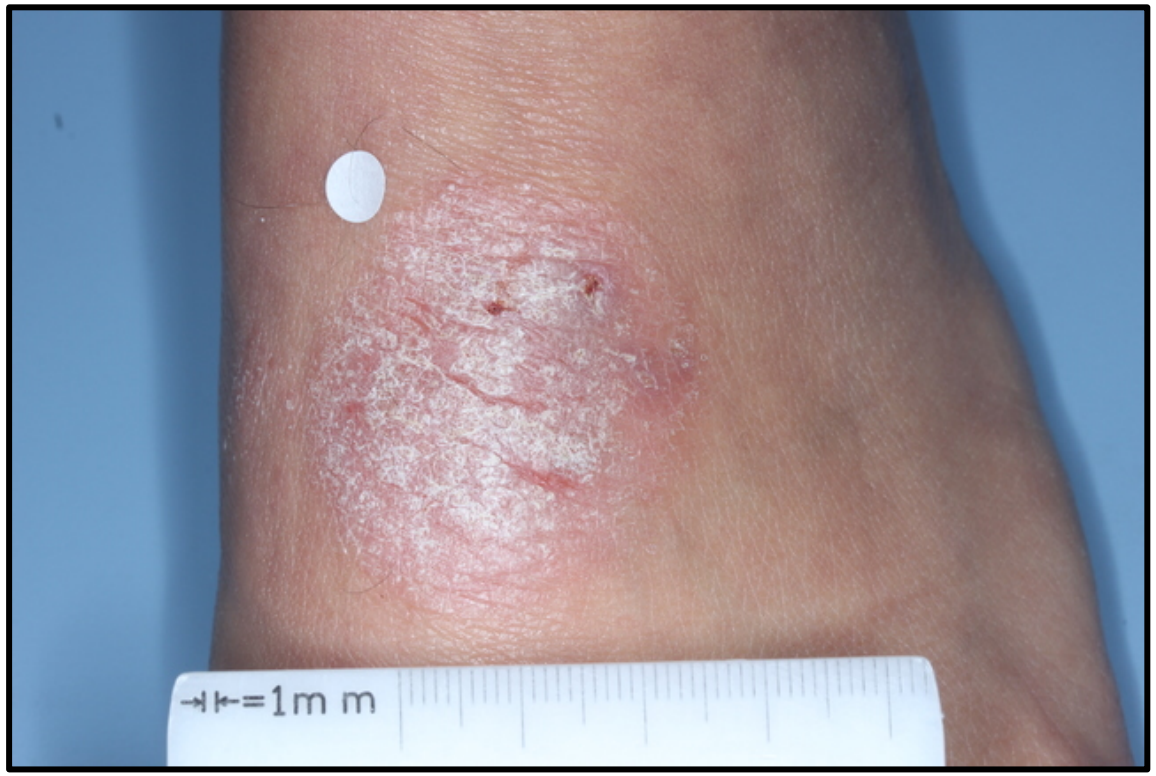
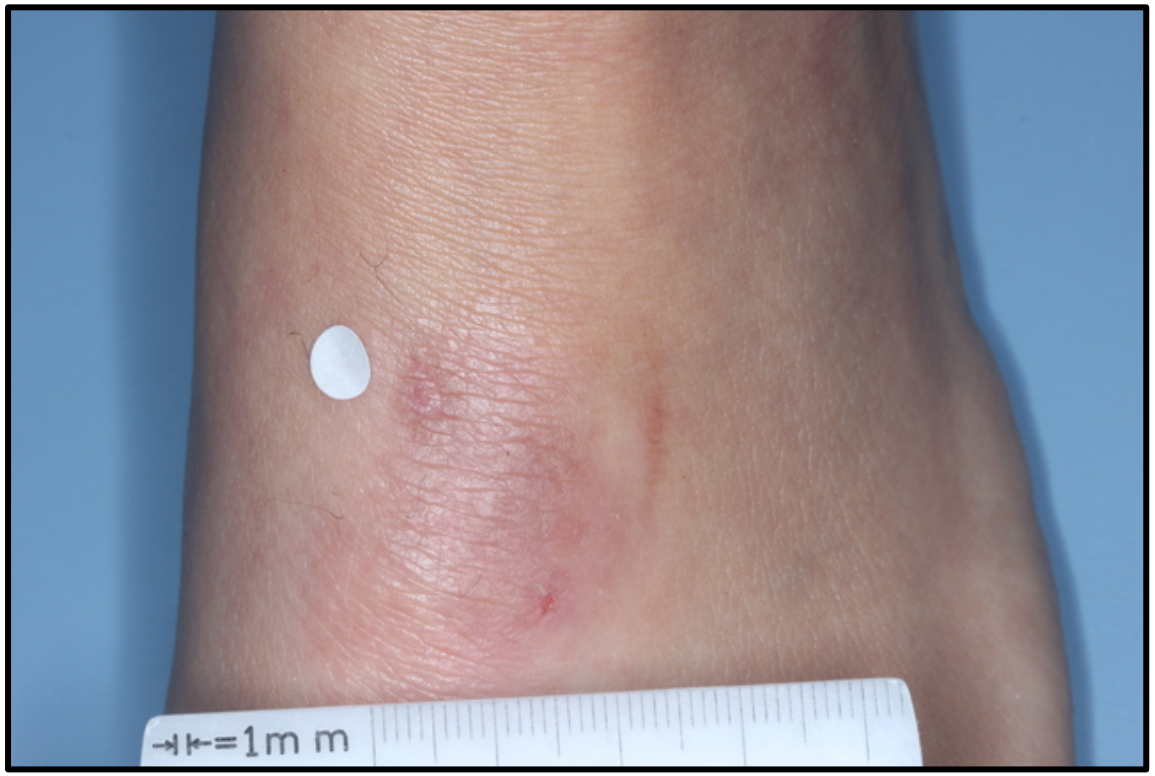
SNA-120: A Novel Topical Non-Steroidal Psoriasis Drug in Phase 3

Before Treatment



After 12 Weeks Treatment with SNA-120 0.05% in Recent Phase 2b Trial



Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201. Subject 08005. Responder Analyses - Composite IGA: Yes; PASI 50: Yes; PASI 75: Yes. IGA: BL 3; 12 Wk 1. PASI (mean): BL 2.8; 12 Wk 0. NRS (mean): BL 6.2; 12 Wk 1.4.

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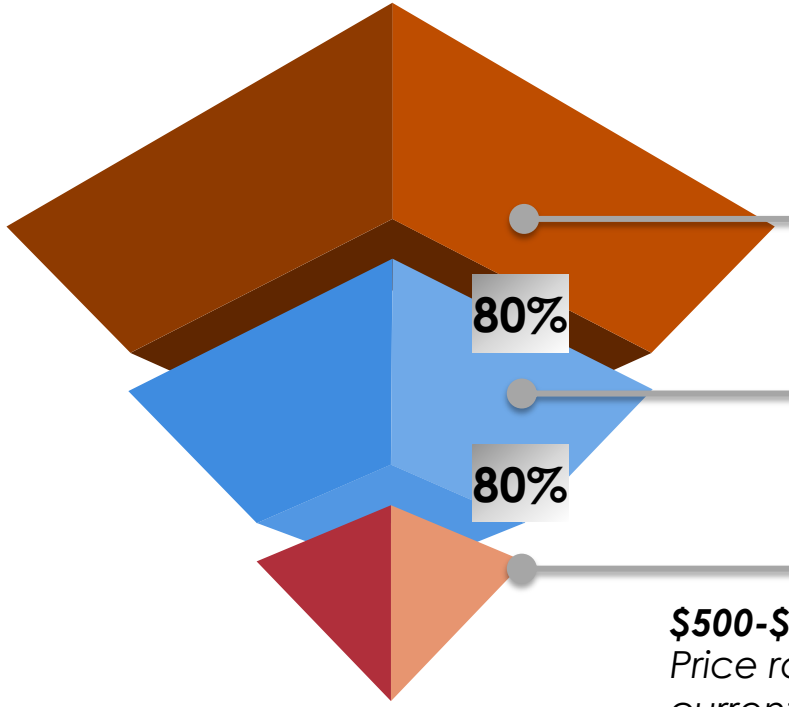
SNA-120, A Topical Non-Steroidal Innovation in Mild to Moderate Psoriasis



7.5 million
Total psoriasis patient population[1]

6.0 million
Mild-to moderate psoriasis patients[1]

4.8 million
Psoriasis patients impacted by pruritus[2]

$500-$950/month
Price range for 60-gram tube of current topical psoriasis therapies[3]

A Novel Topical Non-Steroidal for Mild-to-Moderate Psoriasis

1. American Academy of Dermatology. Skin conditions by the numbers. Accessed November 2018.
2. Stinco et al. *Acta Dermatovenerol Croat* 2014;22(2):122-8.
3. Includes Protopic, Elidel, Enstilar, Taclonex, Dovonex and Calcitriol.

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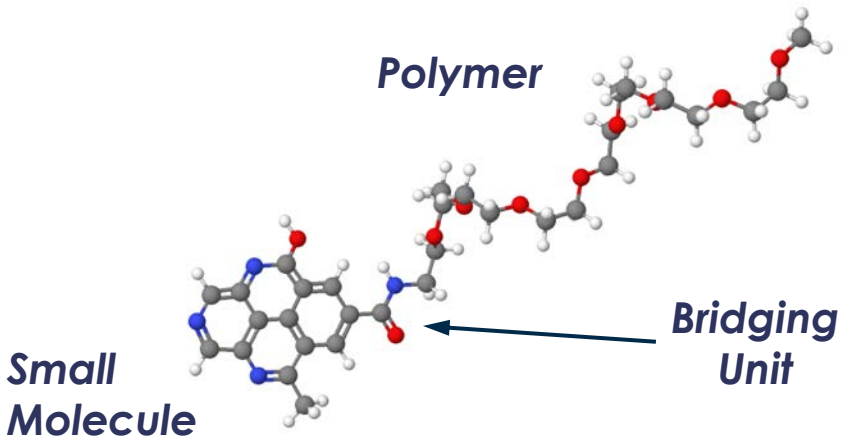
SNA-120, the Lead Asset from Sienna's Topical by Design™ Platform

- **Optimizes** small molecules **for topical administration**
- **High local** drug **concentration**
- **Low systemic exposure**
- Ability to create **new chemical entities (NCEs)** with the **Topical by Design platform**
- **Targeting surfaces** such as **the skin, the eye, the gastrointestinal tract and the respiratory tract**

Topical by Design Molecule Components



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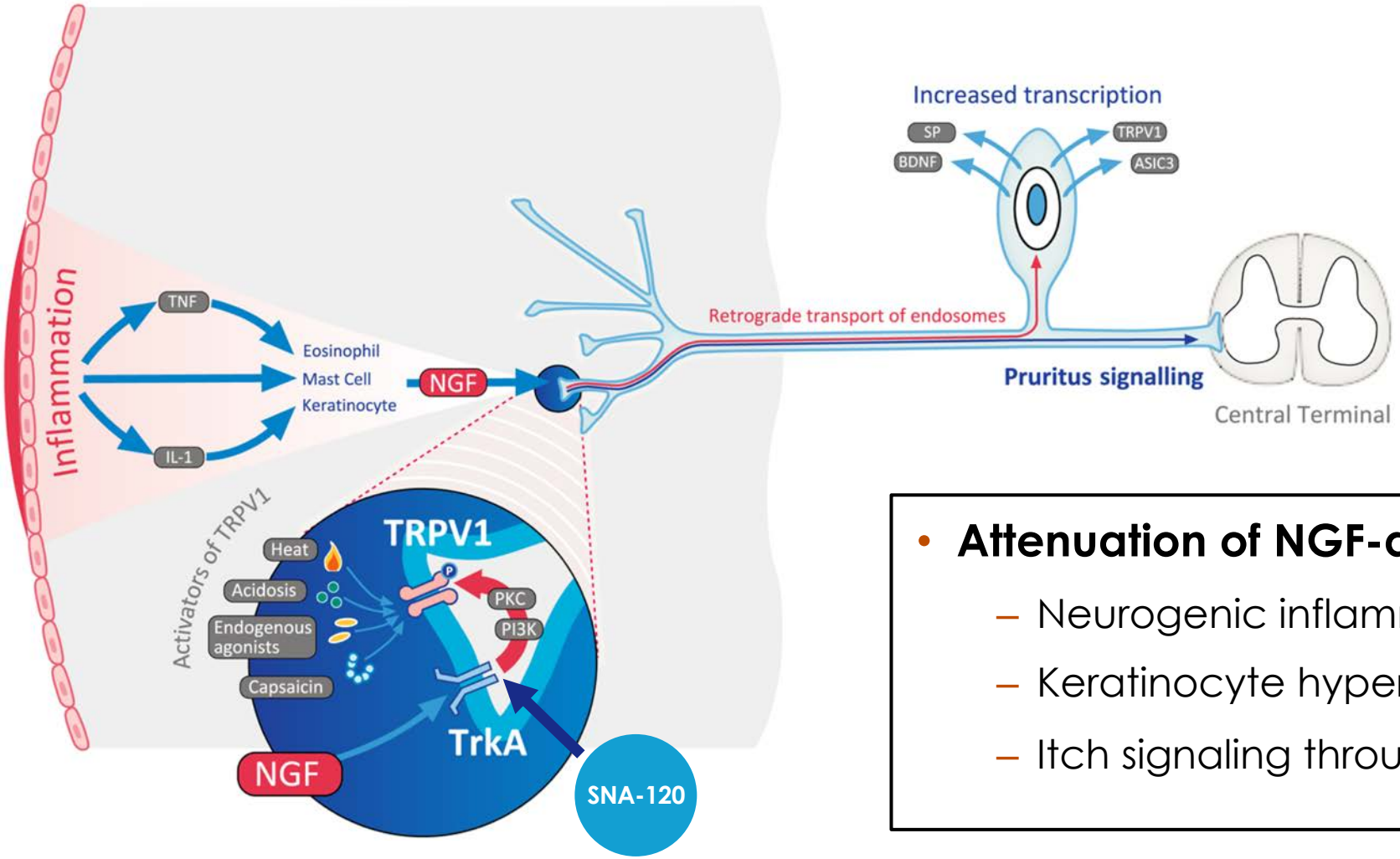
SNA-120 Inhibits TrkA, the High Affinity Receptor for NGF[1], Particularly Important in Psoriasis



- **Attenuation of NGF-driven:**
  - Neurogenic inflammation
  - Keratinocyte hyperproliferation
  - Itch signaling through TRPV1[2]

1. NGF = nerve growth factor
2. TRPV1 = transient receptor potential cation channel subfamily V member 1

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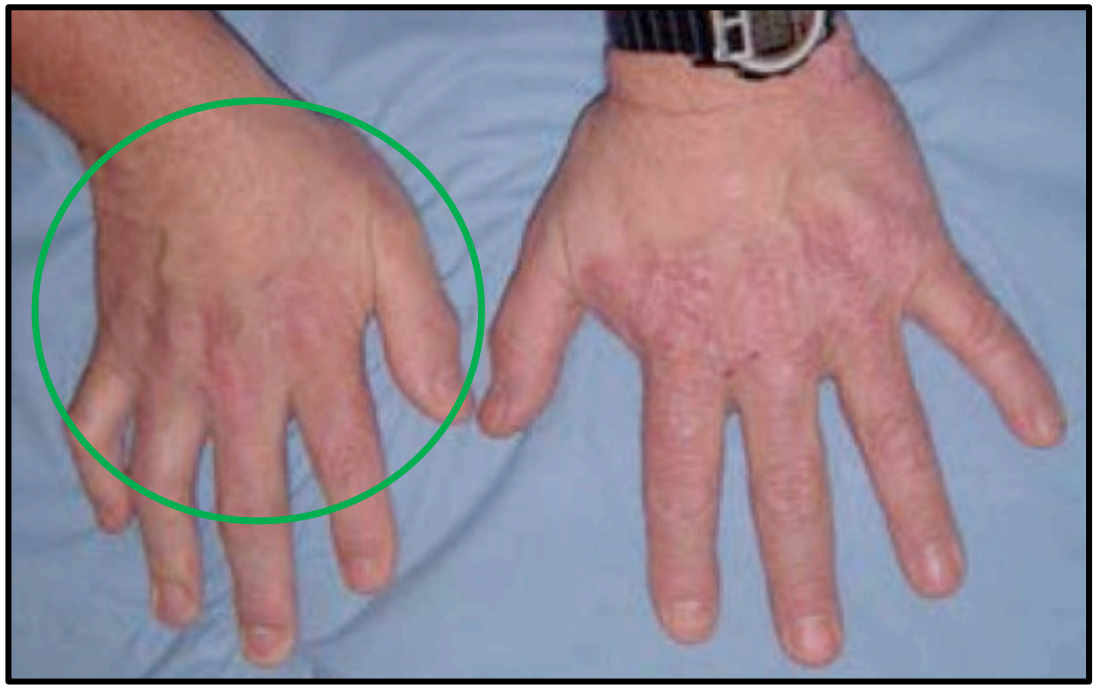
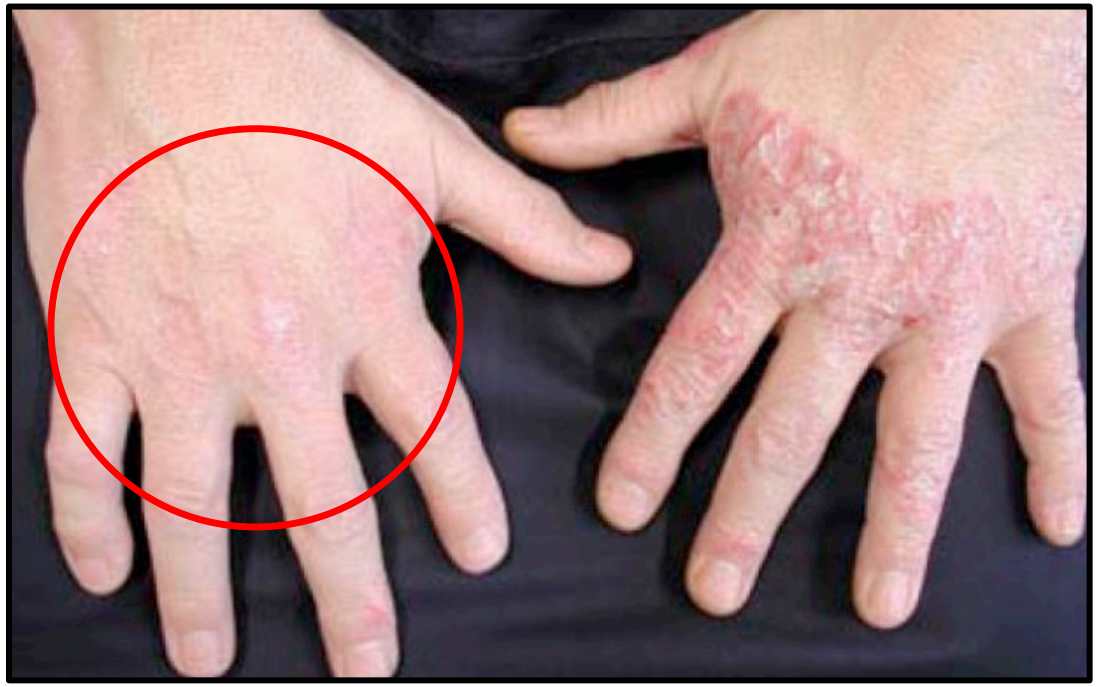
Cutaneous Nerves Play a Role in Psoriasis Pathogenesis

Plaque remission on right hand **following nerve injury** to right hand



Beginning of **plaque reappearance** on right hand **with nerve recovery** in right hand at four months



Modified from Azimi et al. *Br J Dermatol* 2015;172:988-93 (Fig. 1).

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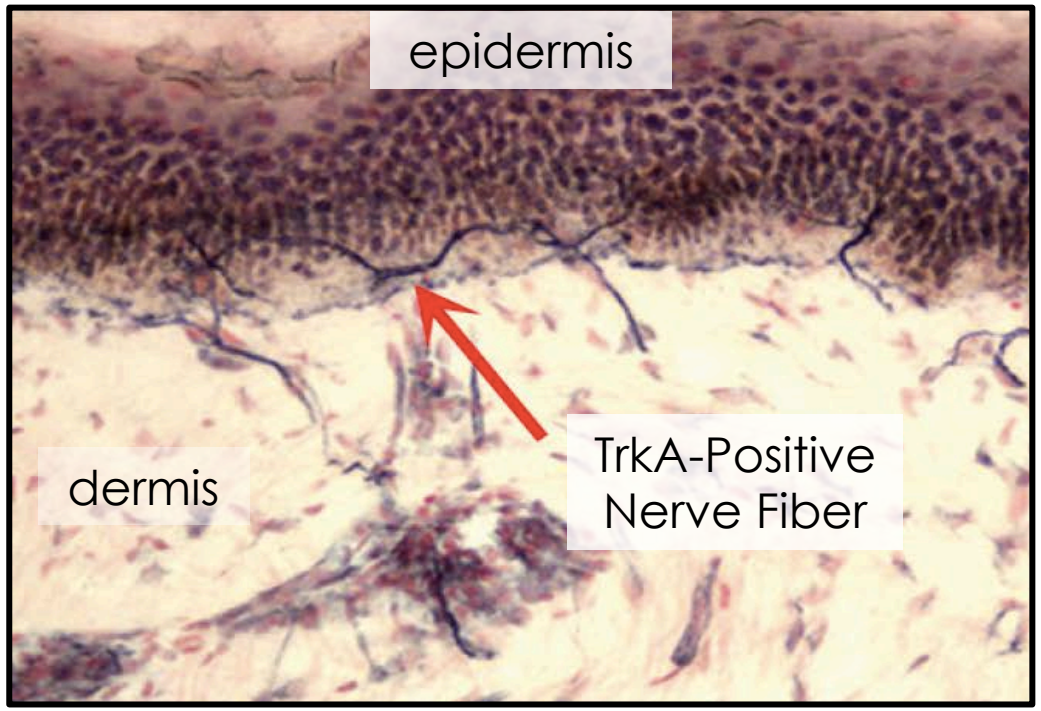
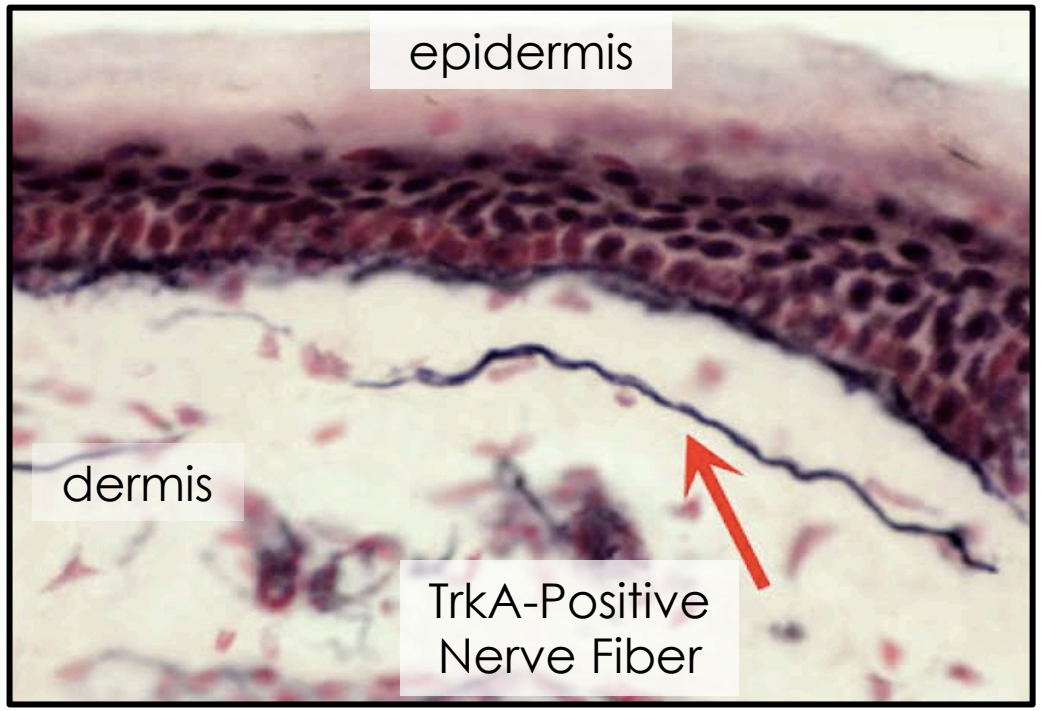
TrkA-Positive Nerve Fibers are Prevalent in Psoriatic Skin





Modified from Roblin et al. *Acta Derm Venereol* 2015;95:542-48 (Fig. 2). Human skin sections showing TrkA-positive intra-epidermal nerve fibers (arrow, left photo) and sub-epidermal nerve fibers (arrow, right photo). Magnification x 20.

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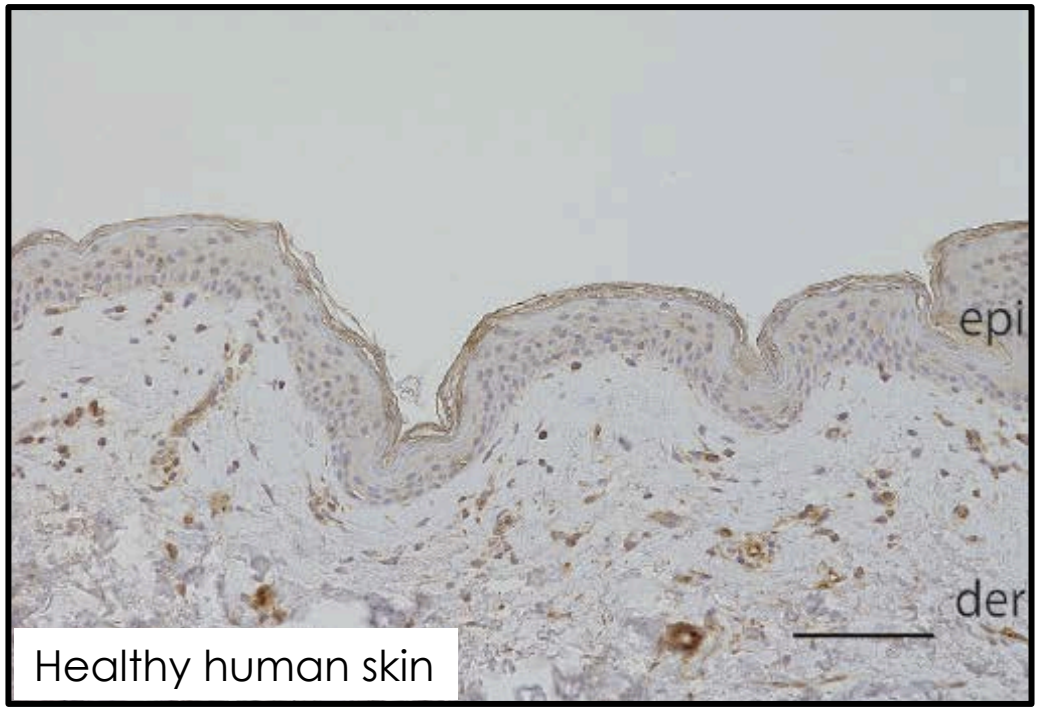
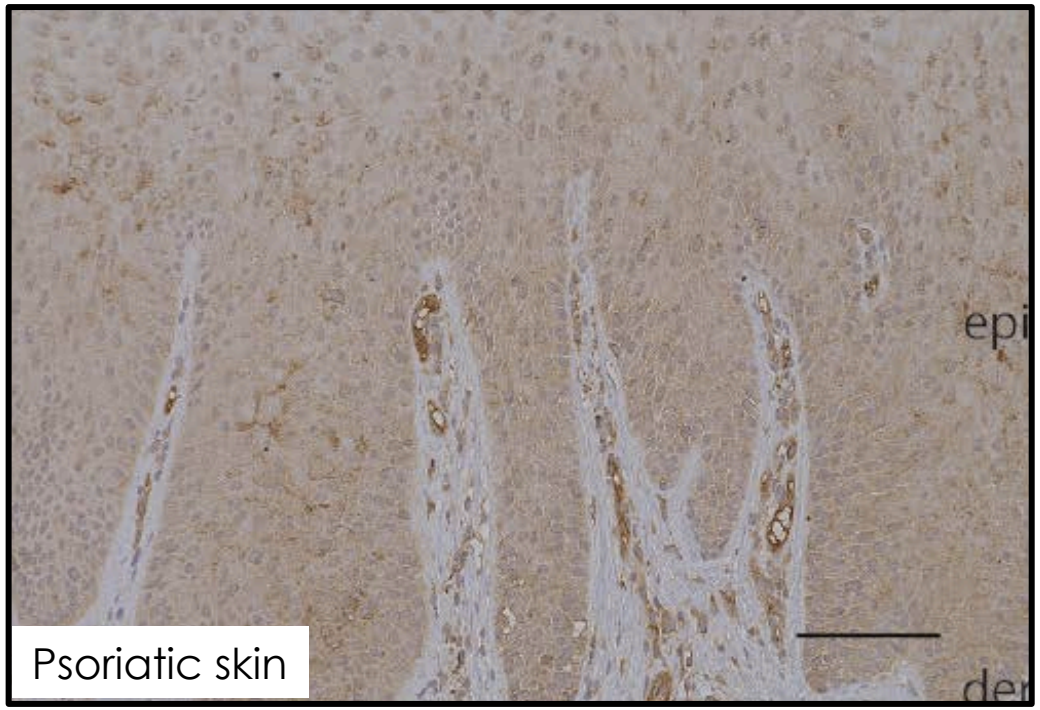
NGF is Highly Expressed in Epidermis of Psoriatic Skin





Modified from Kou et al. *Acta Derm Venereol* 2012;92:521-28 (Fig. 2). Skin samples from healthy volunteer (left photo) and patient with psoriasis (right photo) were immunostained for NGF. NGF expression was increased in the epidermis (epi) of patients with psoriasis compared with healthy volunteers. Scale bars=100 um. Dermis (der).

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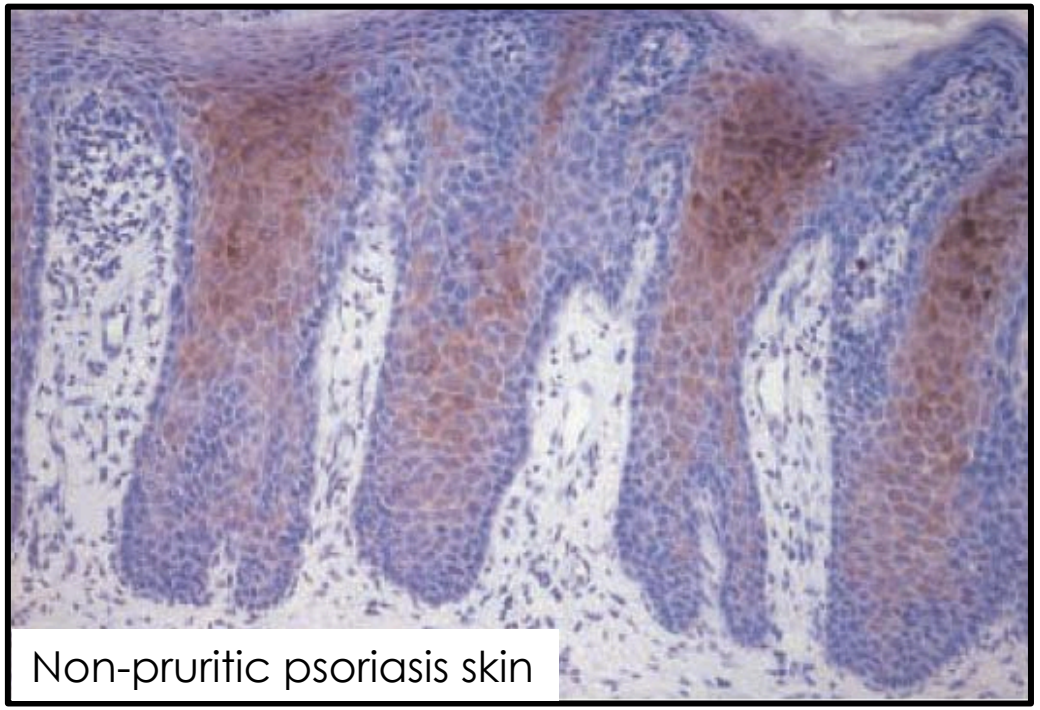
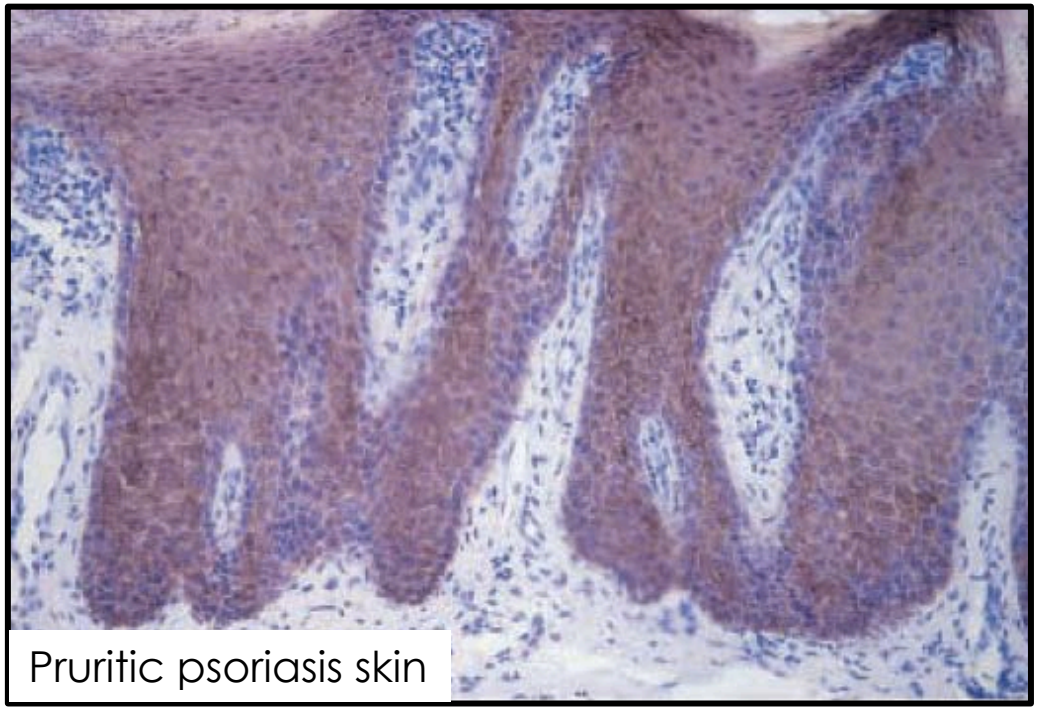
NGF Expression is Greater in Pruritic Psoriatic Skin





Modified from Nakamura et al. *Br J Dermatol* 2003;149:718-30 (Fig. 3). Marked diminution of NGF immunoreactivity in the epidermis of a non-pruritic lesion (left photo). Strong expression of NGF throughout the entire epidermis in a pruritic lesion (right photo). Magnification x 200.

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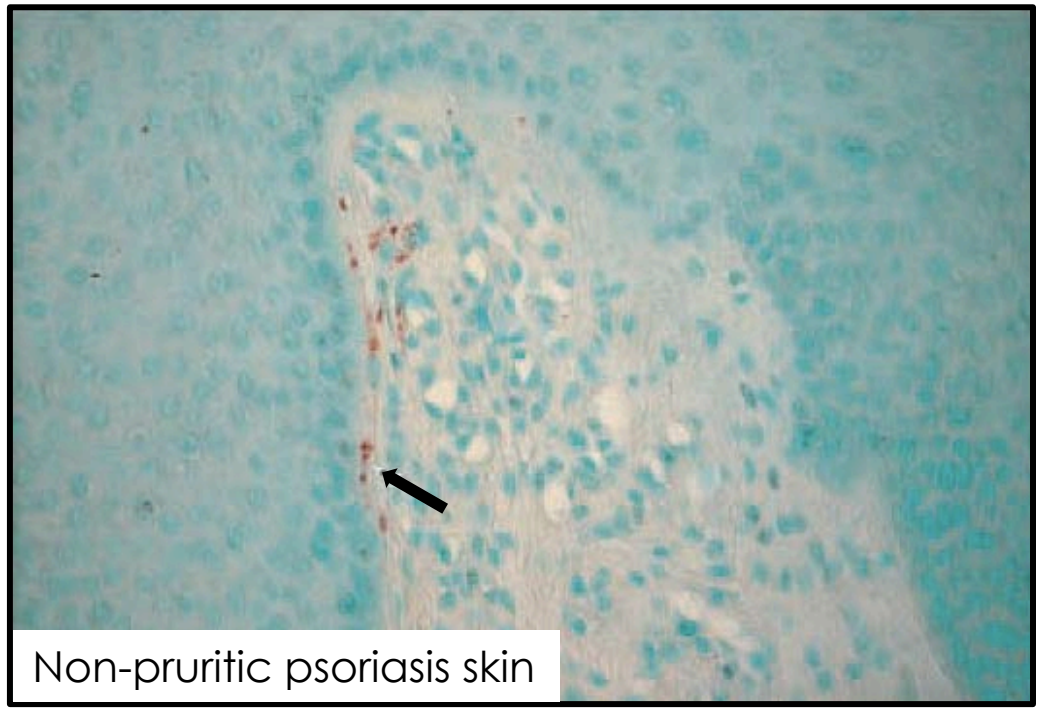
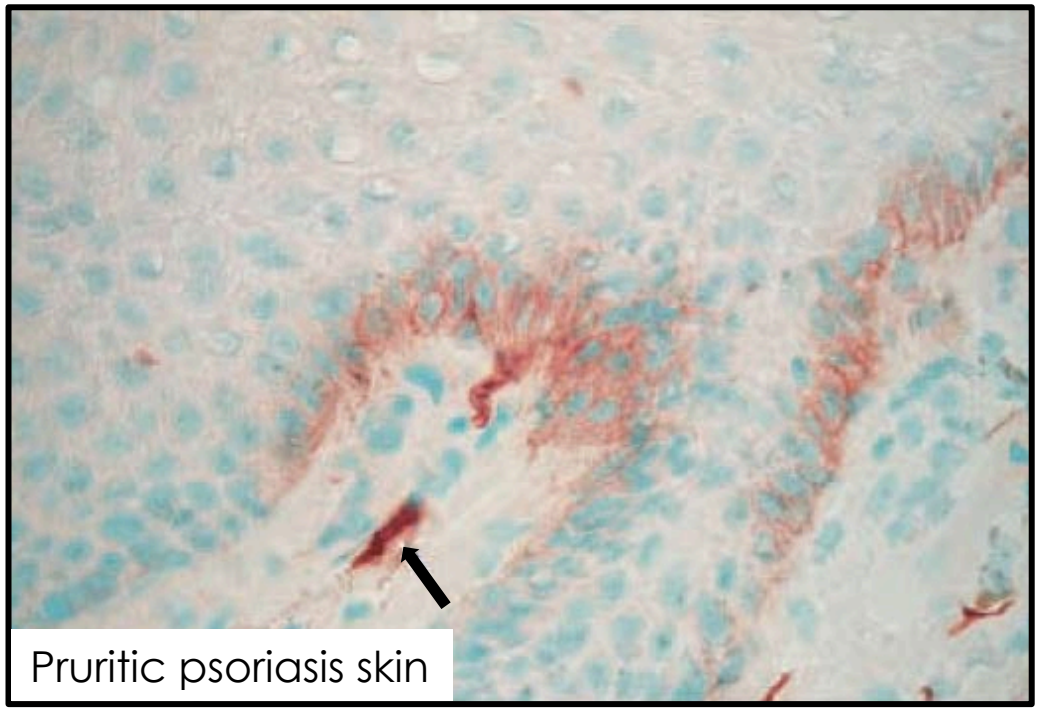
TrkA Expression is Greater in Pruritic Psoriatic Skin





Modified from Nakamura et al. *Br J Dermatol* 2003;149:718-30 (Fig. 4). Immunostaining for TrkA in psoriatic lesional skin. Virtual absence of TrkA expression in the epidermal basal layer in a non-pruritic lesion (left photo); note the few fine nerve fibers expressing TrkA (arrow). Intense immunoreactivity with TrkA in the epidermal basal layer and ascending nerve fiber (arrow, right photo) in a pruritic lesion. Original magnification x 400.

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Clear Iterative Development of SNA-120 to Phase 3, A Novel Topical Non-Steroidal Psoriasis Drug

Creabilis Phase 2b (Study CT327-2003)[1]

- Itchy and non-itchy psoriatics
- Statistically significant efficacy in psoriasis – better in itchy psoriatics
- Statistically significant ~60% improvement in pruritus in itchy psoriatics

Recent Phase 2b (Study SNA-120-201)[1]

- Only itchy psoriatics
- Statistically significant efficacy in psoriasis regulatory endpoint (IGA 2-grade composite[2])
- ~60% improvement from baseline in pruritus

Maximal Use Pharmacokinetic (PK)[1]

- Minimal to no systemic exposure
- Well-tolerated with acceptable safety profile
- ~60% improvement from baseline in pruritus

Phase 3 (planned)

- Primary:
  - Psoriasis (IGA 2-grade composite)
- Secondary:
  - PASI 75[3]
  - Pruritus

1. Data on file, Sienna Biopharmaceuticals, Inc.
2. IGA 2-grade composite = proportion of subjects achieving two-grade improvement from baseline and 'clear' or 'almost clear' in Investigator Global Assessment
3. PASI 75 = proportion of subjects achieving 75% reduction in Psoriasis Area and Severity Index score from baseline

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SNA-120 (0.05%) Showed Statistical Significance on FDA Psoriasis Primary Endpoint for Topicals (IGA 2-Grade Composite[1])[2]

	IGA 2-Grade Composite	
Treatment Group	SNA-120 (0.05%)	Vehicle
Proportion of subjects	29%	13%
p-value	0.036	

- **Responder rate on this stringent FDA primary endpoint is clinically and statistically significant, while Vehicle rate is within expected range**
- 0.5% dose was not as effective and not differentiated from vehicle

1. IGA 2-grade composite = proportion of subjects achieving two-grade improvement from baseline and 'clear' or 'almost clear' in Investigator Global Assessment
2. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.

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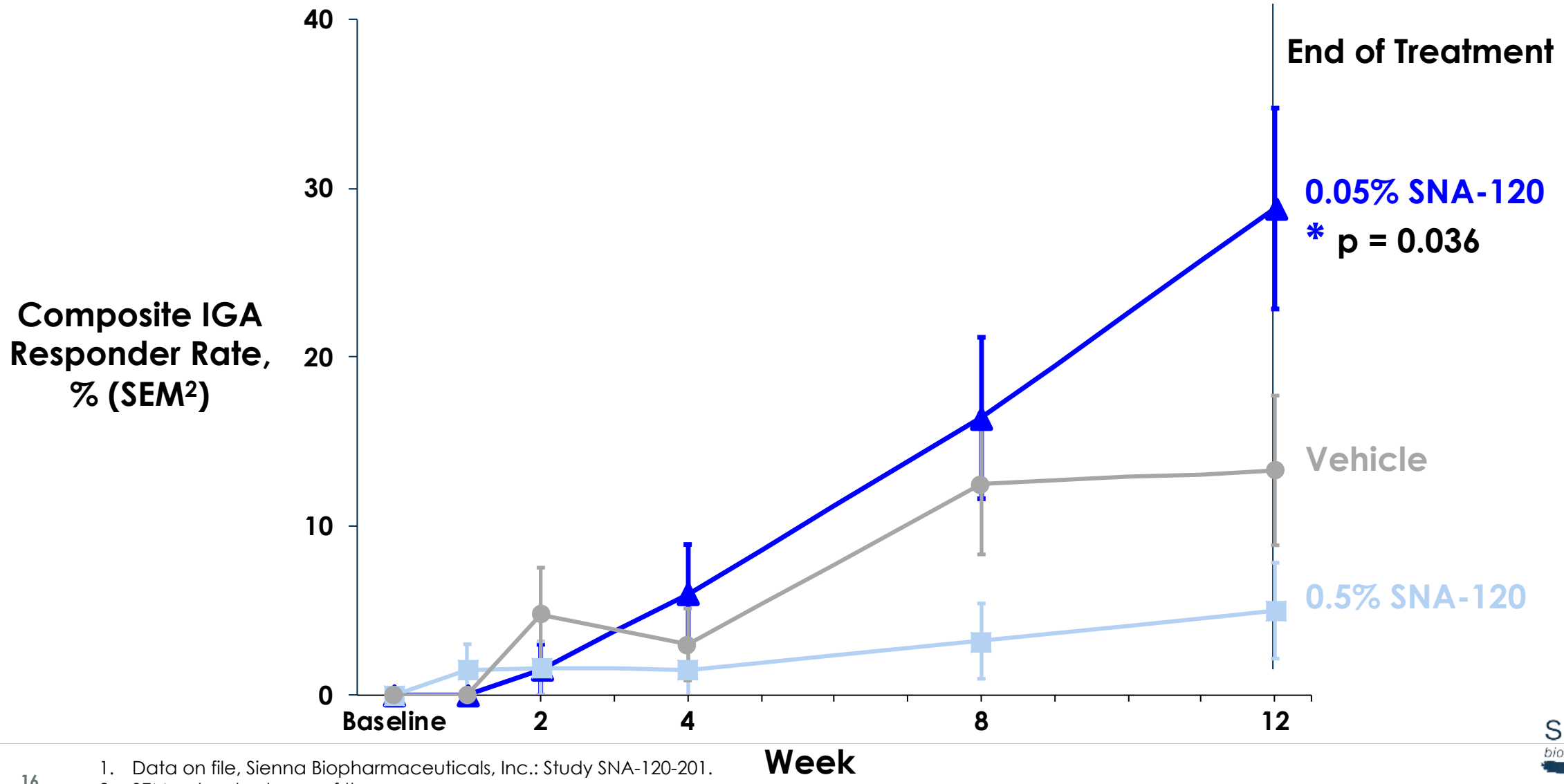
SNA-120 (0.05%) Efficacy Improved Throughout Trial on FDA Psoriasis Primary Endpoint for Topicals (IGA 2-Grade Composite)[1]



1. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.
2. SEM = standard error of the mean

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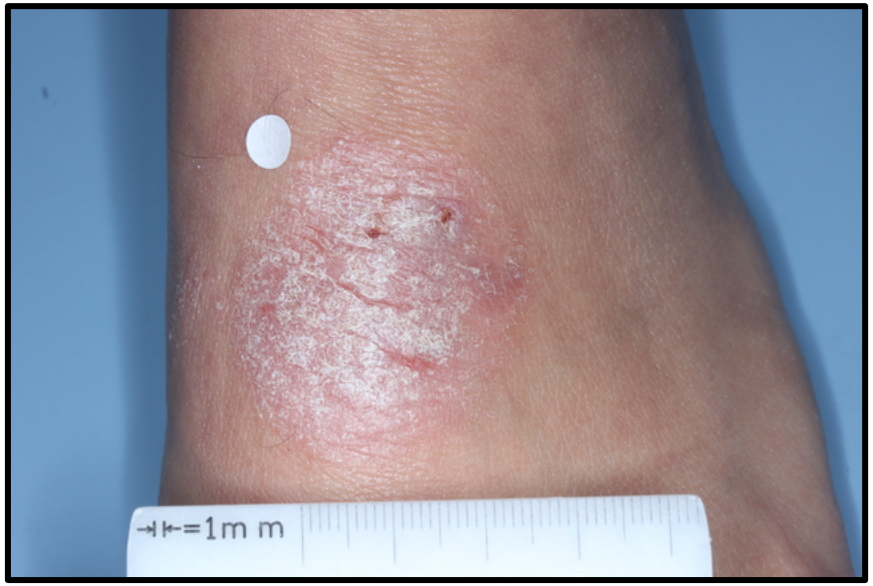
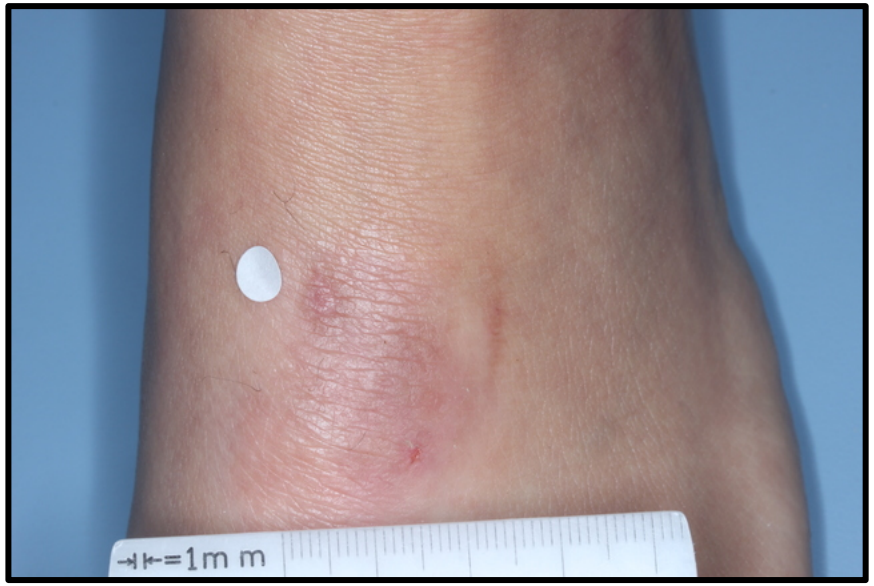
SNA-120 (0.05%) Subject 08005 in SNA-120-201

- Visible clearing of target lesion
- Responder on IGA 2-grade composite and PASI 75





Baseline	
IGA (2 or 3)	3
PASI (mean)	2.8
I-NRS (mean)	6.2

Responder Analyses	
IGA 2-grade Composite	Yes
PASI 50	Yes
PASI 75	Yes

Week 12	
IGA	1
PASI (mean)	0
I-NRS (mean)	1.4

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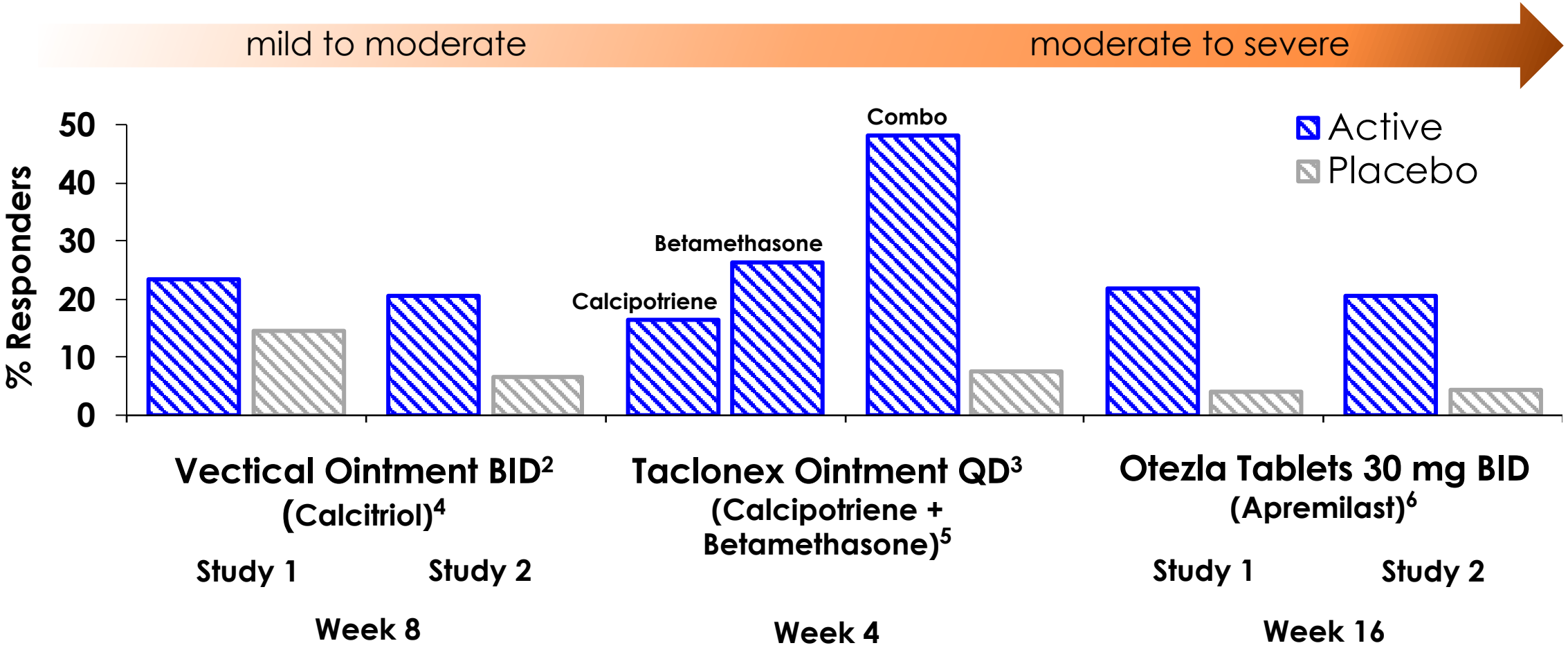
Data on file, Sienna Biopharmaceuticals, Inc.

Published IGA Data for On-Market Psoriasis Therapies[1]



1. Independent study data from Prescribing Information for each listed therapy, not from head-to-head studies
2. BID = twice daily
3. QD = once daily
4. Vitamin D Analog; 2-grade improvement from baseline and 'clear' or 'minimal' on IGA
5. Vitamin D Analog + Mid-Potency Corticosteroid; 'clear' or 'very mild' on IGA
6. Phosphodiesterase 4 (PDE4) Inhibitor; 'clear' or 'almost clear' on IGA

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SNA-120 (0.05%) Statistically Significant on Both IGA 2-Grade Composite and PASI 75[1,2]

	IGA 2-Grade Composite		PASI 75	
Treatment Group	SNA-120 (0.05%)	Vehicle	SNA-120 (0.05%)	Vehicle
Proportion of subjects	29%	13%	27%	13%
p-value	0.036		0.045	

- **Similar results on two stringent endpoints that are measured in different ways = confidence in robustness of results**
- 0.5% dose was not as effective and not differentiated from vehicle

1. PASI 75 = proportion of subjects achieving 75% reduction in Psoriasis Area and Severity Index score from baseline
2. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.

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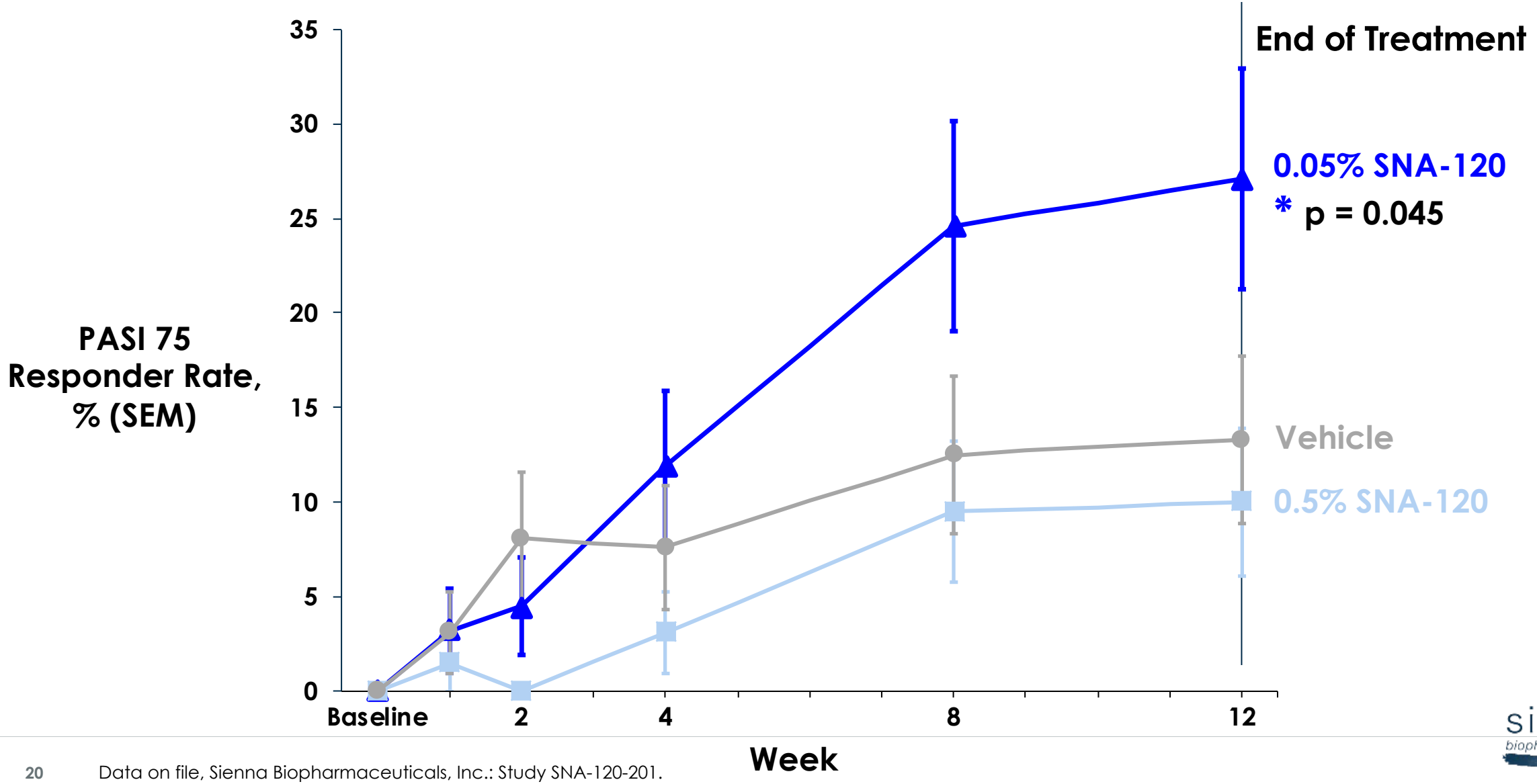
SNA-120 (0.05%) Efficacy Improved Throughout Trial on PASI 75, Similar to IGA 2-Grade Composite



Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.

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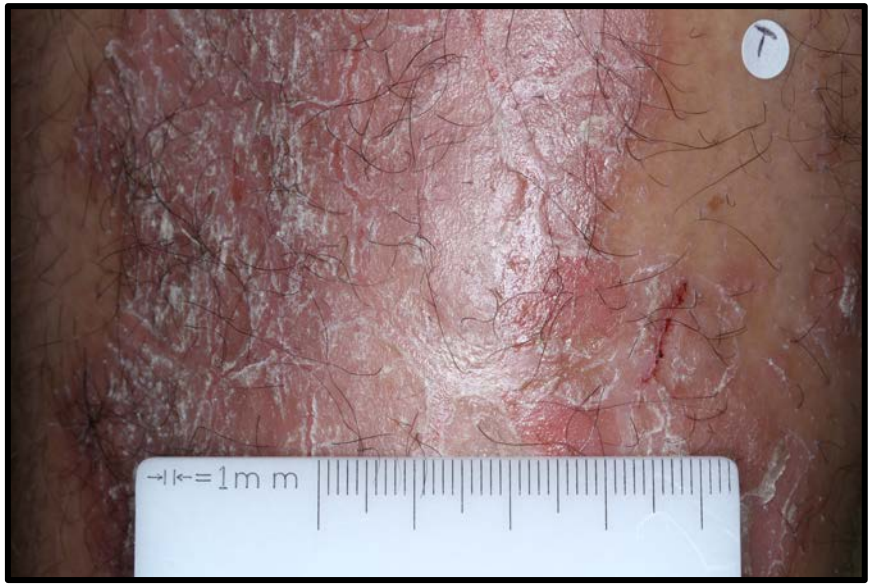
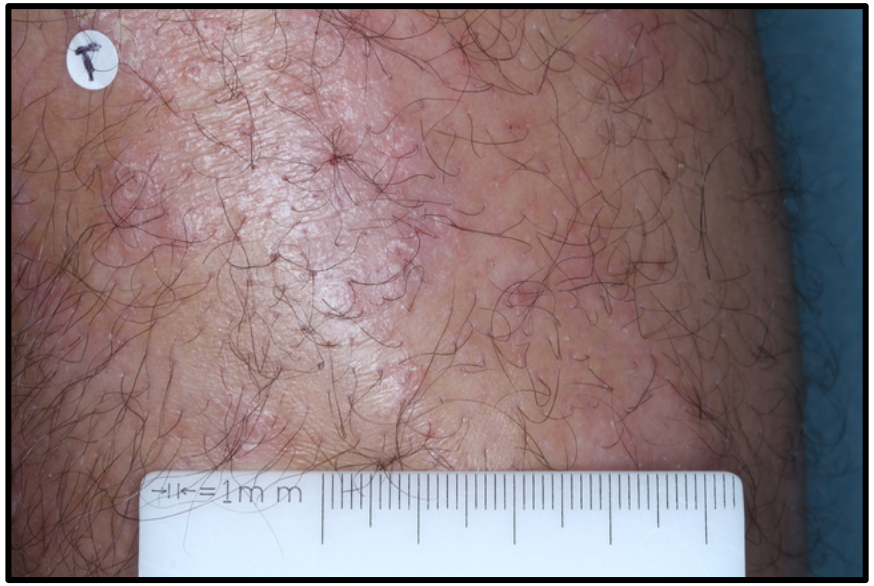
SNA-120 (0.05%) Subject 02012 in SNA-120-201

- Visible clearing of target lesion
- Non-responder on IGA 2-grade composite and PASI 75





Baseline	
IGA (2 or 3)	3
PASI (mean)	4.9
I-NRS (mean)	7

Responder Analyses	
IGA 2-grade Composite	No
PASI 50	Yes
PASI 75	No

Week 12	
IGA	2
PASI (mean)	2.4
I-NRS (mean)	1.4

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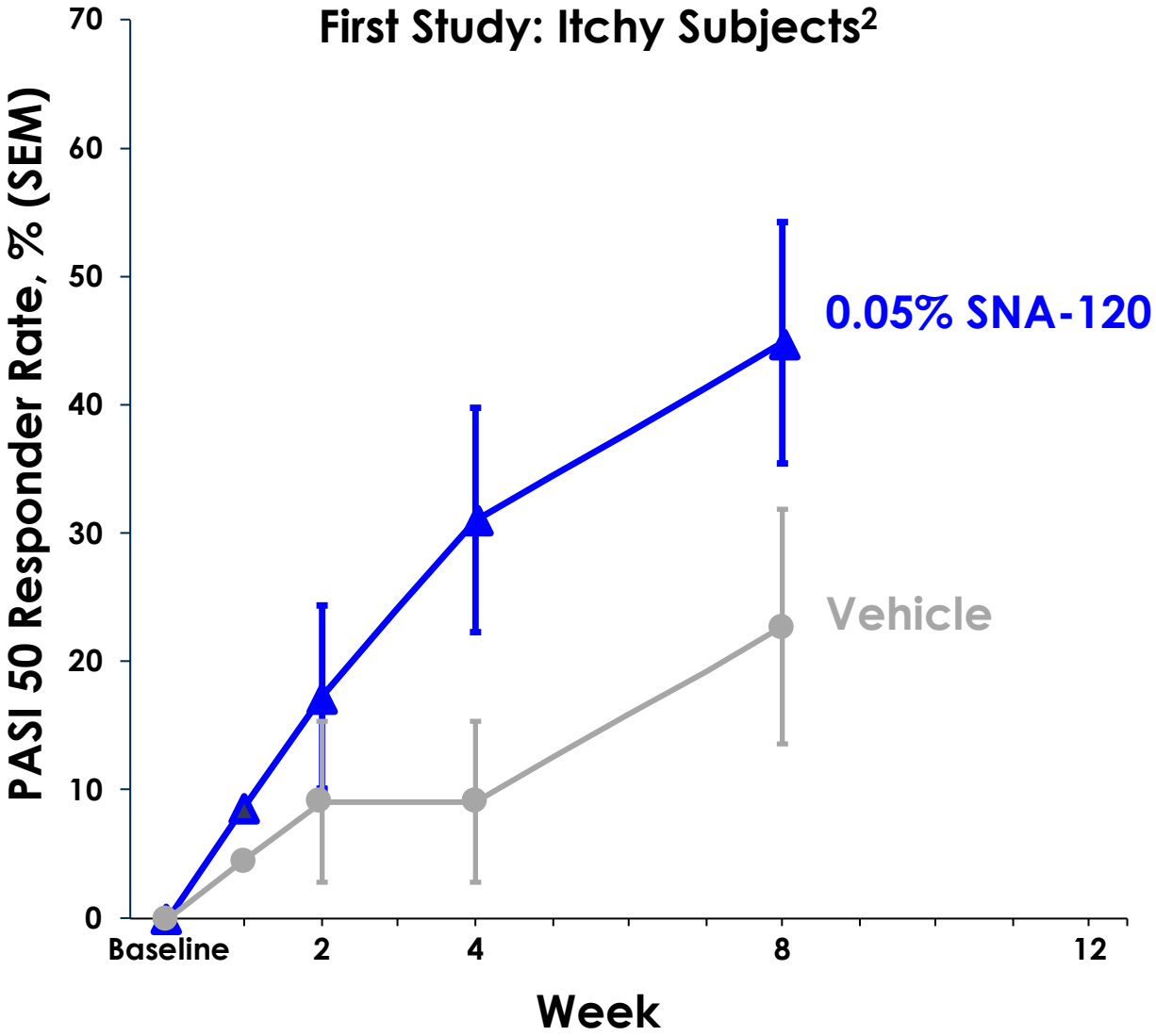
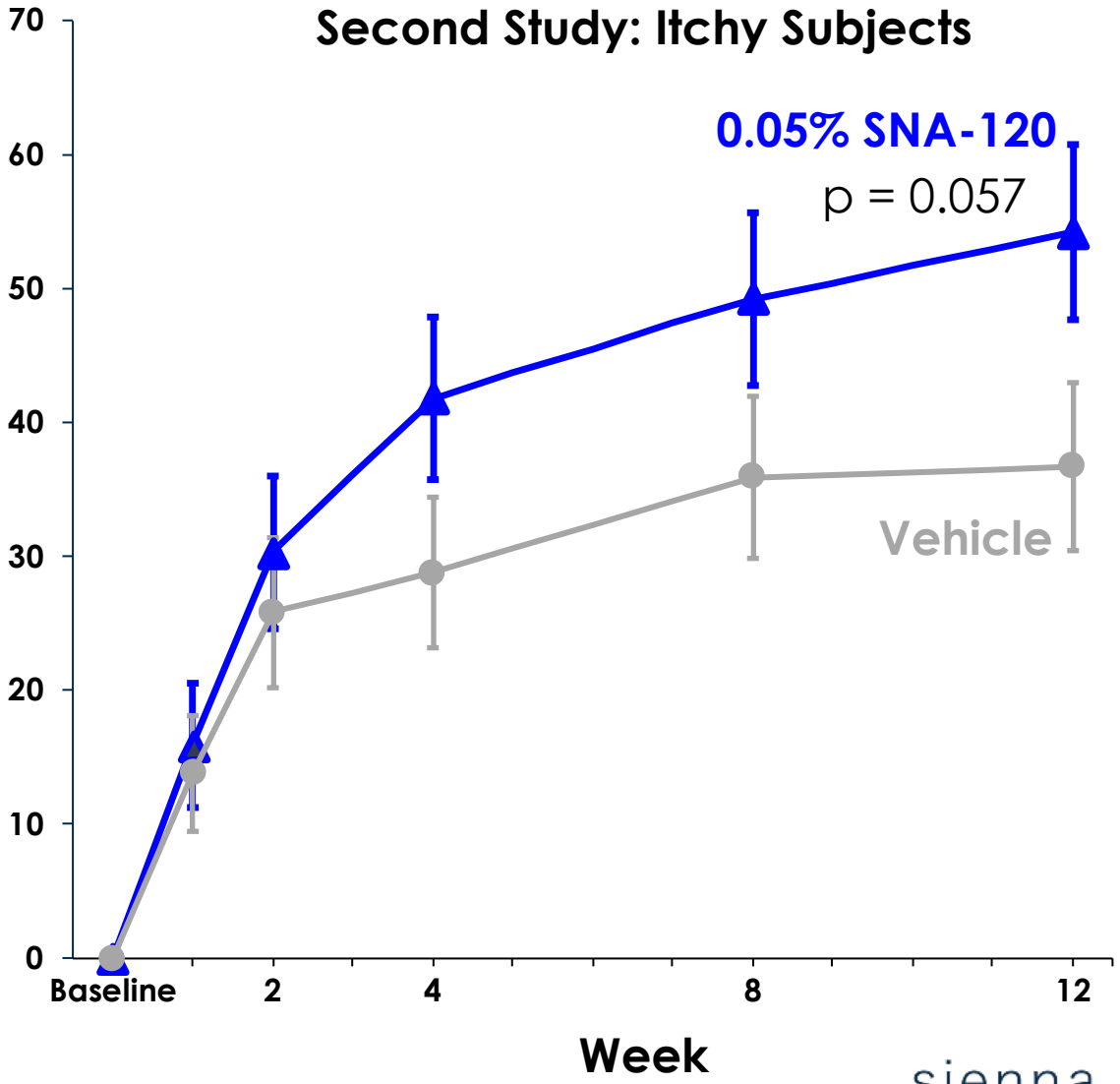
Data on file, Sienna Biopharmaceuticals, Inc.

Consistent Psoriasis Results (PASI 50) in Both CT327-2003 and SNA-120-201 for 0.05% Dose[1]





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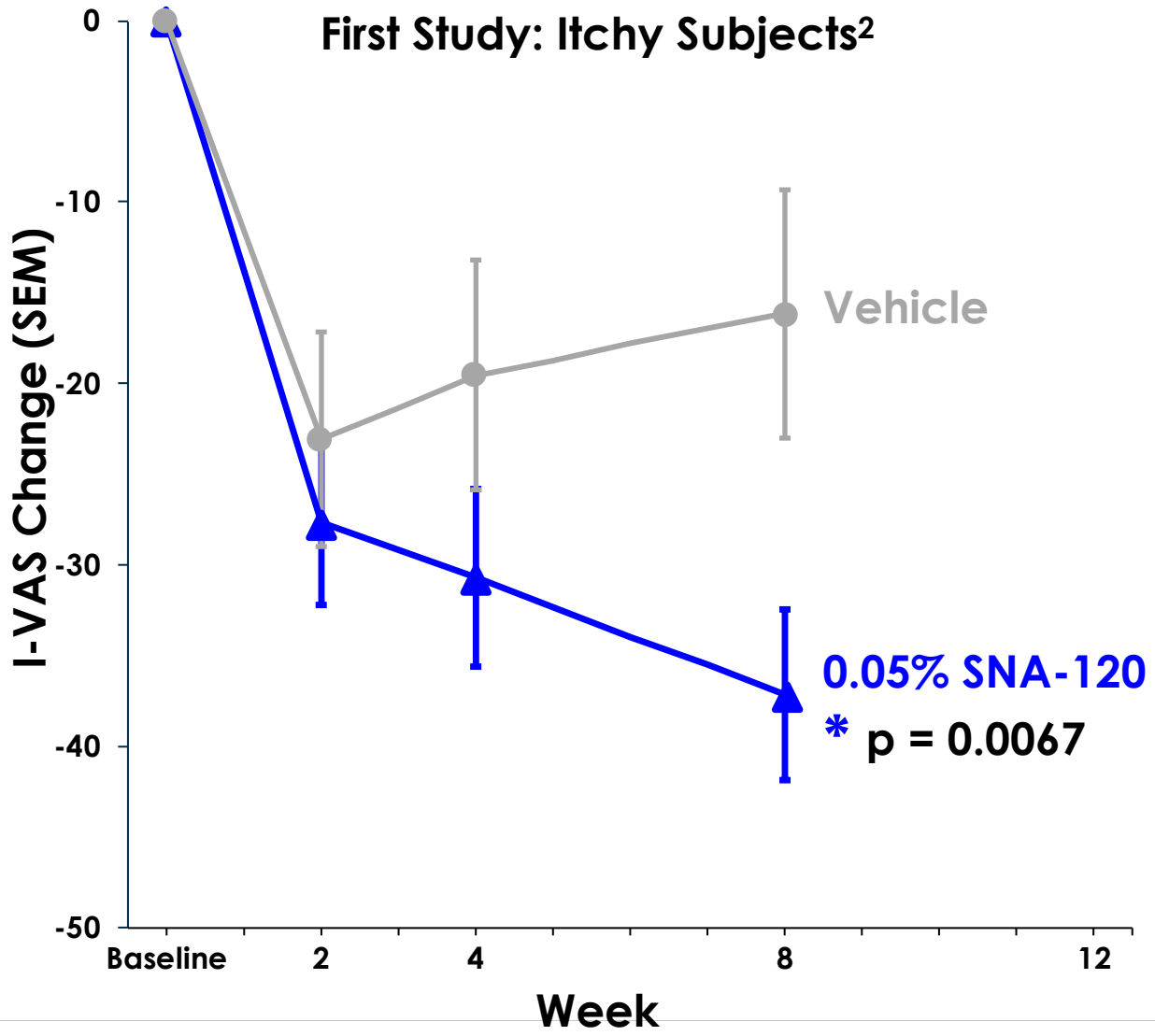
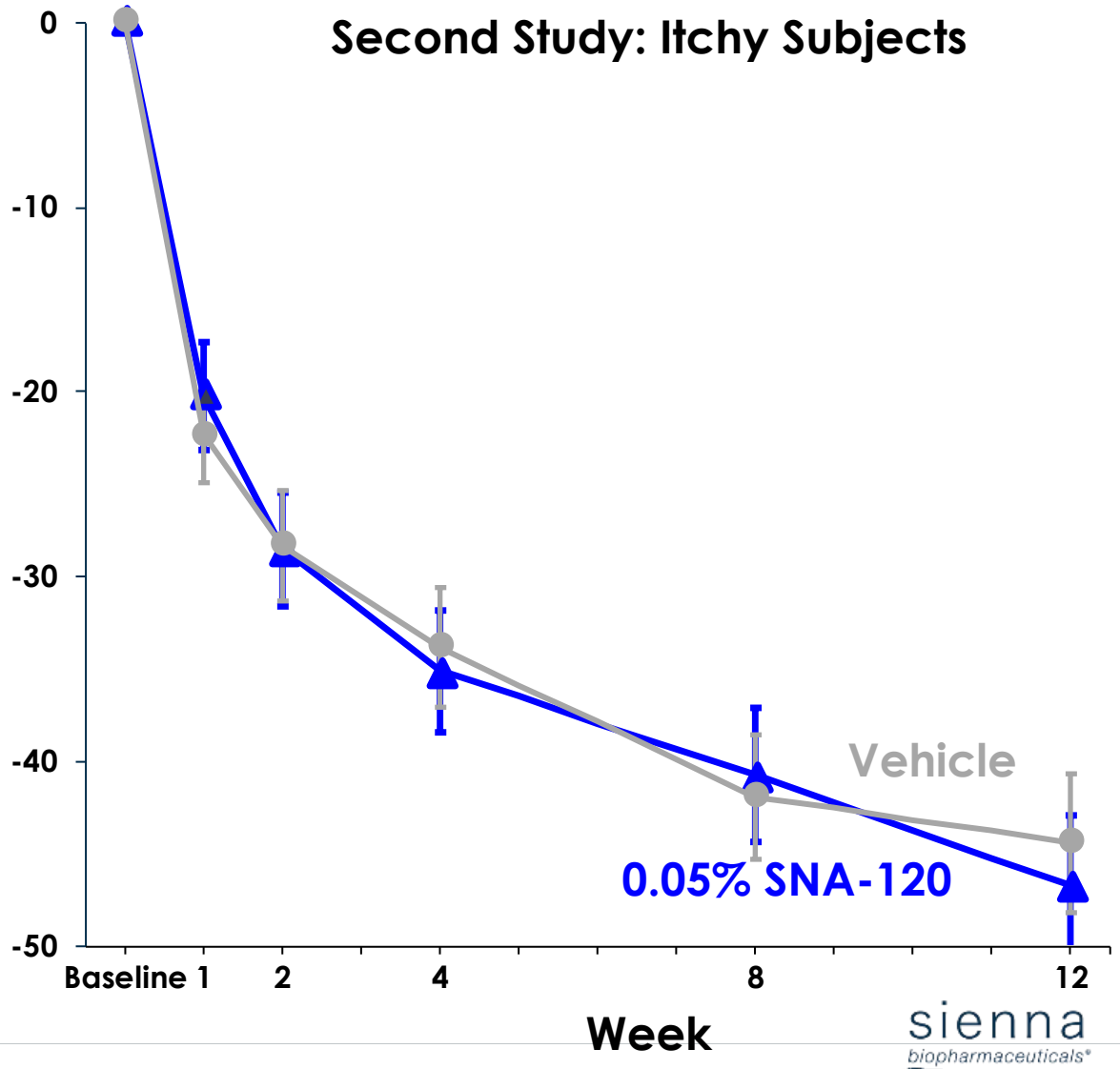
1. Data on file, Sienna Biopharmaceuticals, Inc.
2. Impact on pruritus in subgroup with baseline pruritus VAS ≥ 40 mm.

Consistent Pruritus Results (I-VAS) in Both CT327-2003 and SNA-120-201 for 0.05% Dose, Yet Different Vehicle Response[1]





1. Data on file, Sienna Biopharmaceuticals, Inc.
2. Impact on pruritus in subgroup with baseline pruritus VAS ≥ 40 mm.

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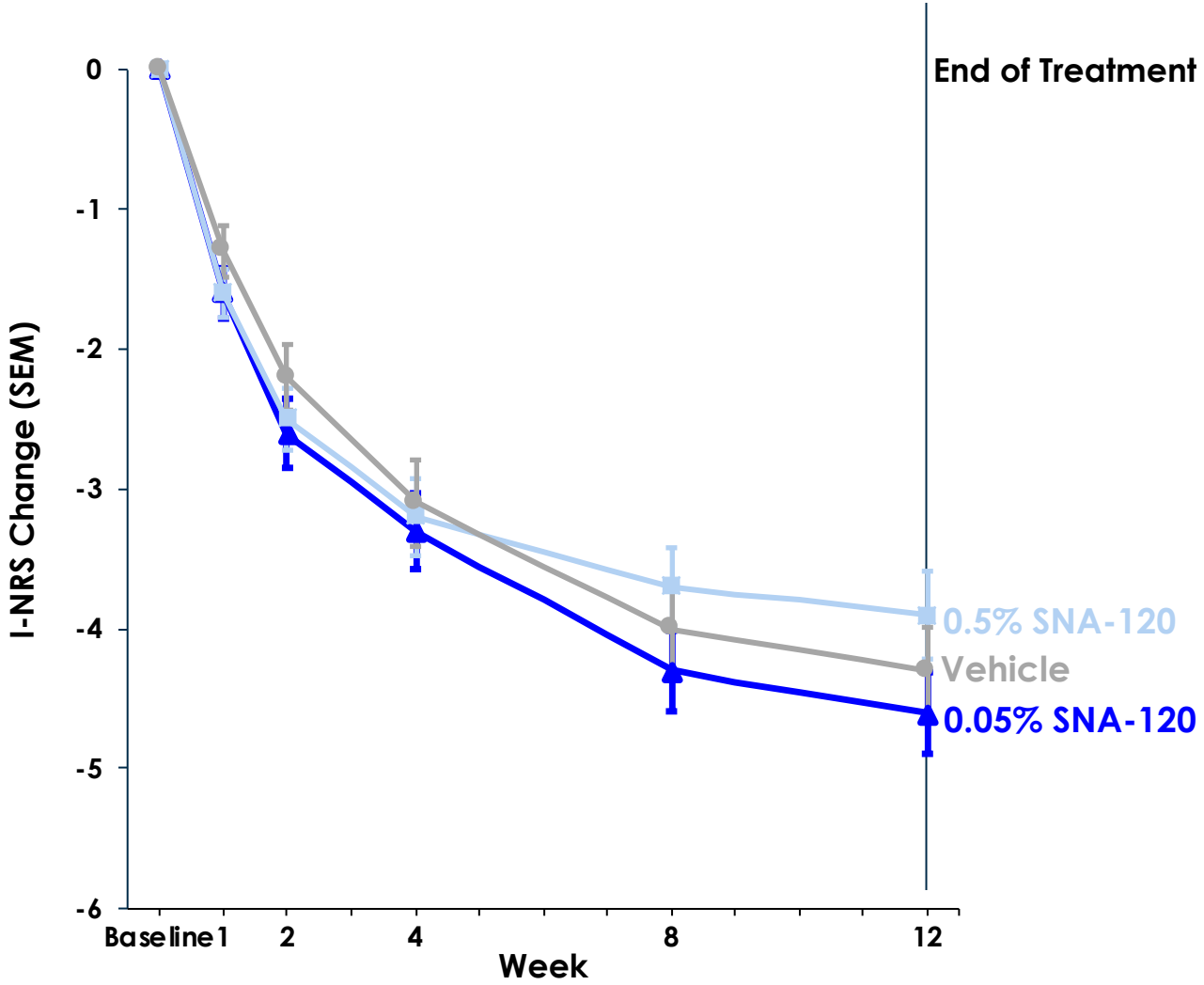
SNA-120 (0.05%) Reduced Pruritus Severity on I-NRS ~60% from Baseline[1]

Study SNA-120-201 Primary Endpoint		
Treatment Group	**SNA-120 (0.05%)**	**Vehicle**
I-NRS at Baseline (mean)	7.3	7.4
I-NRS Change at Week 8 (SD[2])	-4.3 (2.4)	-4.0 (2.6)



1. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.
2. SD = standard deviation

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SNA-120 Was Well-Tolerated with No Serious Treatment-Related Adverse Events (AEs)[1]

- Treatment-related AEs were observed in only 2 subjects and included dermatitis (0.5% group) and pain and pruritus (Vehicle group)
- Most common AEs (≥ 2 subjects) in any group were nasopharyngitis, nausea, diarrhea, cellulitis and urinary tract infection
- Majority of treatment-emergent AEs were mild to moderate
- There were 6 serious AEs in 3 subjects, but none were considered drug related

SNA-120 has been administered to 500+ subjects for up to 12 weeks, observed to be well-tolerated across all trials, with minimal to no demonstrable systemic exposure[2], further validating Topical by Design™ platform

1. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.
2. Excludes Study SNA-120-201, as data not yet available.

SNA-120: A Novel Topical Non-Steroidal Psoriasis Therapy

- Large commercial opportunity
- Clinically and statistically significant efficacy on FDA psoriasis primary endpoint for topicals in SNA-120-201 with n=70 per arm[1]
- Clear regulatory path
  - End-of-Phase 2 meeting with FDA requested for April 2019
  - Two pivotal Phase 3 trials (n~300 each), expected to start in 2H 2019
- Small focused team will execute on an FDA-agreed upon plan
- Significant upside with Topical by Design Platform in Dermatology, Gastroenterology, Ophthalmology and Respiratory

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1. Data on file, Sienna Biopharmaceuticals, Inc.: Study SNA-120-201.