13 October 2022

Positive BTX 1702 Phase 1b/2 Clinical Study for Rosacea

Key highlights

- **Positive data achieved from BTX 1702 Phase 1b/2 randomised, double blind, vehicle-controlled rosacea clinical study**
- **10% BTX 1702 dose showed statistically significant results in the FDA designated endpoint of reduction in inflammatory lesions when compared to vehicle**
- **Both the 10% and 20% BTX 1702 doses showed clinically meaningful results**
- **Efficacy for the BTX 1702 active arms continued to improve at each time point assessed**
- **No serious adverse events were observed**
- **Review of photo evidence from the clinical study demonstrates significant reduction of redness in target patients and reduction in visible lesions**

Philadelphia and Phoenix US, 13 October 2022: Clinical dermatology company, Botanix Pharmaceuticals Limited (ASX: BOT, "Botanix" or "the Company"), is pleased to announce positive data from its BTX 1702 Phase 1b/2 papulopustular rosacea clinical study ("the Study").

A summary of the Study design and endpoints is included in a presentation attached to this press release. A webinar to discuss the Study results will be held at 8am Perth time this morning and the *Zoom details are at the end of this release*.

The BTX 1702 10% gel dose of the study **achieved statistical significance in the FDA designated endpoint of reduction in inflammatory lesions (absolute reduction, p=0.02 and percentage reduction, p=0.03)** and also approached statistical significance for the investigator's global assessment "IGA for papules and pustules" (grade of 0 or 1 at day 57, p=0.059 and 2 grade improvement from baseline, p=0.059).

The BTX 1702 10% gel dose was also found to be very safe and well tolerated when compared to Permetrex™ vehicle (control) gel. The BTX 1702 20% dose was not superior to the 10% dose, but was safe and well tolerated and provides a significant safety margin for the target 10% dose. Efficacy of both the 10% and 20% BTX 1702 doses increased at each time point measured during the 8-week Study.

Botanix President and Executive Chair Vince Ippolito said*: "We are very pleased with the outcomes of this Study and the statistically significant performance of the 10% BTX 1702 synthetic CBD dose against the Permetrex™ vehicle alone.*

"Going into this Study, we wanted to push the dose of synthetic CBD to test the safety and efficacy boundaries in this serious form of rosacea and this has been successfully achieved. The outcomes show that the drug is safe at high doses, but also very effective at the lowest tested dose."

Study Design and Endpoints

The BTX 1702 Phase 1b/2 clinical study was a randomised, double blind, vehicle-controlled study in patients with moderate to severe papulopustular rosacea. The Study was designed to investigate the safety and tolerability of BTX 1702 in adults over an 8-week treatment period, with two different concentrations of BTX 1702 tested along with a vehicle (control) arm. The Study enrolled 133 patients in 16 dermatology clinical sites across Australia and New Zealand. Patients were randomised into 3 separate treatment groups consisting of BTX 1702 10% gel (n=45) applied twice daily, BTX 1702 20% gel (n = 45) applied twice daily and vehicle gel (control n= 43) applied twice daily. Patients aged 18 to 65 years old with moderate to severe papulopustular rosacea that met the relevant eligibility and inclusion criteria were enrolled in the Study with 84% of the patient population comprising females and 16% males.

The primary endpoints for the Study were safety and tolerability. Additionally, several exploratory efficacy endpoints were evaluated, including: absolute reduction and percent change, from baseline in inflammatory lesions; the proportion of patients achieving at least clear or almost clear, and a 2-grade improvement from baseline on the 5-grade Investigator's Global Assessment (IGA) scale and the change in the Clinician's Erythema Assessment (CEA) scale. Endpoints were assessed at baseline and completion of the 8-week treatment period (day 57) and for some endpoints, also at days 15 and 29 of the Study.

Study results

There were no serious adverse events observed during the Study and all arms (vehicle gel, 10% and 20% BTX 1702 gel) were safe and well tolerated. There were no serious adverse events and most adverse events that did occur, were localised and mild in nature. Patients enrolled in the 10% BTX 1702 arm experienced no burning and stinging, while patients enrolled in the vehicle and 20% BTX 1702 arms experienced some minor burning and stinging (less than 5%).

For the exploratory efficacy endpoints, both doses of BTX 1702 showed clinically positive results, with the 10% showing greater results, being statistically significant compared to vehicle, for reductions in inflammatory lesion counts and improvement in investigator's global assessment (IGA) endpoints. As outlined in the attached presentation, improvements were seen at each time point measured in the Study of the efficacy endpoints.

A summary of the exploratory efficacy endpoints at the end of 8 weeks (Day 57) is set out below in Table 1.

Exploratory Efficacy Endpoints – Full Analysis Set

	Vehicle (control)	10% BTX 1702	20% BTX 1702
Absolute reduction in inflammatory lesion count on Day 57	-12.8	-17.7 *(p=0.02)*	-16.9 *(p=0.04)*

Percentage reduction in inflammatory lesion count on Day 57	-26.3%	-44% *(p=0.03)*	-32.2% *(p=0.47)*
IGA Success (Grade of 0 or 1 on Day 57)	9.3%	24.4% *(p=0.059)*	22.2% *(p=0.09)*
IGA Success (2-point improvement on Day 57)	9.3%	24.4% *(p=0.059)*	24.4% *(p=0.059)*
Success as measured by a CEA grade of 0 or 1 on Day 57	15.4%	23.8% *(p=0.34)*	14% *(p=0.85)*
Success as measured by a 2-grade improvement of CEA grade at Day 57	15.4%	23.8% *(p=0.34)*	14% *(p=0.85)*

IGA = Investigator's Global Assessment scale (none, mild, moderate, severe)
CEA = Clinician's Erythema Assessment

Botanix medical adviser and former Chief Medical Officer of Medicis Pharmaceutical Corporation, Dr Ira Lawrence commented*: "To achieve this level of inflammatory lesion reduction and improvement in both IGA and CEA within 8 weeks is very exciting, particularly with such an excellent safety profile.*

"There is the potential for even greater efficacy if the treatment period is extended to 12 weeks duration, especially if the efficacy continues to improve, as it did at each time point assessed in this study, and could represent the possibility of best-in-class performance with BTX 1702."

Based on the results from the Study, the Company believes that the 10% BTX 1702 dose is the superior formulation with the most attractive safety and efficacy profile to take into further clinical development and has the potential to be the best-in-class treatment for papulopustular rosacea. The higher 20% BTX 1702 dose produced some safety and tolerability issues not seen in the 10% dose and the efficacy observed was not superior to the 10% BTX 1702 dose.

Available data from competitive products that have published efficacy outcomes after 8 weeks of treatment, suggests that 10% BTX 1702 is comparable in lesion reduction and IGA improvement at the same point in time, with a possible improvement in safety and tolerability.[1] Separately, the reduction in redness, as measured by the CEA outcome compares very favourably with products designed to reduce redness.[2]

[1] See Prescribing information for https://www.galderma.com/us/sites/default/files/2019-01/Soolantra_Cream_PI.pdf and https://www.galderma.com/us/sites/default/files/2022-03/Epsolay_PI.pdf as an example
[2] See Prescribing Information for https://www.rhofade.com/_assets/pdf/Rhofade-PI_201-11-13.pdf as an example

Rosacea market opportunity

The market for treatments for rosacea (including papulopustular) is expected to reach US$2.6 billion by 2025 and is growing at a CAGR of 6.8%.[3] Rosacea affects more than 430 million people worldwide and the global incidence among adults is estimated at 5.5% with the majority of patients consisting of women over the age of 35 years.[4] There are currently more than 16 million Americans affected by the illness with approximately 5 million medical treatment prescriptions in the US alone each year.[5]

There is currently a need for new rosacea treatments and BTX 1702 has the potential combine reduction in inflammatory lesions, antimicrobial effects and general improvement in skin condition in a single product.

Botanix will review the full data set for the Study once the final clinical study report is completed and the Company has had the opportunity to engage with the FDA on the development program.

1204A canine dermatitis pilot study complete

Botanix also confirms that the 1204A canine dermatitis pilot study has completed, and that an initial review of the data from the study suggests that a significant number of dogs enrolled in the study did not meet the specific inclusion criteria and as a result, the Company may not gain useful efficacy data from the study. The 1204A active arms appear to safe and well tolerated in the study and Botanix will continue to review the study, to establish if any additional insights are possible to be gained from this pilot study.

Valuable pipeline addition pending FDA approval for Sofpironium Bromide

The success of the BTX 1702 study significantly adds to the Botanix pipeline of dermatology products and with the recent submission of Sofpironium Bromide for FDA approval, helping to accelerate Botanix's transition to a revenue generating dermatology company.

Botanix has begun building its commercial capability and is preparing for the important mid-cycle review with FDA for Sofpironium Bromide which occurs 6 months after filing of the NDA. The Company continues to review other opportunities to further bolster its pipeline with additional late stage or revenue producing dermatology products, that can be acquired for modest cost and which contribute to profitability and value.

[3] Grand View research January 2019
[4] Gether L, et al. Br J Dermatol. 2018;179:282-289;
[5] National Rosacea Society. www.rosacea.org; and Symphony Health Solutions, PHAST

Zoom Call Details:

Oct 13, 2022 08:00 AM Perth time
Topic: BTX 1702 Rosacea Data Discussion

Please click the link below to join the webinar:
https://us02web.zoom.us/j/82793897592?pwd=U3dOKzJnU3BRL0pxNEpsM0xLcnhzdz09

Webinar ID: 827 9389 7592
Passcode: 764915
International numbers available: https://us02web.zoom.us/u/ksLhVY2Y5

Release authorised by

Vince Ippolito
President and Executive Chairman

About Botanix Pharmaceuticals

Botanix Pharmaceuticals Limited (ASX:BOT) is a dermatology company based in Philadelphia and Phoenix (US) which is committed to the development of novel treatments for a range of common skin diseases. The Company has a mature dermatology pipeline with its first product, Sofpironium Bromide, for the treatment of primary axillary hyperhidrosis, filed for FDA approval in Q3 CY2022 with approval expected in Q3 2023. The Company also has a pipeline of other products in late-stage clinical studies for the treatment of moderate to severe rosacea (successful Phase 1b/2 study in 4Q 2022), dermatitis and acne respectively. Botanix is also developing a topical antimicrobial product for the eradication of bacteria on the skin surface, initially in patients who are undergoing hemodialysis.

Botanix leverages its proprietary drug delivery system (Permetrex™) for direct skin delivery of active pharmaceuticals in all skin diseases, which is utilised in its existing development programs and is being explored with a view to being utilized in a number of other product opportunities. To learn more please visit: http://www.botanixpharma.com/

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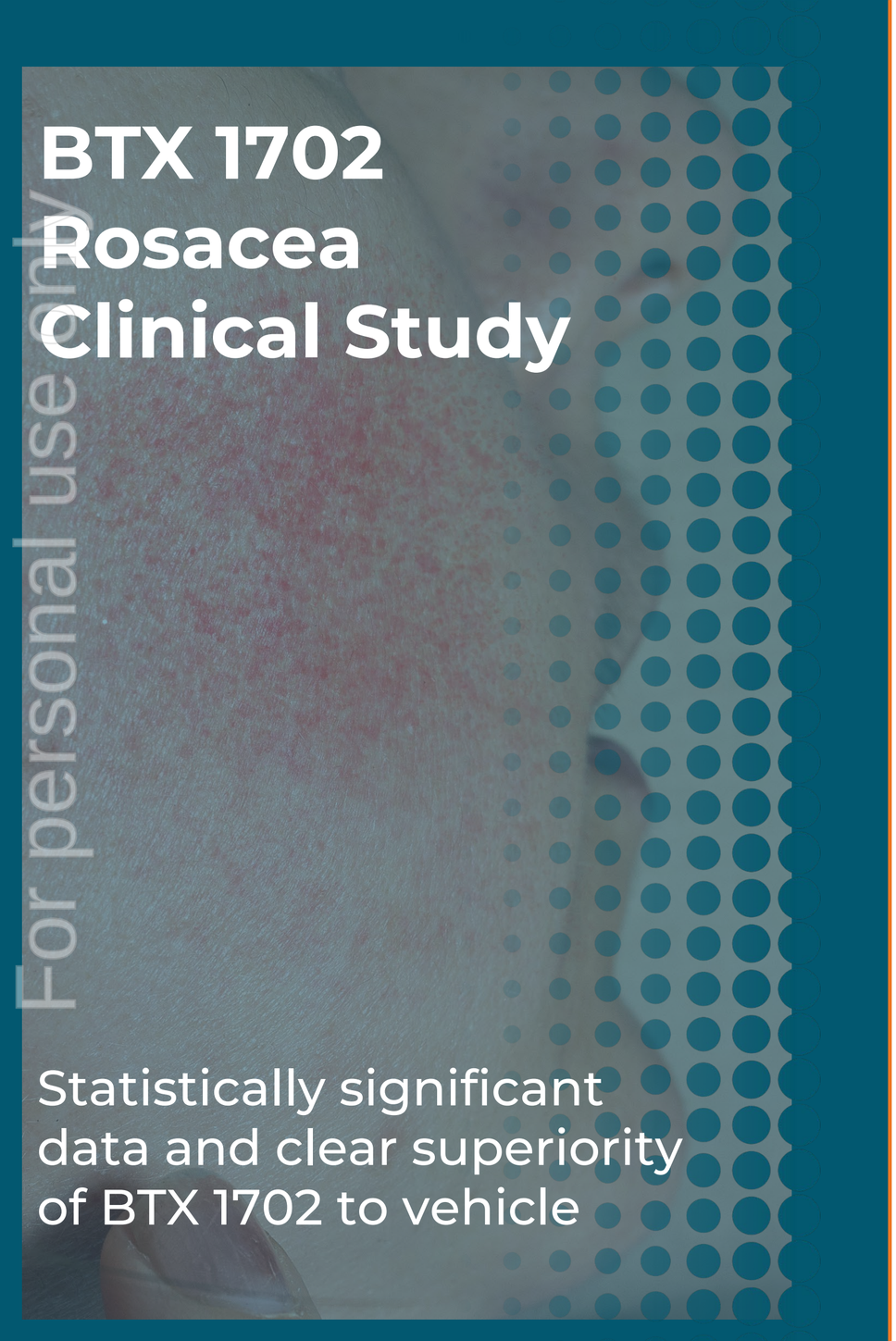
BTX 1702 Rosacea Clinical Data

October 2022

Successful Phase 1b/2 study

botanix

BTX 1702 Rosacea Clinical Study



Statistically significant data and clear superiority of BTX 1702 to vehicle

Positive Phase 1b/2 study

Randomised, double blind, controlled Phase 1b/2 clinical study in 133 subjects, with moderate to severe papulopustular rosacea

Safe and well tolerated

No serious adverse events in any arm of the study, with the 10% BTX 1702 active arm showing superior safety and tolerability

Clinically relevant improvements

Both 10% and 20% BTX 1702 active arms showed clinically meaningful improvements across all efficacy endpoints

Statistical significance

Improvements in reduction in inflammatory lesions was statistically significant for 10% target dose

Highlights Permetrex™ performance

Permetrex™ technology enabled formulation of very high doses and successful delivery into the skin for efficacy and safety results

BTX 1702: Rosacea Phase 1b/2 design and endpoints

Study Details
Three dose groups - 133 patients:

- BTX 1702 high dose - twice daily (BID): 45 patients
- BTX 1702 low dose - twice daily (BID): 45 patients
- Permetrex™ Vehicle - twice daily (BID): 43 patients

Sites: 16 dermatology sites across Australia and NZ

Patients: Adults (18 - 65 years) with moderate to severe papulopustular rosacea

Treatment Period: 8 weeks

Inclusion Criteria

- Moderate to severe papulopustular rosacea on the face
- At least 15 inflammatory lesions (papules/pustules)
- Rosacea severity of moderate (3) or severe (4) on a 5-point Investigator Global Assessment (IGA) scale
- Clinician's Erythema Assessment (CEA) scale of moderate (3) or severe (4)

Primary Endpoints

Safety and tolerability:

- Adverse events
- Cutaneous (Topical Application) Tolerability measures

Secondary Endpoints

- Percent change in inflammatory lesion counts (ILC) from baseline at days 15, 29 and 57
- Absolute change in inflammatory lesion counts (ILC) from baseline at days 15, 29 and 57
- Change in Investigator's Global Assessment (IGA) treatment success from baseline at days 29 and 57 (2-point change and number 'clear' or 'almost clear')
- Change in Clinician's Erythema Assessment (CEA) scale

Safety and Tolerability

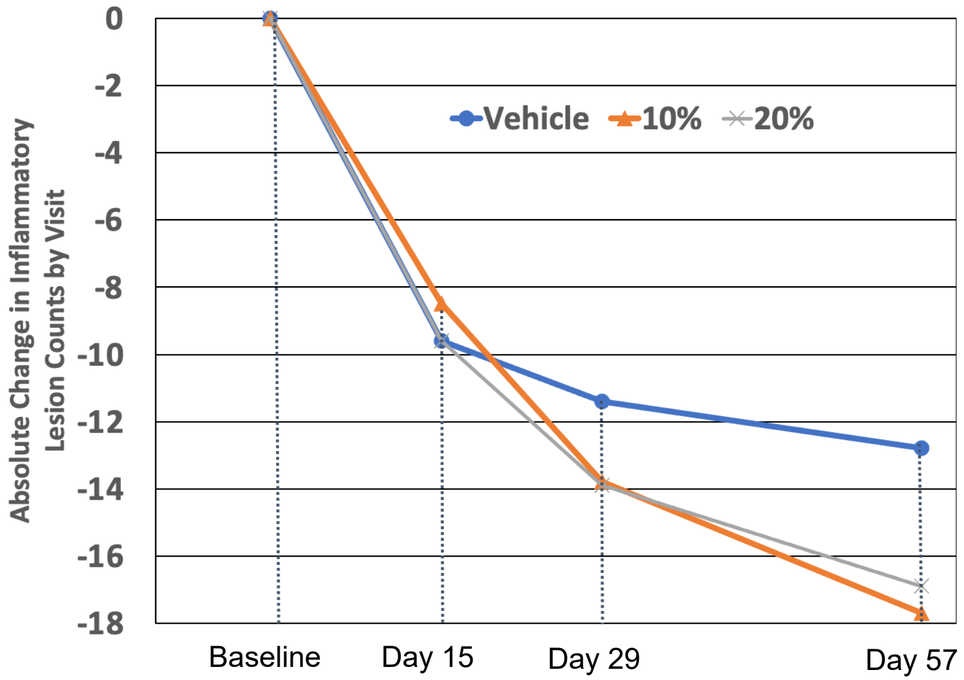
All doses of BTX 1702 were safe and very well tolerated

- All treatment arms (vehicle 10% and 20%) were very well tolerated
- No treatment related serious adverse events reported
- Most common (but not serious) adverse event was local to the application site
- Patients in the 10% BTX 1702 arm reported no burning or stinging whatsoever, with only 5% in the 20% arm reporting minor burning and stinging

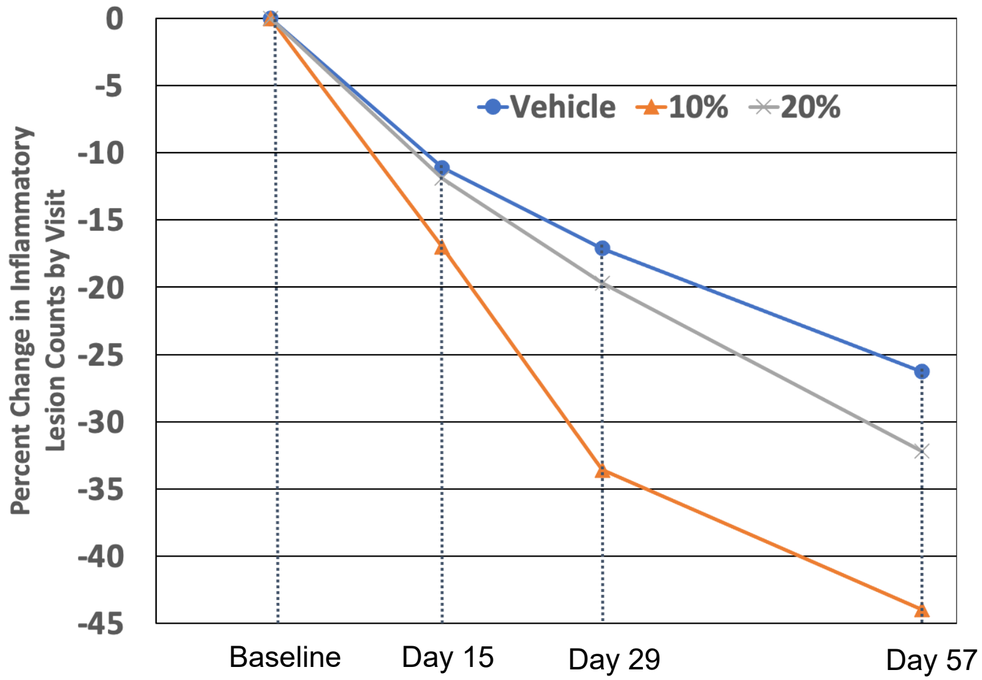
Efficacy endpoint – change in inflammatory lesion count (ILC)

Clinically meaningful results with 10% BTX 1702 also statistically significant

Absolute Change in Inflammatory Lesion Counts (ILC) by Visit



Percentage Change in Inflammatory Lesion Counts (ILC) by Visit

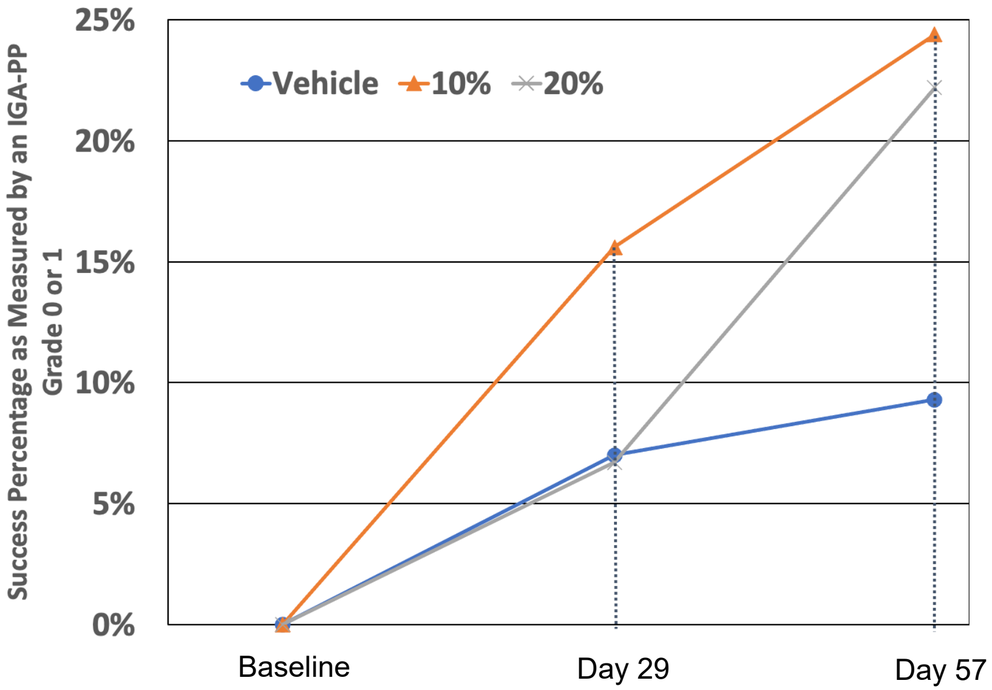


When compared to vehicle, the 10% BTX 1702 formulation showed statistically significant reductions in both the absolute (p=0.02) and percent (p=0.03) changes in inflammatory lesion counts

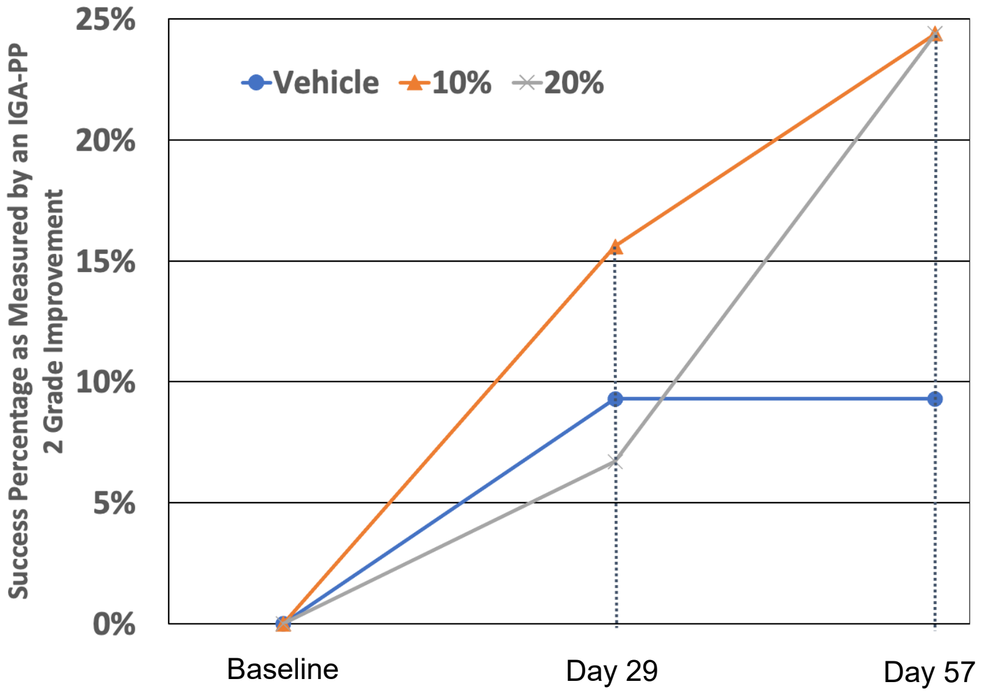
Efficacy endpoint – Investigators Global Assessment for papules and pustules (IGA-PP)

Clinically meaningful improvement in all BTX 1702 active arms

Success (%) as Measured by an IGA-PP* Grade of 0 or 1



Success (%) as Measured by an IGA-PP* 2 Grade Improvement



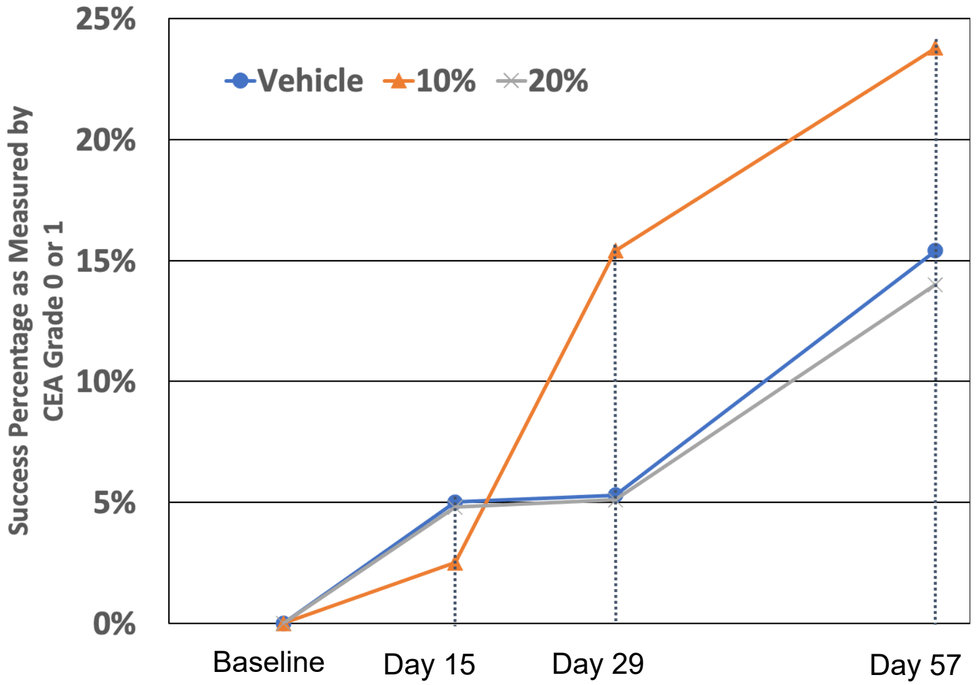
IGA-PP scale is 0 – clear, 1 – almost clear, 2 – Mild, 3 – Moderate, 4 - Severe

Both the 10% and 20% BTX 1702 formulations showed clinically meaningful reductions in IGA-PP compared to vehicle

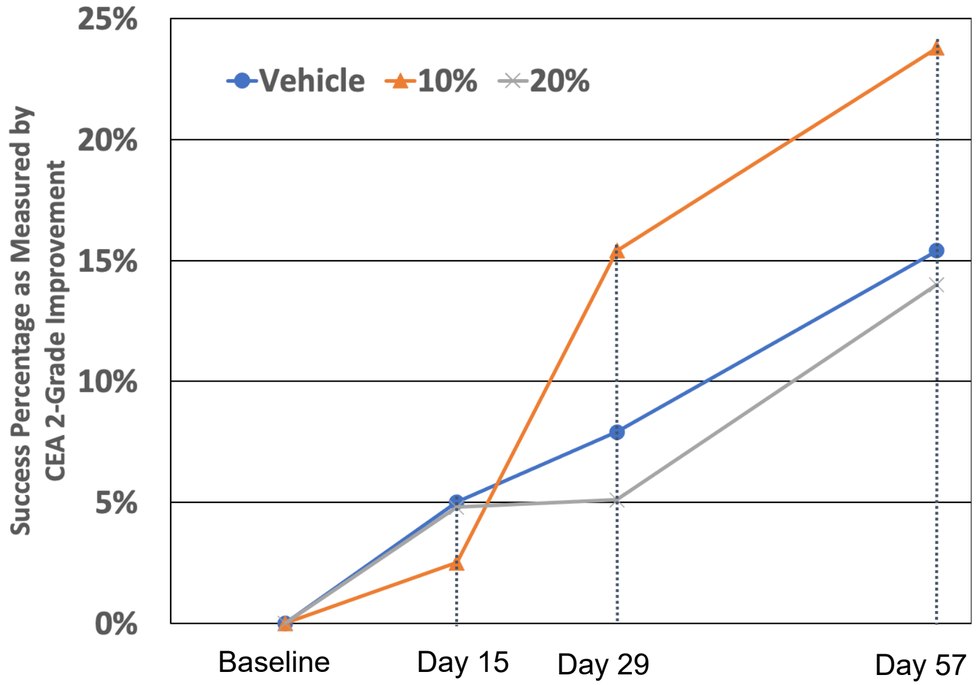
Efficacy endpoint – change in Clinician's Erythema Assessment (CEA)

Clinically meaningful results with strong trend for 10% BTX 1702

Success (%) as Measured by an CEA Grade of 0 or 1 Visit Day v Baseline



Success (%) as Measured by a 2-Grade Improvement CEA Grade Visit Day v Baseline

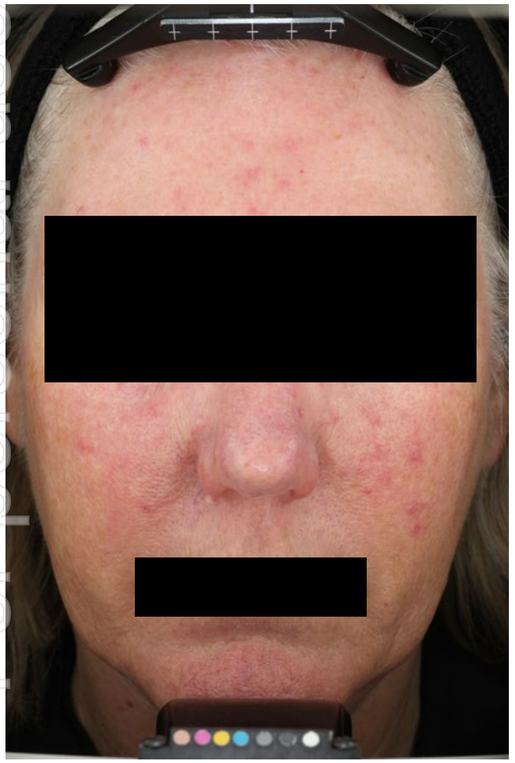


CEA scale is 0 – clear, 1 – almost clear, 2 – Mild , 3 – Moderate, 4 – Severe

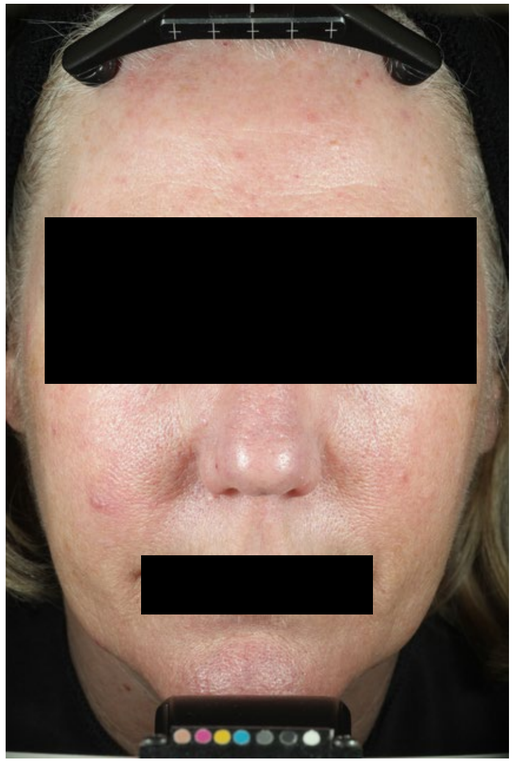
The 10% BTX 1702 formulation showed clinically meaningful reductions in CEA compared to vehicle

Example patient images from Canfield image capture technology

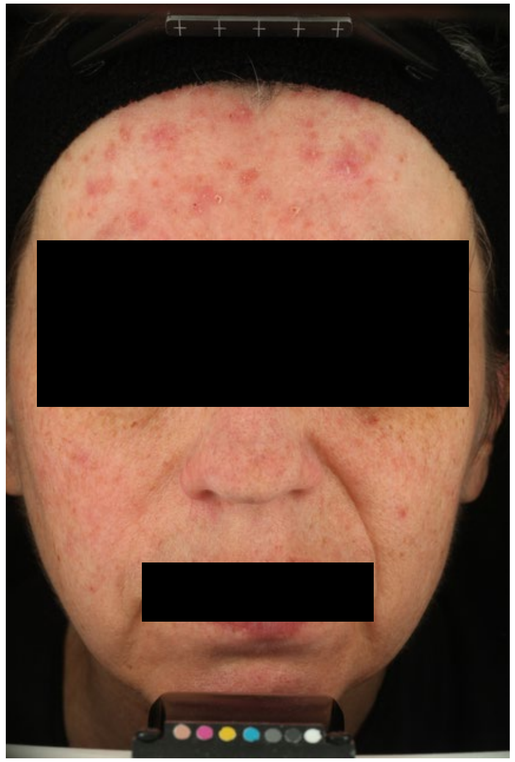
Clear visual improvements and key tool for future studies



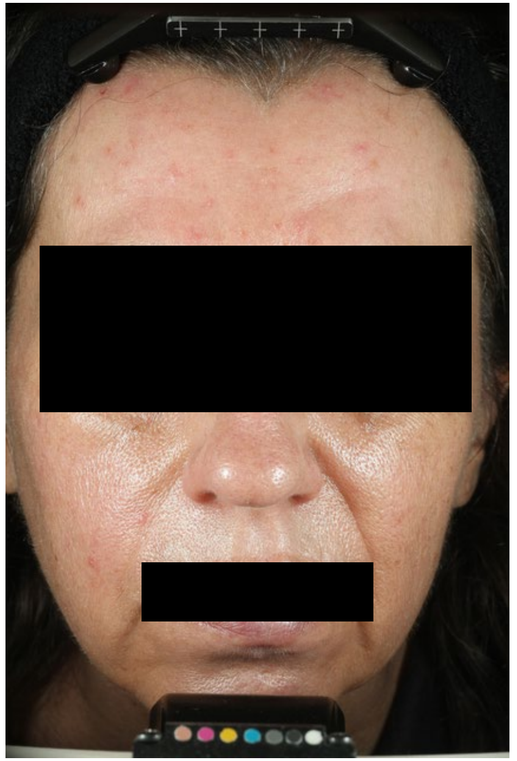
Baseline



Day 57



Baseline



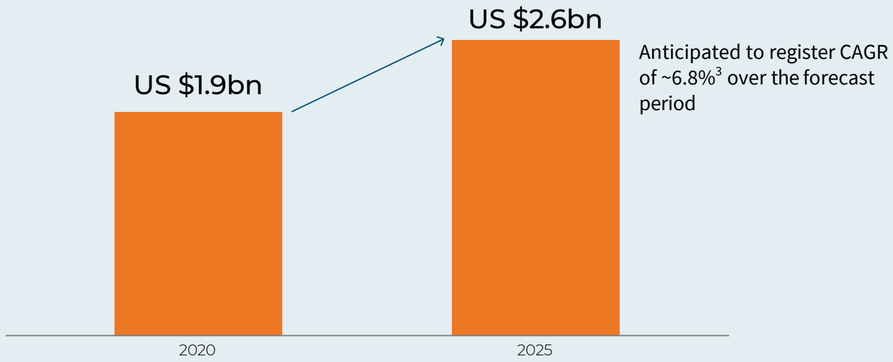
Day 57

Reduction in inflammatory lesions and improvements in redness, shown for moderate and severe patient examples

BTX 1702: high impact of rosacea on patients and significant market opportunity

- Papulopustular rosacea is a highly visible chronic skin disease characterised by redness (inflammation) and acne-like-break- outs[1]
- Patients diagnosed with Rosacea tend to have higher incidences[2] of:
  - Depression
  - Social Anxiety
  - Embarrassment
  - Decreased quality of life

A rapidly growing market:
Rosacea market projected to grow to US$2.6bn by 2025[3]



- Affects ~5.5% of the global population[4], ~430m individuals , women are more likely to be affected than men
- 85% of patients are > 30 years old[5]
- Currently over 16m Americans affected[6] by rosacea, with ~5m medical treatment prescriptions[7] in the US alone
- Active treatment seekers looking for new solution to rosacea

1. Blount BW, Pelletier AL. Am Fam Physician. 2002;66:435-440.; 2. Moustafa F. J Am Acad Dermatol. 2014;71:973-980; 3. Grandview Research. www.Grandview research.com; 4. Gether L, et al. Br J Dermatol. 2018;179:282-289; 5. Aimee Two, et al, JAAD, Volume 72, Issue 5, May 2015; 6. National Rosacea Society. www. rosacea.org; 7. Symphony Health Solutions, PHAST

Summary

10% BTX 1702 dose showed excellent safety and efficacy outcomes

Outstanding results

Both BTX 1702 arms showed clinically meaningful, and in some cases, statistically significant results

10% BTX 1702 dose to be progressed

Efficacy and safety of the 10% dose achieved and demonstrated safety margin provided by the higher 20% dose

Validates synthetic CBD platform

Choice to test higher doses than in previous studies validated with improved efficacy versus vehicle and no new safety signals

Efficacy is improving at all time points

Potential for further efficacy improvements with longer treatment period

Opens up pathway for acne program

Rosacea outcomes in similar disease opens up higher dose options for pivotal acne studies

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