



# TNT Bio, Inc.

## Business Case Competition

### Team Houston

Collin Johnson - Ph.D. Candidate at BCM

Anton Zhang Ph.D. - Postdoc at Rice University

# TEAM MEMBERS



## Collin Johnson

- ❖ Ph.D. Candidate in Translational Biology & Molecular Medicine
- ❖ Innovation consulting fellow for local non-profit organization (Enventure)
- ❖ Aspiring fiction writer and diligent tennis player

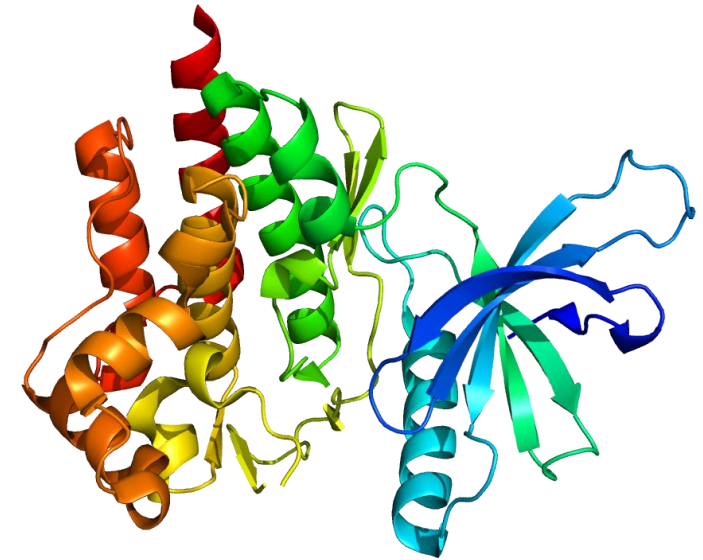


## ZiAng (Anton) Zhang

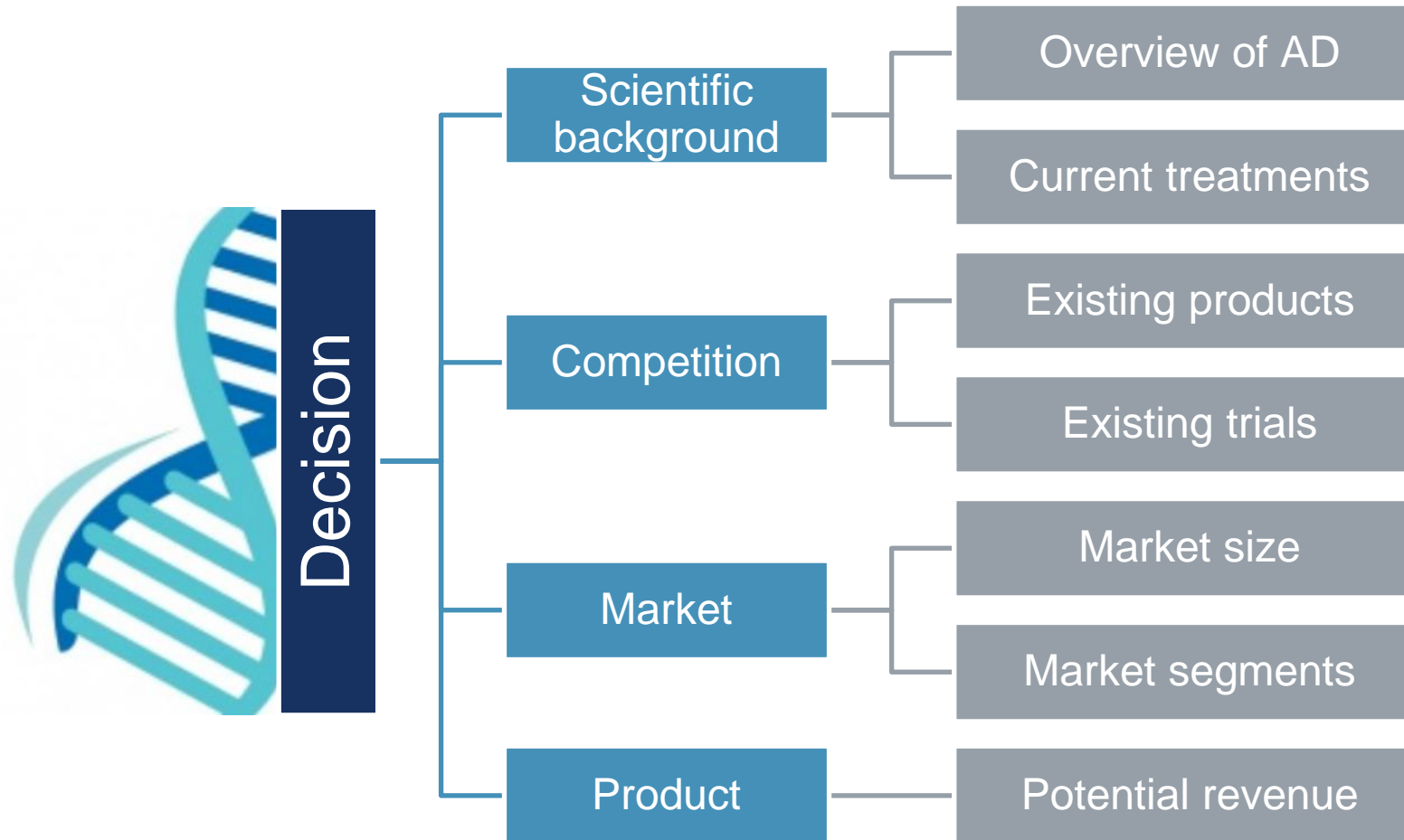
- ❖ Ph.D. in Materials Science, Rice University 2016
- ❖ Tech entrepreneur, co-founder of *Farmin*
- ❖ AVP Education, Consulting Club at the Texas Medical Center
- ❖ Avid reader

# EXECUTIVE SUMMARY

- **Recommendation:**
  - Prioritize TNT-002, the topical TYK2 inhibitor
- **Rationale:**
  - Stronger scientific innovativeness
  - Larger potential market
  - Easier barrier to entry



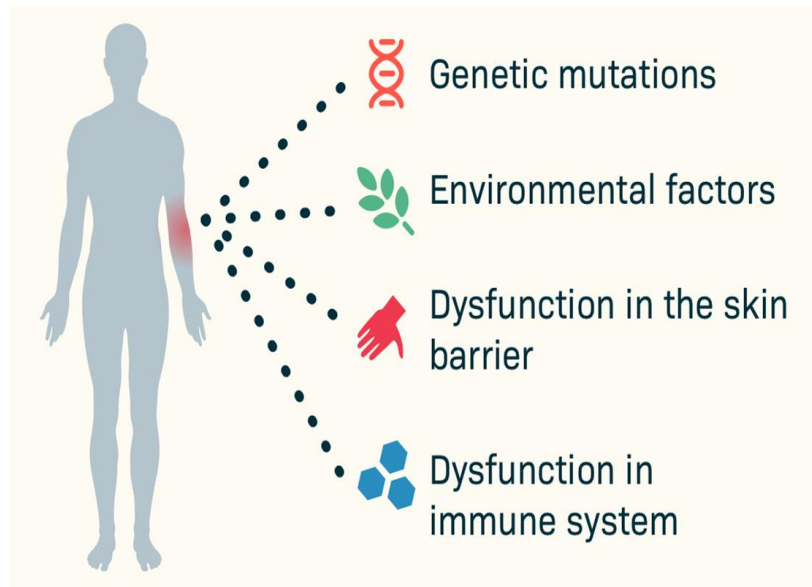
# FRAMEWORK



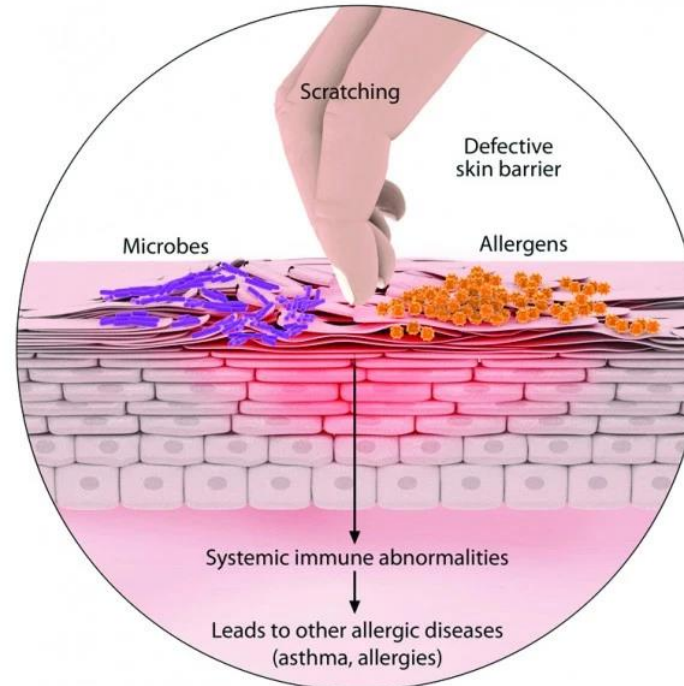


# SCIENTIFIC BACKGROUND - JAK-STAT signaling in AD

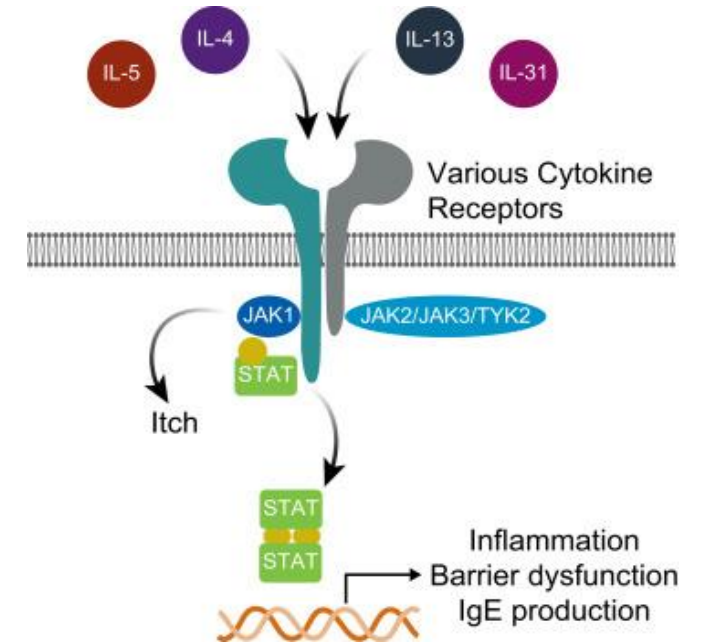
## Causes of Atopic Dermatitis:



## Skin Barrier Dysfunction



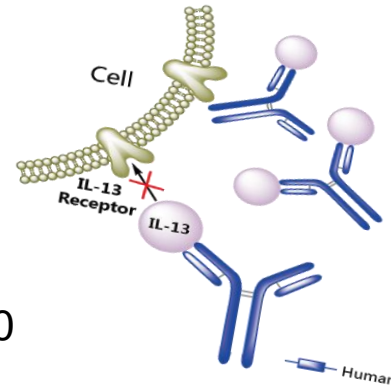
## Elevated immune signaling



# Disadvantage of TNT-013 – IL-13 Monoclonal Therapy

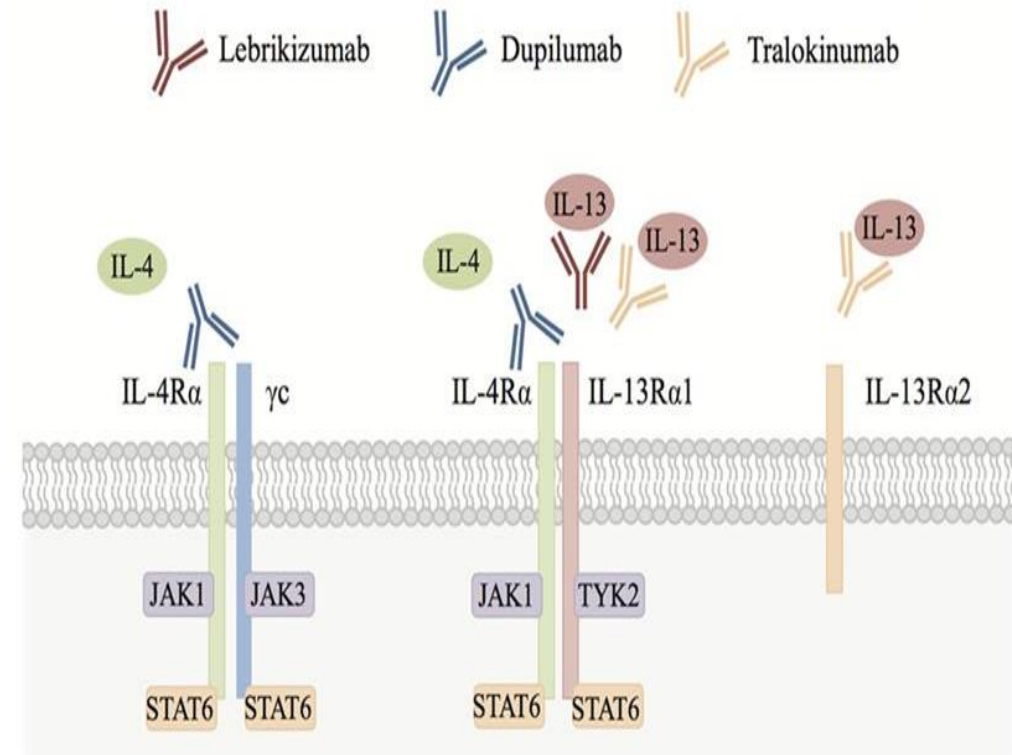
## Dupilumab Phase 4 Study (DRS)

- matured, state-of-the-art care
- Sponsor: Northwestern University
- Primary completion date: March 31, 2020



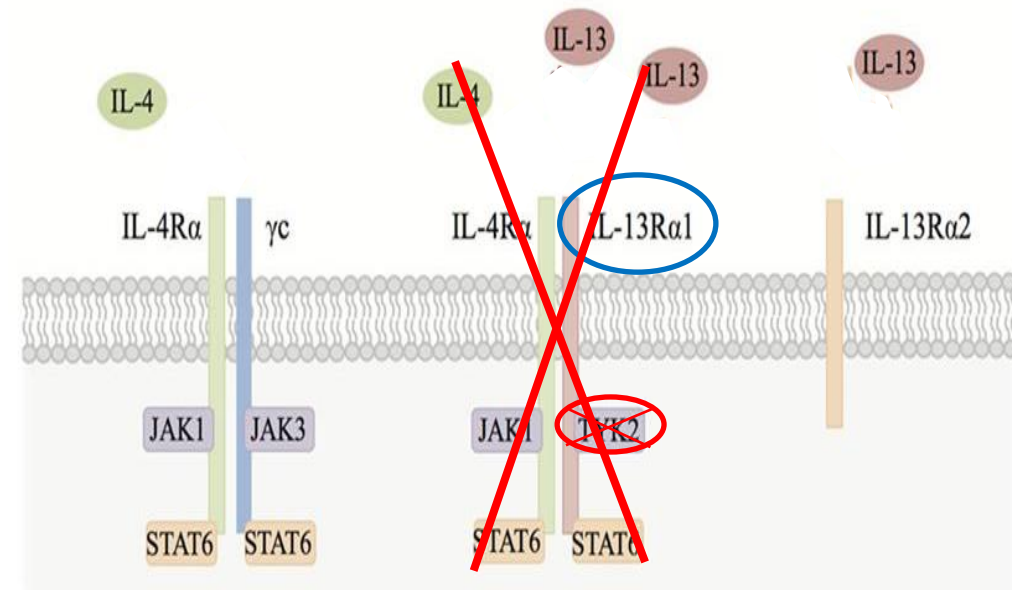
## Tralokinumab Phase 3 in Combination With Topical Corticosteroids for Moderate to Severe Atopic Dermatitis

- Sponsor: LEO Pharma (licensing by AstraZeneca)
- Recruitment Status: Completed
- First Posted: December 6, 2017
- Last Update Posted: January 29, 2020
- ❖ *3rd Pivotal Study*



# Advantage of TNT-002 – TYK2 Inhibitor

- TYK2 is expressed ubiquitously & specifically is associated with the **IL-13 Receptor**
- Topical application provides a localized immune shutdown and directly address barrier dysfunction
- TYK2 deficiency does not lead to pathology in mice under conventional housing conditions; in contrast:
  - Lack of JAK1 and JAK2 associated with lethality
  - Lack of JAK3 associated with severe combined immunodeficiency (SCID)
- JAK inhibitors work faster than biologics
- Good bio-availability; lack of systemic immunogenicity
- ❖ “Oral, Selective TYK2 Inhibitor Delivered Significant Skin Clearance in Patients with Moderate to Severe Plaque Psoriasis in Phase 2 Trial”



# COMPETITION

## Competitions for TNT-013 (sub-Q monoclonal antibody)

Target IL-13 specifically

- Tralokinumab (Phase 3)
- Lebrikizumab (Phase 3)

Target IL-4 and IL-13

- Dupilumab (Approved)

Target IL-12/IL-17/IL-22/IL-31

- Ustekinumab (Phase 3)
- CIM 331 (Phase 3)
- ILV-094 (Phase 2)
- Secukinumab (Phase 2)

## Competitions for TNT-002 (Topical TYK2 inhibitor)

Target TYK2 specifically

- N/A

Target JAKs including TYK2

- Delgocitinib (Approved in Japan)
- Tofacitinib (Phase 2)
- Ruxolitinib (Phase 2)

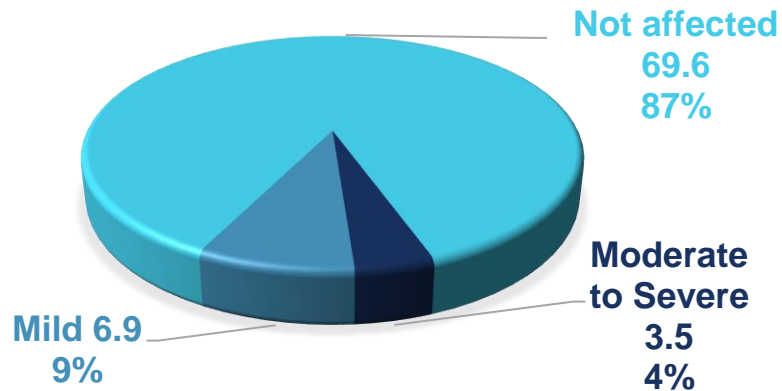
Target JAK1/JAK2/JAK3

- Baricitinab (Phase 3)
- PF-04965842 (Phase 3)

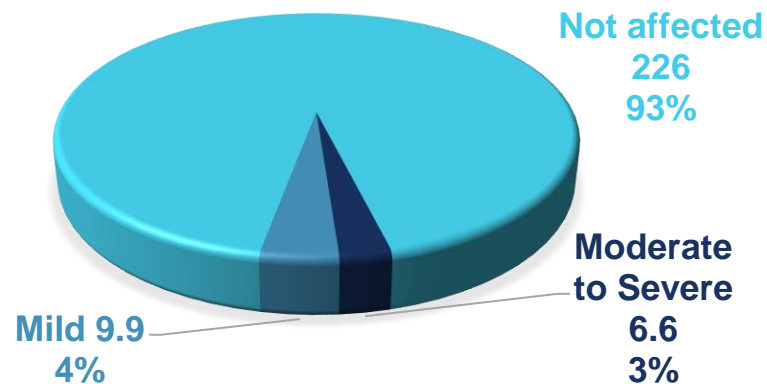


# MARKET SIZE

AD IN CHILDREN (MILLION)

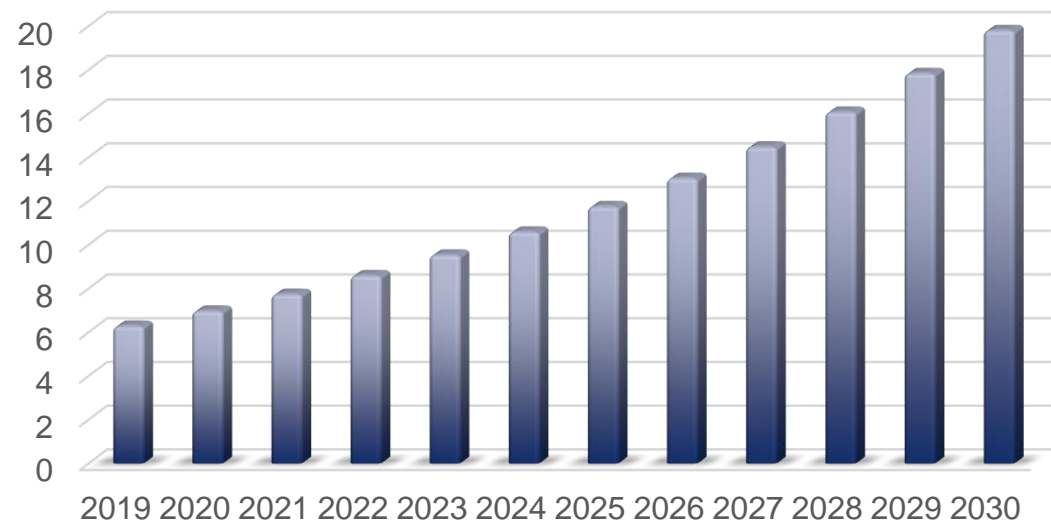


AD IN ADULT (MILLION)



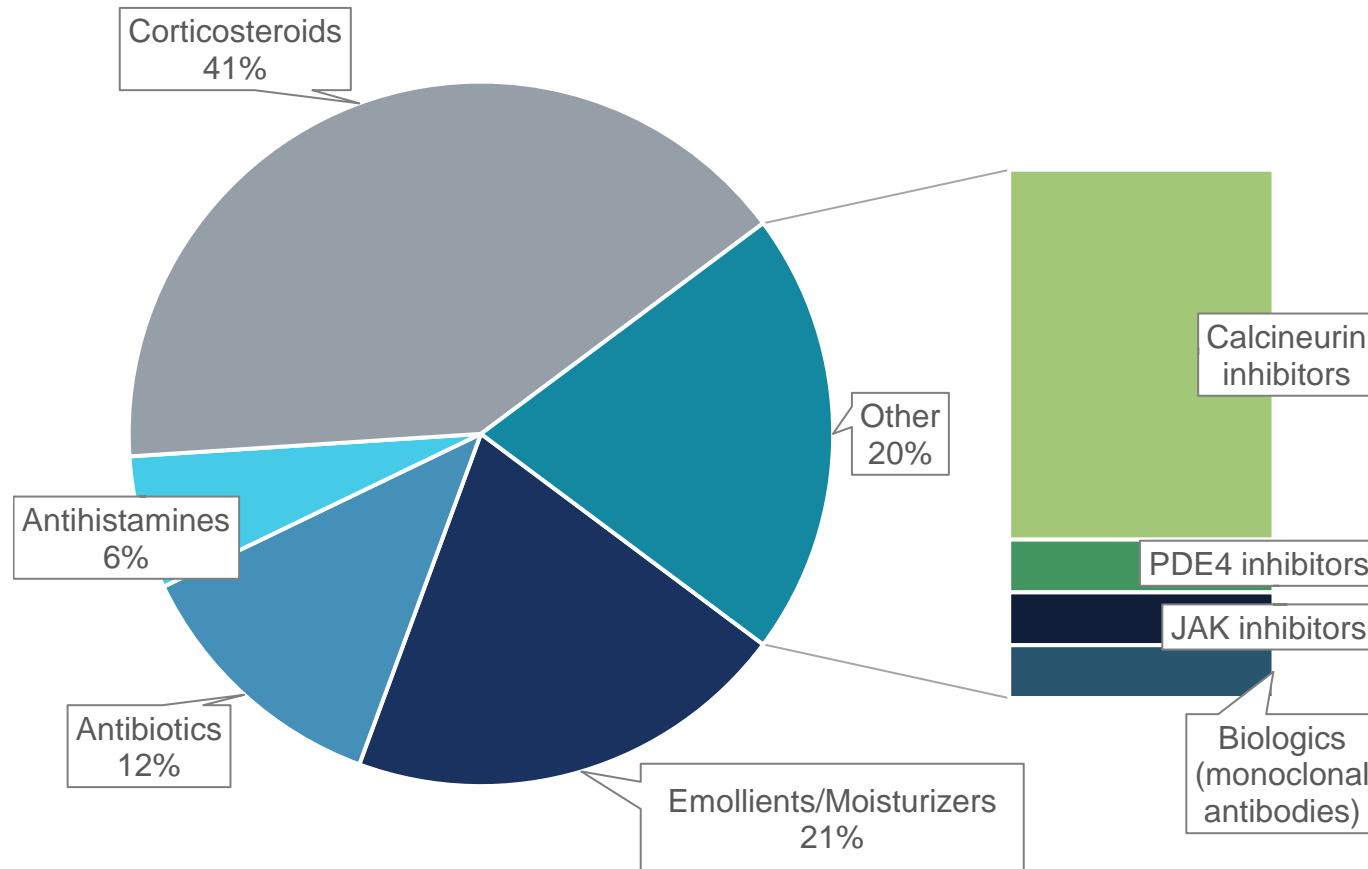
- Total US headcount (2018): 10.4 (children) + 16.5 (adult) = 27 million
  - Patient CAGR projected from 2017: ~2.5%
- Total US market size (2019): 6.3 billion
  - Market CAGR projected from 2017: 11.1%

Total US Market (billion USD)



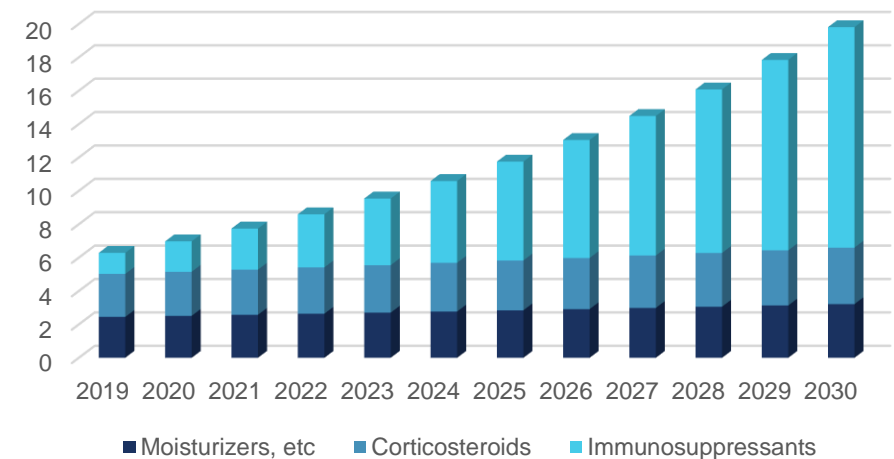
# MARKET SEGMENTS

Market share by treatment method (2018)



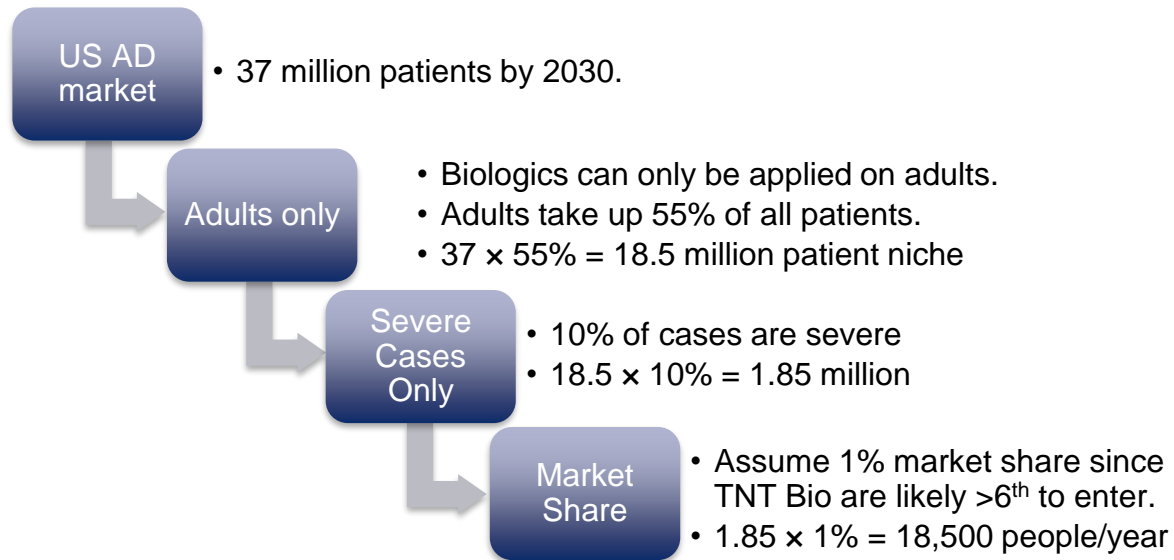
- Total markets will be \$11.8 billion by 2025 and \$19.8 billion by 2030
- The market for immunosuppressants will reach \$5.9 and \$13.2 billion, respectively

US market segments (billion USD)

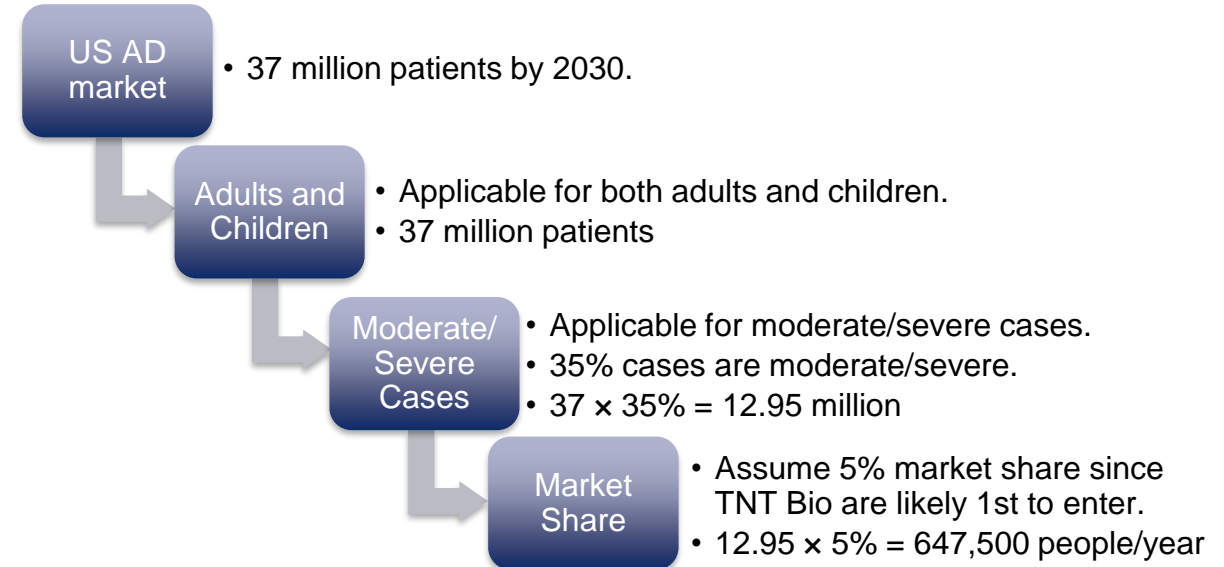


# POTENTIAL REVENUE

## Revenue analysis of 2030 for TNT-013 (sub-Q monoclonal antibody)



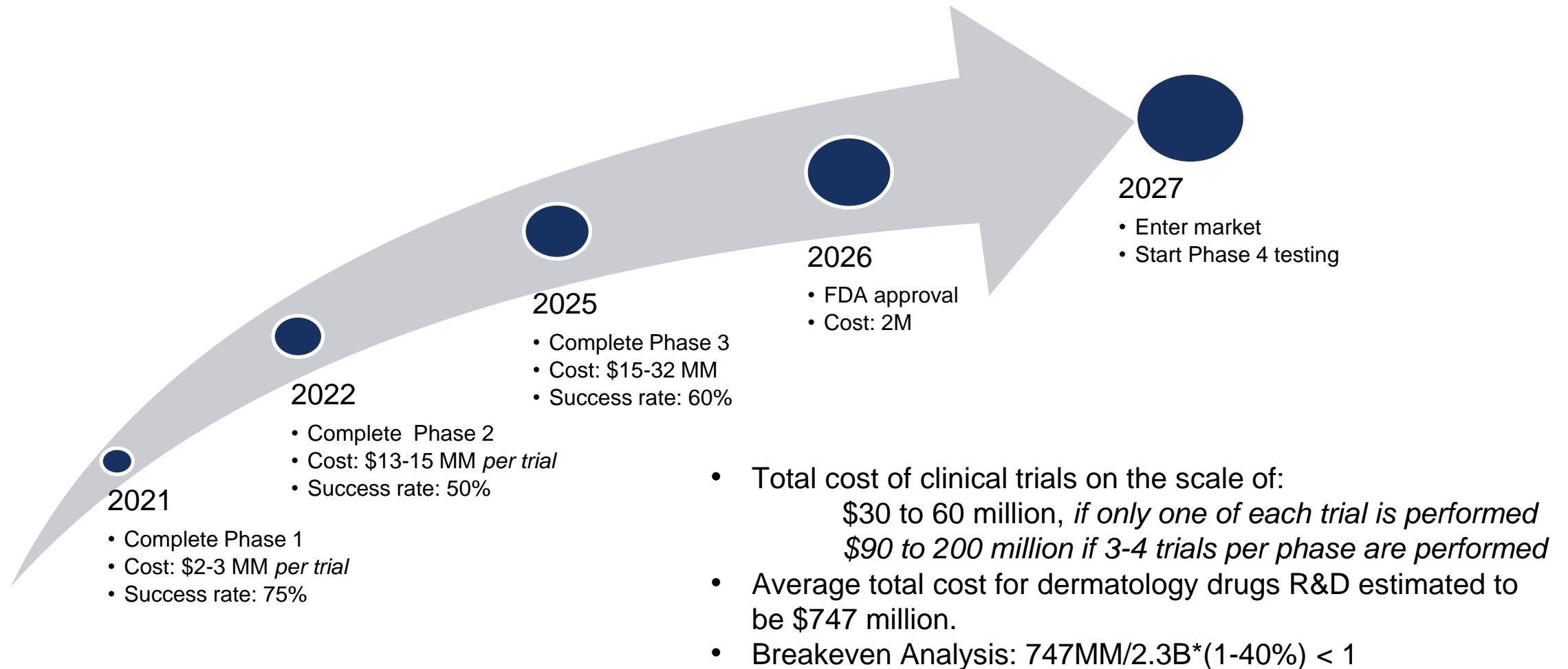
## Revenue analysis of 2030 for TNT-002 (topical TYK2 inhibitor)



- Typical price of biologics (Dupilumab): \$37,000 /year /patient
- Revenue for TNT-013:  $18500 \times 37000 = \$0.7$  billion USD

- Typical price of immunosuppressant (Pimecrolimus, a calcineurin inhibitor): \$3,600 /year /patient
- **Revenue for TNT-002:  $647,500 \times 3,600 = \$2.3$  billion USD**

# PRODUCT TIMELINE





# SWOT Analysis

S

Innovative technology  
Only topical for moderate/severe  
Only TYK2 inhibitor  
Faster than biologics  
Low side effects

W

Still in Phase 1  
Long term side effects uncertain

O

Growing market  
Insurance willingness to cover  
Recognition in the medical community  
Joint usage with other drugs/treatments

T

Other solutions potentially being developed  
Changes in regulations

# CONCLUSION

- **Recommendation:**
  - Prioritize TNT-002, the topical TYK2 inhibitor
- **Next steps:**
  - Pricing strategy
  - Reimbursement strategy
  - Sales/marketing strategy



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# Thank you for your attention.

Team Houston — Collin Johnson & Anton Zhang Ph.D.



# REFERENCES

## Clinical Trials:

- AstraZeneca (Tralokinumab) P3 trial in Asthma: <https://clinicaltrials.gov/ct2/show/NCT02161757>
- LeoPharma (Tralokinumab) P3 trial in AD: <https://clinicaltrials.gov/ct2/show/NCT03363854>
- Dermira, Inc (Lebrikizumab) P3 trial in AD: <https://clinicaltrials.gov/ct2/show/NCT04146363>
- Northwestern University (Dupilumab) P4 in AD: <https://clinicaltrials.gov/ct2/show/NCT03411837?cond=dupilumab&draw=2&rank=1>

## Atopic Dermatitis disease state literature:

- [https://www.jidonline.org/article/S0022-202X\(19\)30007-7/fulltext](https://www.jidonline.org/article/S0022-202X(19)30007-7/fulltext)
- Mueller et al., Biochim Biophys Acta, 2002
- Damsky et. al., J Am Acad Dermatol, 2017
- Ciechanowicz et. al., J Dermatolog Treat., 2019
- Leitner et. al., Cytokine, 2017
- Neubauer et. al., Cell, 1998
- Pesu et al., Immunol Review, 2005
- O'Shea et al., Nat Rev Drug Discov, 2004

## Estimates for Dermatology R&D:

- <https://www.biopharmadive.com/news/new-drug-cost-research-development-market-jama-study/573381/>



# REFERENCES – cont'd

## **Systemic Treatment of Adult Atopic Dermatitis: A Review**

■ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5336433/>

## **Dermatitis Drugs Market**

■ <https://www.fortunebusinessinsights.com/industry-reports/dermatitis-drugs-market-100658>

## **Atopic Dermatitis Drugs Market**

■ <https://www.grandviewresearch.com/industry-analysis/atopic-dermatitis-drugs-market>

## **Adult Dermatitis in America - an Overview**

■ <https://www.aafa.org/media/2209/Atopic-Dermatitis-in-America-Study-Overview.pdf>

## **Therapeutic pipeline for atopic dermatitis: End of the drought?**

■ [https://www.jacionline.org/article/S0091-6749\(17\)31199-5/pdf](https://www.jacionline.org/article/S0091-6749(17)31199-5/pdf)

## **Pharma's first-to-market advantage**

■ <https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/pharmas-first-to-market-advantage>

## **Global Atopic Dermatitis Treatment Market \$10.7 Billion by 2027**

■ <https://www.ihealthcareanalyst.com/global-atopic-dermatitis-treatment-market/>

## **DUPIXENT MAY BE RIGHT FOR YOU**

■ <https://www.dupixent.com/atopicdermatitis>

## **Calcineurin Inhibitors: 40 Years Later, Can't Live Without ...**

■ <https://www.jimmunol.org/content/191/12/5785>

## **Round 1: Biologics, JAK inhibitors training up for atopic dermatitis 'boxing match'**

■ <https://www.mdedge.com/dermatology/article/204315/atopic-dermatitis/round-1-biologics-jak-inhibitors-training-atopic>

## **Newer treatments of psoriasis regarding IL-23 inhibitors, phosphodiesterase 4 inhibitors, and Janus kinase inhibitors**

■ <https://onlinelibrary.wiley.com/doi/full/10.1111/dth.12555>

## **Atopic Dermatitis: Global Drug Forecast and Market Analysis to 2027**

■ <https://store.globaldata.com/report/gdhc172pidr--atopic-dermatitis-global-drug-forecast-and-market-analysis-to-2027/>

## **The price of innovation: new estimates of drug development costs**

■ [https://simon.rochester.edu/faculty\\_research\\_pdf/ron.hansen/intellcont/Price%20of%20Innovation-1.pdf](https://simon.rochester.edu/faculty_research_pdf/ron.hansen/intellcont/Price%20of%20Innovation-1.pdf)

# Supplemental: Clinical Trial Cost Analysis

ID	Phase	# Enrolled Patients	Indication	Target	Administration Type	Cost of Trial*
Bristol-Myers	2	267	moderate-to-severe	TYK2	Oral	13,350,000
Tofacitinib (Pfizer)	2	69	mild to moderate	JAK1/3	Topical	3,450,000
Ruxolitinib (Incyte Corp)	1	41	mild to moderate	JAK1/2	Topical	2,050,000
Ruxolitinib (Incyte Corp)	1	60	mild to moderate	JAK1/2	Topical	3,000,000
Ruxolitinib (Incyte Corp)	2	307	mild to moderate	JAK1/2	Topical	15,350,000
Ruxolitinib (Incyte Corp)	3	618	mild to moderate	JAK1/2	Topical	30,900,000
Baricitinib (Eli Lilly & Co.)	3	300	moderate-to-severe	JAK1/2	Oral	15,000,000
Baricitinib (Eli Lilly & Co.)	3	615	moderate-to-severe	JAK1/2	Oral	30,750,000
Baricitinib (Eli Lilly & Co.)	3	465	moderate-to-severe	JAK1/2	Oral	23,250,000
Baricitinib (Eli Lilly & Co.)	3	624	moderate-to-severe	JAK1/2	Oral	31,200,000
Baricitinib (Eli Lilly & Co.)	3	450	moderate-to-severe	JAK1/2	Oral	22,500,000
Lebrikizumab (Dermira, Inc.)	2	400	moderate-to-severe	Biologic	Subcutaneous	20,000,000
Tralokinumab Phase 3 Trial	3	380	moderate-to-severe	Biologic	Subcutaneous	19,000,000
Dupilumab (Northwestern University)	4	500	moderate-to-severe	Biologic	Subcutaneous	25,000,000

\*Cost based on assumption of \$50,000 spendings per patient enrolled

# Supplemental: AD Clinical Trials

**TABLE I.** Recent controlled trials in patients with AD

Agent	Trade name	Target	Drug	Phase	Manufacturer	ClinicalTrials.gov
Dupilumab		IL-4R $\alpha$	Anti-IL-4R $\alpha$ mAb	Phase III published	Regeneron, Tarrytown, NY	NCT02277743 NCT02277769
Crisaborole		PDE4	Topical PDE4 Inhibitor	Phase III published	Pfizer, New York, NY	NCT02118766 NCT02118792
Ustekinumab	Stelara	IL-12/23p40	Anti-p40 mAb	Phase II published	Janssen, Titusville, NJ	NCT01806662
Tralokinumab		IL-13	Anti-IL-13 mAb	Phase II completed	MedImmune, Gaithersburg, Md	NCT02347176
Tofacitinib		JAK1/3	Topical JAK1/3 Inhibitor	Phase II published	Innovaderm, Montreal, Quebec, Canada	NCT02001181
Lebrikizumab		IL-13	Anti-IL-13 mAb	Phase II completed	Hoffmann-La Roche, Basel, Switzerland	NCT02340234
CIM331/ Nemolizumab		IL-31R	Anti-IL-31R mAb	Phase II completed	Chugai, Tokyo, Japan	NCT01986933
QGE031		IgE	Anti-IgE mAb	Phase II completed	Novartis, Basel, Switzerland	NCT01552629
Apremilast	Otezla	PDE4	PDE4 inhibitor: oral small molecule	Phase II completed	Celgene, Summit, NJ	NCT02087943
QAW039/ Fevipiprant		CRTH2	CRTH2 inhibitor: oral small molecule	Phase II completed	Novartis	NCT01785602
ILV-094		IL-22	Anti-IL-22 mAb	In Phase II	Pfizer	NCT01941537
GBR830		OX40	Anti-OX40 mAb	In Phase II	Glenmark, Mumbai, India	NCT02683928
Secukinumab	Cosentyx	IL-17	Anti-IL-17 mAb	In phase II	Novartis	NCT02594098
OC000459		CRTH2	CRTH2 Inhibitor: oral small molecule	In phase II	Atopix, Chiesi, Parma, Italy	NCT02002208
Baricitinib		JAK1/2	Jak1/2 inhibitor: oral small molecule	In phase II	Eli Lilly, Indianapolis, Ind	NCT02576938
PF-04965842		JAK1/2	Jak1/2 inhibitor: oral small molecule	In phase II	Pfizer	NCT02780167
ZPL389		H4R	Histamine H4 receptor inhibitor: oral small molecule	Phase II completed	Ziarco Pharma, Canterbury, United Kingdom	NCT02424253
BMS-981164		IL-31	Anti-IL-31 mAb	Phase I completed	Bristol-Myers Squibb, New York, NY	NCT01614756
AMG157/ Tezepelumab		TSLP	Anti-TSLP mAb	Phase I completed	Amgen, Thousand Oaks, Calif	NCT00757042
MK-8226		TSLPR	Anti-TSLPR mAb	In phase I	Merck, Kenilworth, NJ	NCT01732510

CRTH2, Prostaglandin D<sub>2</sub> receptor 2; H4R, histamine H4 receptor; IL-4R, IL-4 receptor; TSLPR, thymic stromal lymphopoietin receptor.

Brunner et. al., American Academy of Allergy, Asthma & Immunology, 2017.