BTLA Agonist (ANB032) R&D Event

May 25, 2023
1:15pm PT / 4:15pm ET
Forward looking statement

This presentation and any accompanying oral presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: the timing of initiation of the Company’s clinical trials, including rosnilimab’s clinical trials in rheumatoid arthritis and in a second indication; the timing of the release of data from the Company’s clinical trials, including imsidolimab’s Phase 3 clinical trial in GPP, rosnilimab’s Phase 2b clinical trial in rheumatoid arthritis and ANB032’s Phase 2b clinical trial in atopic dermatitis; the timing of ANB033’s IND filing; statements regarding efficacy, safety and proof of mechanism from blinded data from rosnilimab’s clinical trial in alopecia areata and the timing of release of additional data from this trial; the Company’s ability to find a licensing partner for imsidolimab or etokimab and the timing of any such transaction; and the Company’s projected cash runway. Statements including words such as “plan,” “continue,” “expect,” or “ongoing” and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause the company’s actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to the company’s ability to advance its product candidates, obtain regulatory approval of and ultimately commercialize its product candidates, the timing and results of preclinical and clinical trials, the company’s ability to fund development activities and achieve development goals, the company’s ability to protect intellectual property and other risks and uncertainties described under the heading “Risk Factors” in documents the company files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this presentation, and the company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

Certain information contained in this presentation may be derived from information provided by industry sources. The Company believes such information is accurate and that the sources from which it has been obtained are reliable. However, the Company cannot guarantee the accuracy of, and has not independently verified, such information.

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.
## Agenda for today

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>SPEAKER</th>
</tr>
</thead>
</table>
| AnaptysBio: Best-In-Class Immune Cell Modulators                      | Dan Faga
Chief Executive Officer                                          |
| Checkpoint Agonism and ANB032, a BTLA Agonist                         | Martin Dahl, Ph.D.
Senior Vice President, Research                                        |
| Unmet Needs in Atopic Dermatitis (AD) and Need for Additional Targets | Emma Guttman, M.D., Ph.D.
Professor and Chair of Dermatology
Icahn School of Medicine, Mount Sinai                                  |
| Targeting AD with ANB032: Translational Data                          | Martin Dahl, Ph.D.
Senior Vice President, Research                                        |
| ANB032: Phase 1 Results and AD Phase 2b Trial                         | Paul Lizzul, M.D., Ph.D.
Chief Medical Officer                                                    |
| Closing Remarks                                                        | Dan Faga
Chief Executive Officer                                                 |
| Q&A                                                                   | AnaptysBio                                                            |
Best-in-class immune cell modulating antibodies restore immune balance across autoimmune & inflammatory diseases

<table>
<thead>
<tr>
<th>Immune Cell Modulators</th>
<th>Cytokine Antagonists (legacy programs for out-licensing)</th>
</tr>
</thead>
</table>
| Rosnilimab (PD-1 agonist) | **Imsidolimab** (IL-36R)  
Phase 2b in Rheumatoid Arthritis  
**Etokimab** (IL-33)  
Phase 2b/3-ready in epithelial driven diseases |
| ANB032 (BTLA agonist) | Phase 2b in Atopic Dermatitis |
| ANB033 (CD122 antagonist) | IND-enabling |

<table>
<thead>
<tr>
<th>Research-driven</th>
<th>Strong capital position</th>
<th>GSK immuno-oncology financial collaboration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinical pipeline of immunology targets</td>
<td>Cash runway to YE 2026</td>
<td>Significant royalty potential</td>
</tr>
</tbody>
</table>
Two decades of leadership in antibody discovery

Research-stage out-licensing

Single-cytokine antagonists

Immune cell modulators

First AnaptysBio-discovered antibody FDA and EU approved in 2021: JEMPERLI (dostarlimab), a PD-1 antagonist

2005: AnaptysBio founded

2011: 1st gen. PD-1 agonist variants out-licensed to Celgene

2014: Checkpoint antagonists out-licensed to Tesaro (GSK)

2018: Etokimab (IL-33): P2b in AD

2019: Imsidolimab (IL-36R): P2 in GPP

2023: ANB032 (BTLA agonist): P2b in AD

2023: Rosnilimab (PD-1 agonist): P2b in RA

Pivotal P3 data of imsidolimab in GPP: Q4:2023
**Checkpoint agonists restore immune balance**

**Checkpoint agonists:**
“hit the brakes”

**Checkpoint antagonists:**
“release the brakes”

**Immune cells** (e.g., T, B, dendritic)

**Checkpoint receptors** (e.g., PD-1, BTLA)

- **Treat cancer:**
  - Up-regulate immune cells

- **Treat inflammation:**
  - Down-regulate immune cells
**ANB032 has potential to treat wide range of systemic inflammatory diseases**

**BTLA agonists modulate immune cells:**
inhibit activated T cell proliferation, reduce inflammatory cytokine secretion and modulate DC function including inducing Tregs

- Th1 cell
- Th2 cell
- Th17 cell
- Th22 cell
- Dendritic cell (DC)
- Treg
- B cell

**Atopic dermatitis:**
> $16 billion global sales by 2030**

AD market to grow significantly given unmet patient need

- Th1, Th2, Th17, Th22 and DCs drive atopic dermatitis pathogenesis
  - SOC only directly targets Th2 pathway

Expect ANB032 to drive deeper responses across broader patient population
  - Restore immune balance

* Therapeutic area classes include dermatology, rheumatology, gastroenterology, metabolic, neurology and respiratory. ** GlobalData, AD Global Drug Forecast and Analysis, 2030.
ANB032’s mechanism of action matches atopic dermatitis disease pathogenesis

Checkpoint agonism may deliver differentiated outcomes while restoring immune balance in inflammatory and autoimmune diseases.

BTLA agonism inhibits activated T cell proliferation, reduces inflammatory cytokine secretion and modulates DC function including induction of Tregs.

Th1, Th2, Th17, Th22 and dendritic cells drive AD pathogenesis.

ANB032, supported with translational preclinical and Phase 1 safety data, has potential for deep responses across a broad patient population in AD.

Global Phase 2b trial initiated with top-line data expected by year-end 2024.
## Agenda for today

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>SPEAKER</th>
</tr>
</thead>
</table>
| AnaptysBio: Best-In-Class Immune Cell Modulators                      | Dan Faga  
Chief Executive Officer                                           |
| Checkpoint Agonism and ANB032, a BTLA Agonist                        | Martin Dahl, Ph.D.  
Senior Vice President, Research                                       |
| Unmet Needs in Atopic Dermatitis (AD) and Need for Additional Targets | Emma Guttman, M.D., Ph.D.  
Professor and Chair of Dermatology  
Icahn School of Medicine, Mount Sinai                                 |
| Targeting AD with ANB032: Translational Data                         | Martin Dahl, Ph.D.  
Senior Vice President, Research                                       |
| ANB032: Phase 1 Results and AD Phase 2b Trial                        | Paul Lizzul, M.D., Ph.D.  
Chief Medical Officer                                                   |
| Closing Remarks                                                      | Dan Faga  
Chief Executive Officer                                                 |
| Q&A                                                                  | AnaptysBio                                                               |
Modulating immune cells by targeting checkpoint receptors may restore immune balance

Healthy

Inflammatory cascade: Initiation and Amplification

DC maturation and antigen presentation

Resolution of Inflammation

Potential for Tolerance

Time

Immune Response

Inflammatory cycle in disease

Treg
Checkpoint agonists can restore immune balance to deliver differentiated outcomes

**Efficacy**
- Inhibits activated immune cells, acting directly on dysregulation
- Deep responses across broad patient population

**Durability**
- Restoring immune balance

**Safety**
- Agonist class well-tolerated to date
- No evidence of carcinogenicity with T cell modulators, such as abatacept, in decades of use

---

**Checkpoint agonists**

Differentiated safety and efficacy

- Single cytokine blockers
- On-target activity (acceptable tox)
- TYK2
- On mechanism but off-target activity (unacceptable tox)

---

JAKi (Approved doses; suboptimal PD)
Ligands on opposing cells bind to receptors, forming tight synapses to initiate checkpoint agonism

Checkpoint receptors on immune cells:
- regulated by kinases (on) and phosphatases (off)

Checkpoint ligands on opposing cells:
- engage initiating kinases
- exclude phosphatases

* Figure adapted from Frontiers in Immunology. 2018 Oct 8; 9: 2306; Immunoreceptor tyrosine-based inhibitory motif (ITIM)
AnaptysBio’s checkpoint agonists optimize inhibitory signaling by enabling tight immune synapse formation

Fc independent checkpoint receptor agonism

Fc receptor binding affinity AND membrane proximal binding optimizes agonism

* Figure adapted from Frontiers in Immunology. 2018 Oct 8; 9: 2306
B and T lymphocyte attenuator (BTLA) is a potent modulator of T cells, B cells and dendritic cells (DC)

Expressed only on immune cells and preferentially on activated immune cells

Dysregulation of BTLA pathway accelerates onset and exacerbates disease

Adapted from Xu et al, J. Cell Biol. 2020 Vol. 219 No. 6
**Proof of mechanism:**

**Agonism of BTLA pathway in dermatitis model**

BTLA knock-out mice have exacerbated T cell-mediated skin disease

BTLA agonist-treated WT mice have reduced T cell-mediated skin disease

Infiltrating CD4 T cells (similar for CD8)

Proliferating CD8 T cell IFNγ

Infiltrating CD4 T cells (similar for CD8)

Infiltrating CD8 T cell IFNγ

---

Nakagomi et al, Journal of Investigative Dermatology, 2013; Surrogate Murine BTLA agonist third-party data
ANB032: Best-in-class BTLA agonist antibody

ANB032: IgG4 antibody (non-depleting)
- Binds to BTLA on epitope proximal to immune cell
- Fc receptor binding profile contributes to differentiated potency
- Non-blocking of HVEM engagement with optimized antigen binding affinity

ANB032’s agonist signal modulates immune cells
- Inhibits activated T cell proliferation
- Reduces inflammatory cytokine secretion
- Modulates DC function, including inducing Tregs
**ANB032’s optimized Fc receptor engagement significantly enhances BTLA agonism**

Jurkat BTLA SHP2 Recruitment Assay methodology: BTLA and SHP2 are fused with complementary enzyme fragments, when SHP2 is recruited to activated phosphorylated BTLA, the enzyme donor and enzyme acceptor form active β-gal that is detected by chemiluminescence.
ANB032 demonstrates best-in-class in-vivo efficacy in humanized murine model of GvHD

All antibodies given at the same biweekly dose.
Checkpoint agonism leverages natural immune regulatory mechanisms to safely resolve inflammation and restore balance.

BTLA is a key checkpoint that modulates activity of T, B and dendritic cells.

ANB032 optimized Fc receptor engagement and proximal binding epitope significantly enhances BTLA agonism.

ANB032 has demonstrated preclinical proof of mechanism and best-in-class efficacy in vivo.
# Agenda for today

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>SPEAKER</th>
</tr>
</thead>
<tbody>
<tr>
<td>AnaptysBio: Best-In-Class Immune Cell Modulators</td>
<td>Dan Faga</td>
</tr>
<tr>
<td></td>
<td>Chief Executive Officer</td>
</tr>
<tr>
<td>Checkpoint Agonism and ANB032, a BTLA Agonist</td>
<td>Martin Dahl, Ph.D.</td>
</tr>
<tr>
<td></td>
<td>Senior Vice President, Research</td>
</tr>
<tr>
<td><strong>Unmet Needs in Atopic Dermatitis (AD) and Need for Additional Targets</strong></td>
<td>Emma Guttman, M.D., Ph.D.</td>
</tr>
<tr>
<td></td>
<td>Professor and Chair of Dermatology</td>
</tr>
<tr>
<td></td>
<td>Icahn School of Medicine, Mount Sinai</td>
</tr>
<tr>
<td>Targeting AD with ANB032: Translational Data</td>
<td>Martin Dahl, Ph.D.</td>
</tr>
<tr>
<td></td>
<td>Senior Vice President, Research</td>
</tr>
<tr>
<td>ANB032: Phase 1 Results and AD Phase 2b Trial</td>
<td>Paul Lizzul, M.D., Ph.D.</td>
</tr>
<tr>
<td></td>
<td>Chief Medical Officer</td>
</tr>
<tr>
<td>Closing Remarks</td>
<td>Dan Faga</td>
</tr>
<tr>
<td></td>
<td>Chief Executive Officer</td>
</tr>
<tr>
<td>Q&amp;A</td>
<td>AnaptysBio</td>
</tr>
</tbody>
</table>
Unmet Needs in Atopic Dermatitis and Need for Additional Targets

Emma Guttman-Yassky, M.D., Ph.D.
Waldman Professor of Dermatology
System Chair, Department of Dermatology
Icahn School of Medicine at Mount Sinai, New York, NY
Immediate Past President, International Eczema Council
Most common inflammatory skin disease (~7% of adults in US, 15% of children)

20-30% of patients have moderate-to-severe disease

Large unmet need for long-term disease control

The therapeutic drought is finally ending!
Impact of moderate-to-severe AD\textsuperscript{1-6}

Moderate to Severe AD in childhood may disrupt education\textsuperscript{6}

Potential for suicidal ideation

Anxiety, depression, low self-esteem\textsuperscript{1,4,5}

Sleep disturbance and daytime fatigue due to itch and pain\textsuperscript{1-3,5}

Work disability: not able to work in a full-time job

Poor qualifications, limited career prospects, financial problems

Poor tolerance for heat—causes flares of AD\textsuperscript{2}

Exercise and vacations in warm climates impossible; limits QoL

AD = atopic dermatitis; QoL = quality of life

Greater understanding of disease pathogenesis is enabling development of novel therapies.
Dupilumab (anti-IL-4Rα) targets IL-4 and IL-13
**EASI-50/75/90 in pooled solo 1 & 2 monotherapy 16-week studies**

<table>
<thead>
<tr>
<th>EASI-50(^a) (Secondary endpoint)</th>
<th>EASI-75(^a) (Primary endpoint)</th>
<th>EASI-90(^a) (Secondary endpoint)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="chart1.png" alt="" /></td>
<td><img src="chart2.png" alt="" /></td>
<td><img src="chart3.png" alt="" /></td>
</tr>
</tbody>
</table>

*Placebo qw (n=460)  Dup 300 mg q2w (n=457)  Dup 300 mg qw (n=462)*

*P<0.0001 vs placebo.

The only licensed dose for dupilumab in moderate-to-severe AD patients is 300 mg Q2W.

Baseline EASI mean scores (SD): placebo, dupilumab 300 mg q2w, and dupilumab 300 mg qw were 34.0 (14.4), 32.4 (13.3), and 32.5 (13.3), respectively.

Dup=dupilumab; EASI=Eczema Area and Severity Index; EASI-50/75/90=proportion of patients with ≥ 50%/75%/90% improvement in EASI score from baseline; q2w=every 2 weeks; qw=weekly; SD=standard deviation.

Where are we: Less than 25% AD patients are completely satisfied with SOC

AD = atopic dermatitis; BSA = body surface area
AD is highly heterogeneous and involves multiple immune cytokines (e.g., IFN-γ, IL-4, IL-13, IL-17, IL-22)

AD exhibits **variable patterns**
- Disease activity
- Disease severity
- Location (e.g., face, genitals)

**Morphology and distribution of AD lesions differ between age groups**

- **Infantile phase**
- **Childhood phase**
- **Adult phase**

❖ Adult-onset AD has **greater Th1 activation** compared to pediatric-onset

**Immune activation may vary between age of onset, disease duration, and ethnicity**, resulting in heterogeneous presentation

**Other factors varying between patients**
- Response to therapy
- IgE status
- Trigger-induced events
- Impact on itch, sleep, and QoL

AD, atopic dermatitis; IgE, immunoglobulin E; QoL, quality of life; Th, T helper cell
## What’s in the pipeline for AD patients?

<table>
<thead>
<tr>
<th>Target</th>
<th>Compound</th>
<th>Phase</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-13</td>
<td>Tralokinumab</td>
<td>FDA-, EMA-approved</td>
<td>LEO</td>
</tr>
<tr>
<td>IL-13</td>
<td>Lebrikizumab</td>
<td>3</td>
<td>Lilly</td>
</tr>
<tr>
<td>IL-13</td>
<td>Cendakimab</td>
<td>2</td>
<td>BMS</td>
</tr>
<tr>
<td>IL-13RA1</td>
<td>ASLAN004</td>
<td>2</td>
<td>ASLAN</td>
</tr>
<tr>
<td>IL-4RA</td>
<td>CBP201</td>
<td>3</td>
<td>Connect Biopharma</td>
</tr>
<tr>
<td>IL-31</td>
<td>Nemolizumab</td>
<td>3</td>
<td>Galderma/Chugai</td>
</tr>
<tr>
<td>IL-22RA1</td>
<td>LEO138559</td>
<td>2</td>
<td>LEO</td>
</tr>
<tr>
<td>OX40</td>
<td>KHK4083/AMG 4051</td>
<td>3</td>
<td>Amgen (KHK)</td>
</tr>
<tr>
<td>OX40L</td>
<td>Amlitelimab/KY1005</td>
<td>2b</td>
<td>Sanofi</td>
</tr>
<tr>
<td>BTLA agonist</td>
<td>ANB032</td>
<td>2b</td>
<td>AnaptysBio</td>
</tr>
<tr>
<td>CCR4</td>
<td>RPT193</td>
<td>2b</td>
<td>RAPT</td>
</tr>
<tr>
<td>S1PR</td>
<td>Etrasimod</td>
<td>3</td>
<td>Arena/Pfizer</td>
</tr>
</tbody>
</table>

**Small Molecules**

<table>
<thead>
<tr>
<th>Immune cell modulator</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-17C, IL-33, TSLP, IL-36, IL-1, IL-17A, IL-5 failed clinical trials in AD</td>
</tr>
</tbody>
</table>

EU=European Union; IL=interleukin; IV=intravenous; TSLP=thymic stromal lymphopoietin.

JAK Inhibitors: Topical: Ruxolitinib (FDA approved in US as of September 2021), Delgocitinib (Approved in Japan)

Other topicals: Roflumilast, Tapinarof (phase 3 in AD)

Oral: Abrocitinib, Upadicitinib, Baricitinib (FDA/EU/UK approval; baricitinib not FDA-approved for AD, only for AA)
Atopic dermatitis emerges as systemic disease

- Systemic inflammation is well established in psoriasis
- Higher immune activation has been recently reported in peripheral blood from AD vs. psoriasis patients
  - Increased activated T cells
  - Increased circulatory cytokines and cardiovascular associated markers
- Several population-based studies showed increased cardiovascular disease in AD

Silverberg JI Allergy 2015 70: 1300–1308
To fully understand the effect of a given treatment, we need an integrated model of skin and blood AD biomarkers.
Both successes and failures have helped to frame pathogenic concepts and therapeutic directions.
AD biology is heterogenous and uniquely fits BTLA MOA

Pathogenesis linked broadly to Th2, Th1, Th17, Th22 as well as dendritic cells

BTLA expressing cells (Th1, Th2, Th17, Th22, B, Dendritic) are clinically validated drivers of disease in atopic dermatitis
ANB032: Best-in-class BTLA agonist antibody

ANB032: IgG4 antibody (non-depleting)
- Binds to BTLA on epitope proximal to immune cell
- Fc receptor binding profile contributes to differentiated potency
- Non-blocking of HVEM engagement with optimized antigen binding affinity

ANB032’s agonist signal modulates immune cells
- Inhibits activated T cell proliferation
- Reduces inflammatory cytokine secretion
- Modulates DC function, including inducing Tregs
## Agenda for today

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>SPEAKER</th>
</tr>
</thead>
</table>
| AnaptysBio: Best-In-Class Immune Cell Modulators                      | Dan Faga  
Chief Executive Officer                                          |
| Checkpoint Agonism and ANB032, a BTLA Agonist                         | Martin Dahl, Ph.D.  
Senior Vice President, Research                                        |
| Unmet Needs in Atopic Dermatitis (AD) and Need for Additional Targets | Emma Guttman, M.D., Ph.D.  
Professor and Chair of Dermatology  
Icahn School of Medicine, Mount Sinai                                 |
| **Targeting AD with ANB032: Translational Data**                      | Martin Dahl, Ph.D.  
Senior Vice President, Research                                        |
| ANB032: Phase 1 Results and AD Phase 2b Trial                         | Paul Lizzul, M.D., Ph.D.  
Chief Medical Officer                                                     |
| Closing Remarks                                                       | Dan Faga  
Chief Executive Officer                                              |
| Q&A                                                                  | AnaptysBio                                                             |
Th1, Th2, Th17, Th22 and dendritic cells in tissue and periphery drive AD pathogenesis

Potential for BTLA expression (ANB032 impact)

Adapted from Nature Reviews Disease Primers volume 4, Article number: 1 (2018).
BTTLA is broadly expressed on immune cells driving atopic dermatitis pathogenesis

DC maturation

DC antigen presentation and co-stimulation of T cells

T cell activation, proliferation and cytokine secretion

Immature DC

Mature DC

T naïve

Stimuli

Th1

Th2

Th17/22

IFNγ

IL-13

IL-17A

IL-22
T cells and dendritic cells are hallmarks of AD skin

BTLa pathway is dysregulated in AD tissue...

BTLa is elevated and HVEM is decreased, suggesting insufficient agonism in diseased skin

Adapted from Guttman et al, Journal of Allergy and Clinical Immunology, 2018.
...and in the periphery

BTLA is elevated and HVEM is decreased, suggesting insufficient agonism in circulating T Cells

- BTLA (MFI)
  - CD4 T cells
  - CD8 T cells

- HVEM (MFI)
  - CD4 T cells
  - CD8 T cells

- HVEM/BTLA Ratio
  - Normalized to Healthy Baseline
  - CD4 T cells
  - CD8 T cells

Atopic Derm

- Healthy
- Atopic Derm
BTLA expression remains elevated after treatment with IL-13 targeted biologic

Analysis based on data sourced from Guttman et al, Journal of Allergy and Clinical Immunology, 2018.
**ANB032 inhibits pathogenic T cell amplification in both periphery and skin**

Inhibition of activated T cell proliferation and reduction of inflammatory cytokine secretion

*Stimuli*
Broad T cell (Th1, Th2, Th17 and Th22) signatures characterize atopic dermatitis
ANB032 inhibits T cell proliferation in AD patient-derived PBMCs

Assay protocol includes incubating AD-patient derived PBMCs with ANB032 and analyzing samples for T cell proliferation three days later.
ANB032 inhibits Th1, Th2, Th17 and Th22 cytokine secretion in AD patient-derived PBMCs

Inhibition of Th1 Cytokine Secretion

Inhibition of Th17 Cytokine Secretion

Inhibition of Th2 Cytokine Secretion

Inhibition of Th22 Cytokine Secretion

(N=6 AD patients)
BTLA highly expressed on mature DCs

**Inflammatory stimuli induce DC maturation**

LPS*

Pathogens
Cytokines
PAMPs
DAMPs

**Immature DC**  
**Mature DC**

- Co-stimulatory molecules
- MHC II Expression
- Secretion of pro-inflammatory cytokines

**LPS stimulated DCs**

- 40% Mature DC
- 50% Immature DC

**Mature DC**

- 92%

BTLA expression

Adapted from Frontiers in Immunology. 2019 Jan 21;9:3176 ; * LPS=Lipopolysaccharide (a TLR4 agonist).
ANB032 modulates dendritic cell function

Reduction of mature dendritic cells (DCs) enhances the direct inhibitory effect on T cells and induces CD4+ FOXP3+ Tregs

ANB032
ANB032 inhibits DC maturation and reduces antigen presentation and co-stimulatory molecules

**Maturation of DCs by LPS**

**Inhibition of DC maturation by ANB032**

**Antigen presentation**

(Gated on total CD11c+ DCs)

**MHC II**

**Co-stimulatory molecules on DCs**

(Gated on total CD11c+ DCs)

**CD80**

**CD86**

**CD40**

ANB032 inhibits DC maturation

Isotype

ANB032

MHC II (HLA DR)

(MFI normalized to isotype LPS)

CD11c

CD80

CD86

CD40

Number of mature DC (normalized to isotype LPS)

ANB032 inhibits DC maturation

Isotype

ANB032
ANB032-treated DCs induce functional Tregs offering potential to restore immune balance.
ANB032 inhibits T- and DC-mediated inflammation that are validated drivers of AD pathogenesis

- BTLA pathway is dysregulated and BTLA is broadly expressed on T cells and dendritic cells that drive all phases of AD pathogenesis.

- ANB032 directly inhibits proliferation of and cytokine secretion from AD patient-derived pathogenic Th1, Th2, Th17, Th22 cells.

- ANB032 modulates dendritic cells which enhances the direct inhibitory effect on T cells and induces Tregs.
## Agenda for today

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>SPEAKER</th>
</tr>
</thead>
</table>
| AnaptysBio: Best-In-Class Immune Cell Modulators                      | Dan Faga
Chief Executive Officer                                         |
| Checkpoint Agonism and ANB032, a BTLA Agonist                        | Martin Dahl, Ph.D.
Senior Vice President, Research                                       |
| Unmet Needs in Atopic Dermatitis (AD) and Need for Additional Targets | Emma Guttman, M.D., Ph.D.
Professor and Chair of Dermatology
Icahn School of Medicine, Mount Sinai                                |
| Targeting AD with ANB032: Translational Data                         | Martin Dahl, Ph.D.
Senior Vice President, Research                                       |
| **ANB032: Phase 1 Results and AD Phase 2b Trial**                    | Paul Lizzul, M.D., Ph.D.
Chief Medical Officer                                                   |
| Closing Remarks                                                      | Dan Faga
Chief Executive Officer                                               |
| Q&A                                                                  | AnaptysBio                                                               |
Understanding disease pathology enables better therapies: AD mirrors psoriasis a decade ago

Atopic Dermatitis

2004: First generation biologic
   TNF

2006 – 2009+: “Me-too / Me better” biologics
   TNF & IL-12/23

2014: First generation oral
   PDE4

2015+: Increasingly effective biologics
   IL-17 / IL-23

2022: Increasingly effective orals
   Tyk2

2022: First generation oral
   JAKi

2021 – 2023+: “Me-too / Me better” biologics
   IL-13

2017: First generation biologic
   IL-13/4

Psoriasis

Understanding disease pathology enables better therapies: AD mirrors psoriasis a decade ago

2004: First generation biologic
   TNF

2006 – 2009+: “Me-too / Me better” biologics
   TNF & IL-12/23

2014: First generation oral
   PDE4

2015+: Increasingly effective biologics
   IL-17 / IL-23

2022: Increasingly effective orals
   Tyk2

2022: First generation oral
   JAKi

2021 – 2023+: “Me-too / Me better” biologics
   IL-13

2017: First generation biologic
   IL-13/4

Understanding disease pathology enables better therapies: AD mirrors psoriasis a decade ago
Opportunity for new biologic class with differentiated outcomes in AD regardless of prior treatment

Atopic dermatitis US prevalence*

5 Million

Diagnosed

2 Million

Diagnosed Moderate-to-Severe

1.2 Million

Biologic eligible Moderate-to-Severe

Target Population

Suboptimal Responders >50%

EASI-75 45-50%

EASI-90 <35%

e.g., dupilumab response profile

Significant room to differentiate:

- Broader response
- Deeper response
- Resolution of inflammation

*Claims analysis to determine market size based on 5 years of claims history; dupilumab responsive profile per prescribing information (label.fda.gov).
BTLA agonists may treat all stages of AD

Healthy | Mild | Increasingly severe atopic dermatitis

Th2 disease | Th1, Th2, Th17, Th22 and dendritic cells driven disease

Biologic-eligible population

BTLA agonist opportunity

Single cytokine antagonist (e.g. IL-13) opportunity

Suboptimal responses, but IL-13s utilized given limited options today
ANB032 demonstrated favorable safety and tolerability with rapid and sustained PK/PD activity

96 healthy volunteers in SAD and MAD cohorts in Phase 1 study

- Favorable ~2-week half-life with IV and SQ dosing
- Full receptor occupancy (RO) within hours and maintained for >30 days

Rapid and sustained target engagement on both T and B cells

- Duration of reduced BTLA expression persisted in dose-dependent manner

Well-tolerated with no dose limiting tox

- No SAEs
- Most AEs mild-to-moderate, short duration, dose independent and resolved without sequelae
- No evidence of infection risk or cancer risk to date
# ANB032 Phase 2b in IL-13 mAb naïve and experienced AD patients

## Efficacy:
~3-month treatment

- ANB032 SC Dose 1
- ANB032 SC Dose 2
- ANB032 SC Dose 3
- Placebo

## Safety/Durability:
~3-month follow up

### Patient population
- Adults with moderate-to-severe atopic dermatitis*
- Include both dupilumab/IL-13 naïve and experienced patients

### Endpoints

<table>
<thead>
<tr>
<th>Primary</th>
<th>Mean change from Baseline in EASI at Week 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary</td>
<td>EASI-75</td>
</tr>
<tr>
<td></td>
<td>vIGA-AD 0 (clear) or 1 (almost clear) and a ≥ 2-point reduction (improvement)</td>
</tr>
<tr>
<td></td>
<td>PNRS (itch), DLQI, SCORAD</td>
</tr>
<tr>
<td></td>
<td>Safety</td>
</tr>
</tbody>
</table>

### Exploratory endpoints
- Th1/Th2/Th17 cytokines and other soluble biomarkers, tissue samples (tape strips, biopsies)

---

* Moderate-to-severe atopic dermatitis: at least 10% of their total body surface area (BSA), an Eczema Area and Severity Index (EASI) score ≥ 16, and a validated Investigator Global Assessment for Atopic Dermatitis (vIGA) score ≥ 3.
Explore predictive markers of treatment response

Goals

• Apply precision medicine to further development of ANB032 in AD and other diseases
• Profile immune impact and mechanistic markers of BTLA agonism
• Map immune changes from baseline onto current and future disease signatures

Periphery biomarkers

• T cell stimulation assay
• Transcriptomics
• Immunophenotyping (e.g., TBNK, Tregs)
• Soluble biomarkers and cytokines relevant to Th1/Th2/Th17/Th22 biology

Tissue biomarkers (tape strips and biopsies)

• Proteomics including cytokines
• Transcriptomics
• Immunophenotyping (e.g. TBNK, Tregs)
## Top-line Week 14 data anticipated by YE 2024

Clinical team has deep experience conducting dermatology clinical trials, including in AD

<table>
<thead>
<tr>
<th>Global Trial</th>
<th>Extensive AD relationships</th>
<th>Recruitment initiatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>40+ dermatology investigators with proven track record enrolling AD trials</td>
<td>Long history of relationships with global KOLs in AD</td>
<td>Robust training program</td>
</tr>
<tr>
<td>North America and Europe trial sites</td>
<td>Strong medical society engagement</td>
<td>Community outreach/advocacy group engagement</td>
</tr>
<tr>
<td></td>
<td>Collaboration with experienced and proven CROs in AD</td>
<td>Social media campaign, patient resources and local advertising</td>
</tr>
</tbody>
</table>
ANB032 may address need for improved treatment outcomes for AD patients

- AD disease heterogeneity is not adequately addressed by standard of care
- ANB032 mechanism could enable broader and deeper responses to resolve inflammation and restore immune balance
- Phase 2b dose-finding study initiated in both IL-13 mAb naïve and experienced patients with moderate-to-severe AD
- Top-line Phase 2b results expected in Q4 2024
# Agenda for today

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>SPEAKER</th>
</tr>
</thead>
</table>
| AnaptysBio: Best-In-Class Immune Cell Modulators                      | Dan Faga  
Chief Executive Officer                                           |
| Checkpoint Agonism and ANB032, a BTLA Agonist                        | Martin Dahl, Ph.D.  
Senior Vice President, Research                                      |
| Unmet Needs in Atopic Dermatitis (AD) and Need for Additional Targets | Emma Guttman, M.D., Ph.D.  
Professor and Chair of Dermatology  
Icahn School of Medicine, Mount Sinai                                |
| Targeting AD with ANB032: Translational Data                         | Martin Dahl, Ph.D.  
Senior Vice President, Research                                      |
| ANB032: Phase 1 Results and AD Phase 2bTrial                         | Paul Lizzul, M.D., Ph.D.  
Chief Medical Officer                                                   |
| Closing Remarks                                                       | Dan Faga  
Chief Executive Officer                                           |
| Q&A                                                                  | AnaptysBio                                                               |
Checkpoint agonism may deliver differentiated outcomes while restoring immune balance in inflammatory and autoimmune diseases.

BTLA agonism inhibits activated T cell proliferation, reduces inflammatory cytokine secretion and modulates DC function including induction of Tregs.

Th1, Th2, Th17, Th22 and dendritic cells drive AD pathogenesis.

ANB032, supported with translational preclinical and Phase 1 safety data, has potential for deep responses across a broad patient population in AD.

Global Phase 2b trial initiated with top-line data expected by year-end 2024.

ANB032’s mechanism of action matches atopic dermatitis disease pathogenesis.
## Immune cell modulator development: Three phase 2 initiations in 2023

<table>
<thead>
<tr>
<th>Antibody Program</th>
<th>Therapeutic Indication</th>
<th>Development Stage and Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rosnilimab</strong></td>
<td>Rheumatoid Arthritis</td>
<td><em>Phase 2b initiation Q3 2023</em></td>
</tr>
<tr>
<td>(PD-1 agonist)</td>
<td></td>
<td><em>Top-line data mid 2025</em></td>
</tr>
<tr>
<td><strong>ANB032</strong></td>
<td>Inflammatory Disease</td>
<td><em>Trial initiation YE 2023</em></td>
</tr>
<tr>
<td>(BTLA agonist)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ANB033</strong></td>
<td>Atopic Dermatitis</td>
<td><em>Phase 2b initiated Q2 2023</em></td>
</tr>
<tr>
<td>(CD122 antagonist)</td>
<td></td>
<td><em>Top-line data YE 2024</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>ANB033</strong></td>
<td><em>IND submission H1 2024</em></td>
</tr>
<tr>
<td></td>
<td>(CD122 antagonist)</td>
<td></td>
</tr>
</tbody>
</table>