Who We Are

• Therapeutic focus: immuno-oncology and autoimmunity
• Proprietary antibody discovery platform: First 40+ targets drugged
• Broad pipeline of novel therapeutic candidates targeting multiple targets of the immune system
• Growing biotech with lab/office/vivarium in Cambridge, MA

Key Milestones

• Developed comprehensive and deep approach to antibody discovery: novel drug candidates and building blocks for next-generation bispecific antibodies. StitchMabs™ HT screening platform.
• Nominated our first clinical candidate
• 2018 “Fierce 15” biotech company
• Completed $132 M in series A financing: OrbiMed, F-Prime, Cowen, Borealis, Thiel, Biomatics, Alexandria, BioMed

2019

• Enroll Phase 1 Study: CTX-471 – novel CD137 agonist: https://clinicaltrials.gov/ct2/show/NCT03881488
• Begin IND enabling studies for our second candidate: first-in-class NKp30 bispecific
• Nominate a third clinical candidate: two new INDs in 2020
• Series B financing; IPO ready
Our Discovery Approach Bridges Innate & Adaptive Immunity

VALIDATED ANTIBODY PANELS TO 40+ TARGETS FORM BUILDING BLOCKS FOR COMBINATION & BISPECIFIC SCREENING

Innate Immunity
- NKG2D
- CD226
- NKp30
- NKp46
- CD16a
- 2B4
- CD89
- SIRPa

Adaptive Immunity
- CD8+ CTL
- CD40
- Ag shedding
- PD-L1
- CD155
- CD112
- CD113
- CD47
- CD277

Tumor
- Her2
- BCMA
- CD38
- CD200
- CD30
- CD137
- TIGIT
- CD112R
- CD96

Neutrophil
- NKG2D
- CD226
- NKp30
- NKp46
- CD16a
- 2B4
- CD89
- SIRPa

Macrophage
- NKG2D
- CD226
- NKp30
- NKp46
- CD16a
- 2B4
- CD89
- SIRPa

Treg
- CD137
- TIGIT
- TNFR2
- OX40
- GITR

MDSC
- PD-L1
- Gal-1
- Gal-3
- IL-6

CD137
- TIGIT
- TNFR2
- OX40
- GITR

CD137
- TIGIT
- TNFR2
- OX40
- GITR

OX40
- GITR
Compass Pipeline: June 2019

<table>
<thead>
<tr>
<th></th>
<th>Discovery</th>
<th>In Vitro</th>
<th>In Vivo</th>
<th>IND Enabling Studies</th>
<th>Phase I</th>
<th>Phase II</th>
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</thead>
<tbody>
<tr>
<td><strong>T-Cell</strong></td>
<td>Activation</td>
<td>CTX-471: Novel CD137 agonist</td>
<td>CTX-471 Combinations</td>
<td>CTX-8371: PD-1 x PD-L1 Bispecific</td>
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<td>CKPT Blockade</td>
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<tr>
<td><strong>NK Cell</strong></td>
<td>Activation</td>
<td>CTX-8573: BCMA x NKp30 Bispecific</td>
<td>NKp30 x TAA Platform</td>
<td>TGFβ x TIGIT Bispecific</td>
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<tr>
<td><strong>Macrophage</strong></td>
<td>Activation</td>
<td>Receptor x TAA Bispecifics</td>
<td>CTX-5861: SIRPα and Combinations</td>
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</table>

TAA: Tumor associated antigen

CKPT: Checkpoint
T-Cells

**Activation**

*CTX-471 - CD137 Agonist*

**Checkpoint blockade**

*CTX-8371 - PD1 x PDL1 Bispecific*
CTX-471: Best in Class CD137 Agonist

NOVEL EPITOPE WITH DIFFERENTIATED ACTIVITY SUPPORTED BY EXTENSIVE PRECLINICAL DATA

**CTX-471 Summary**

**Selection**
- Panel of 70 antibodies
- 8 unique epitope bins
- Comprehensive *in vitro* characterization based on binding, signaling, activation, and drug-like properties
- 4 leads compared *in vivo*

**Molecular Profile**
- Fully human, IgG4 agonist
- Non-ligand competitive
- Differentiated epitope in CRD3/4
- Mouse/human/cyno cross-reactive

CTX-471 binds a unique, non-ligand competitive epitope in CRD3-4 of CD137
Raising the Bar for Preclinical Efficacy - High Burden Tumor Models

**Small CT26 tumor: ~75 mm³**
- Typical size at which treatment begins in mouse efficacy studies
- Tumors this small are modestly sensitive to monotherapy with α-PD-1/L1, α-OX40, α-CTLA4, or α-CD137 (3H3)
- Small tumors can be eradicated by CTX-471 monotherapy

**Large CT26 tumor: ~500 mm³**
- Treating extremely large tumors of this size is generally considered futile
- Tumors this large are highly resistant to monotherapy α-PD-1/L1, α-OX40, α-CTLA4, or α-CD137 (3H3)
- Large tumors can also be eradicated by CTX-471 monotherapy
CTX-471 Induces Regression of ~500 mm$^3$ Tumors

CTX-471 AND CTX-471-AF CLONES WERE TESTED IN CT26 THERAPEUTIC IN VIVO MODEL

- Tumors were allowed to grow to ~500 mm$^3$ before treatment began
- Therapeutic model, not a prevention model
- Unprecedented Monotherapy activity for an I/O Antibody

Low affinity
Intermediate affinity
High affinity
Generation of Long Term Immunological Response

POTENT AND FUNCTIONAL IMMUNOLOGICAL MEMORY – ALL CURED MICE REJECTED THE TUMOR

Survival Curve: Monotherapy Treatment

Survival Curve: Re-challenge

✓ Monotherapy treatment
✓ At > 8 x t_{1/2} all mice of Clone #1 and most mice of Parental survived
✓ All surviving mice re-challenged with CT-26 rejected the tumor

* P values from Log-rank test compared to control
CTX-471-AF-1 Induces Comprehensive Reprogramming Within the Tumor Microenvironment

**Increased Infiltration of Immune Cells in the TME**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CTX-471-AF-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD45</td>
<td>18 ± 1 %</td>
<td>62 ± 25 %</td>
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</table>

**Treg Reduction in the TME**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CTX-471-AF-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOXP-3</td>
<td>31 ± 9 %</td>
<td>7 ± 3 %</td>
</tr>
</tbody>
</table>

**Protection/Reversion of T-cell Exhaustion**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CTX-471-AF-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-1</td>
<td>43 ± 5 %</td>
<td>8 ± 5 %</td>
</tr>
<tr>
<td>TIGIT</td>
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</tbody>
</table>

**Tumor Associated Macrophage Reduction in the TME**

<table>
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<tr>
<th></th>
<th>Control</th>
<th>CTX-471-AF-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD11b</td>
<td>44 ± 4 %</td>
<td>24 ± 11 %</td>
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<tr>
<td>F4/80</td>
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</tbody>
</table>

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Combinations are Synergistically Effective *In Vivo*

CT26HuHER2 ADOPTIVE TRANSFER MODEL – T-CELL MEDIATED ACTIVITY SHOWN FOR CTX-471

Note: Treatment initiated 6-days post tumor inoculation
CTX-471-AF causes Profound Tumor Necrosis of Very Large Tumors
Tumor Rejection by CTX-471-AF is Associated with Increased Frequency and Penetration of CD8⁺ T Cells

Day 7
Day 10
Day 14

Control

CTX-471-AF

Anti-CD8 IHC
**Vision:** a broad T-Cell and NK-cell activator that has efficacy after PD-1/PD-L1 blockade in the immune-sensitive tumors (‘hot tumors’) and activity in selected cold tumors

- Widely expressed on T cells and NK cells
- Activation via CTX-471 leads to efficacy across a broad set of syngeneic tumors in mice
- Demonstrable activity in cold tumors such as colorectal cancer, pancreatic cancer, etc.

**Phase 1** will test the activity of CTX-471 in the relapsed patient population after PD-1 axis blockade

- Immunological architecture is required for response: patients can not be refractory to PD-1 blockade
- Once efficacy has been established in the 2L, 3L, we will proceed to front line therapy

**Tumor types:** all approved PD-1 and PD-L1 indications

- Immunologically responsive based on at least 3 months of stable disease
- High unmet medical need due to limited response to CKPT blockers
- Second line NSCLC is a major commercial opportunity

**Execution**

- IND open as of 3/2019
- 6-8 Centers in the US: Dana Farber, MGH, Wash. U., Mary Crowley CC, Mt. Sinai, ITOR, Hackensack
- Currently screening patients
**Activation**

*CTX-8573 – BCMA x NKp30 Bispecific*

*NKp30 Engager Platform*

**Checkpoint blockade**

*TIGIT x TGFβ Bispecific*
Empirical Identification and Optimization of NK Bispecific Antibodies

COMPASS SCREENING WORKFLOW FOR MULTISPECIFIC CONSTRUCTS

Comprehensive antibody discovery

Panel of BCMA-NKR StitchMabs™ and bispecifics expressed and purified at 24 well scale

Secondary screen – Effect of CD16a engagement

Primary Screen
Primary NK cells
IgG1 Fc

Combinatorial library

Synergistic NK activation
Next Generation NK Cell Bispecific Platform Targeting NKp30 Receptor

- **First in class** bispecific antibody targeting **NKp30 activating receptor** expressed by NK cells
- **Overcomes CD16a deficiency**
- **Lowers the threshold** of NK cell activation and induces NK cell-mediated killing of tumor cells expressing high, medium and **low levels** of TAAs with >100 fold increased potency compared to mAb
- induces **NK cell proliferation** and cytokine release in the presence of target cells
- **Wide therapeutic window** with no activity in the absence of target antigen
- Leverages Compass **common light chain** and StitchMabs™ technologies
NKp30 Bispecific Platform Significantly Enhances ADCC Potency of α-BCMA mAb

SUPERIOR TUMOR CELL KILLING ACTIVITY MAINTAINED IN THE ABSENCE OF CD16A

Target cell killing by primary NK cells

Target cell killing by CD16⁺ KHYG-1 cell line

NCI-H929 target cells
4 hour incubation
Affinity Matured, Afucosylated BCMA x NKp30 Lead CTX-8573 Induces Highly Potent and Selective Lysis of BCMA<sup>pos</sup> Tumor Cells Expressing Different Levels of Antigen

Ag expression level

<table>
<thead>
<tr>
<th>BCMA copies per cell</th>
<th>&gt;500,000</th>
<th>~100,000</th>
<th>&lt;30,000</th>
<th>BCMA negative tumor cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>H929</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MM.1S</td>
<td></td>
<td></td>
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<tr>
<td>RPMI 8226</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>HL-60</td>
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</tbody>
</table>

Methods: Primary NK cells from one donor were cultured for 4 hours with tumor cells. E:T ratio 10:1

Compass Therapeutics
Single Dose of 1st Generation BCMA x NKp30 Bispecific Depletes BM Plasma Cells & Expands BM NK-Cells in Cynomolgus Monkeys
COLLABORATION WITH DR. FRANCOIS VILLINGER AT NEW IBERIA RESEARCH CENTER

Bone marrow plasma cell depletion (ELISpot)

Cyno #1 (AK749J)

Ig secreting cells (normalized to baseline)

Days post treatment

IgG
IgM
IgA

Cyno #2 (B6016)

Ig secreting cells (normalized to baseline)

Days post treatment

IgG
IgM
IgA

Activation & expansion of bone marrow NK-cells

IgG-like PK with 16 day β-phase half-life

30 mg/kg dose

Collaboration with Dr. Francois Villinger at New Iberia Research Center
# Our NKp30xBCMA is Uniquely Suited to Target Severe Autoimmune Indications

<table>
<thead>
<tr>
<th>BCMA Targeting Programs</th>
<th>Multiple myeloma and other cancers</th>
<th>Severe Autoimmune Indications driven by pathological IgGs</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-BCMA (IgG1)</td>
<td>+</td>
<td>-</td>
<td>Insufficient potency on low BCMA expressing cells</td>
</tr>
<tr>
<td>BCMA-ADCs</td>
<td>+</td>
<td>-</td>
<td>Safety</td>
</tr>
<tr>
<td>CAR-T</td>
<td>+</td>
<td>-</td>
<td>Safety &amp; cost</td>
</tr>
<tr>
<td>BCMA x CD3 (‘BiTE’)</td>
<td>+</td>
<td>-</td>
<td>Safety and product profile</td>
</tr>
<tr>
<td>NKp30 x BCMA</td>
<td>+</td>
<td>+</td>
<td>Targets cells expressing high, medium and low BCMA, PK/PD profile</td>
</tr>
</tbody>
</table>
## Potential Indications for a BCMA-Directed Cell Depletion Agent

<table>
<thead>
<tr>
<th>Indication</th>
<th>Prevalence</th>
<th>Limitations of Current Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light-chain amyloidosis¹</td>
<td>~40 cases per 1,000,000 ~12,000 pts in the U.S.</td>
<td>Up to 80% of pts are ineligible for ASCT, and plasma cell directed chemotherapy has been shown to fall short in addressing organ dysfunction caused by amyloid deposition</td>
</tr>
<tr>
<td>Myasthenia Gravis²</td>
<td>~20 cases per 100,000. ~60,000 pts in the U.S.</td>
<td>Corticosteroids and immunosuppressants are associated with a number of significant side effects. Use of Soliris only blocks the activity of complement recruited by the pathogenic IgGs directed against the ACh receptor. It does not address the blocking of the Ach receptor by pathogenic IgGs, nor the receptor cross-linking and internalization by these IgGs.</td>
</tr>
<tr>
<td>Pemphigus Vulgaris³</td>
<td>~1-10 cases per 1,000,000 ~300-3,000 pts in the U.S.</td>
<td>Patients who do not respond to corticosteroids and immunosuppressants are treated with IVIg or Rituxan. Even with IVIg and Rituxan, complete remission may take several months, and some patients do not respond.</td>
</tr>
<tr>
<td>Immune Thrombocytopenia¹</td>
<td>~9.5 cases per 100,000 ~30,000 pts in the U.S.</td>
<td>Treatment for ITP is focused on either reducing the autoimmune destruction of the platelets, or directly stimulating platelet production with specific growth factors. Use of IVIg and plasmapheresis can lead to serious complications, and while thrombopoietin receptor agonists lead to increases in blood platelet counts, they do not address the underlying destruction of the platelets.</td>
</tr>
</tbody>
</table>

Sources: ¹National Organization for Rare Disorders, ²Myasthenia Gravis Foundation, ³International Pemphigus & Pemphigoid Foundation
NKp30 x BCMA effect on serum IgM in a Monkey is similar to 6 courses of Plasmapheresis in humans

TARGETING PATHOGENIC ANTIBOIES IN AUTOIMMUNE DISEASE

Animal #1, Drop of IgM level in serum

Guptill, Autoimmunity, 2016
NKp30 x BCMA effect on serum IgM in a Monkey is similar to Fc/FcRn blockade in humans

TARGETING PATHOGENIC ANTIBODIES IN AUTOIMMUNE DISEASE

Animal #1, Drop of IgM level in serum

Ulrichts, 2017 (ARGX-113)
NKp30 Bispecific Engager Platform Summary

• NKp30 identified as optimal bispecific partner for targeting and activating NK cells through unbiased screen leveraging Compass discovery platform

• Key properties of NKp30 bispecifics
  – **Potent** - Enhance ADCC, cytokine production, and NK-cell proliferation compared to monoclonal antibodies
  – **Large therapeutic window** - Active against target cells with wide range of antigen expression, but no activity in the absence of target
  – **Resistant to CD16a downregulation** - Activate NK cells in the absence of CD16a engagement
  – **Highly manufacturable** - Monoclonal-like drug-like properties and pharmacokinetics
  – **Flexible format** – Common-LC format amenable to multi-TAA or multi-NKR targeting
  – **Potential to target additional effector cell types**

• BCMA x NKp30 program
  – Robust killing of target cells with high, medium, & low BCMA
  – Potent depletion of plasma cells in cynomolgus monkey
  – Cell line development & additional primate studies underway with potential IND’s in multiple myeloma or autoimmune disease in 1H2020

• Her2 x NKp30
  – Bispecifics identified against multiple epitopes of Her2 with improved ADCC potency compared to trastuzumab
  – Lead clone CTX-7144 entering affinity maturation

• Multiple campaigns in progress for additional targets in hematological and solid tumors with preliminary lead ID in 2019
Our Pipeline

Effective Modulation of the Immune System
Compass Therapeutics: 2019 and Beyond
BUILDING A FULLY INTEGRATED BIOPHARMACEUTICAL COMPANY

2015-2016
- Clinical lead CTX-471
- CLC antibodies
- StitchMabs™
- 30 discovery campaigns complete

2017
- Clinical candidate
- 2nd lead: NKp30 x BCMA
- Candidates for IND3, IND4
- Multiple CLC mAbs
- Bispecifics with unique activity
- Several I&I programs advancing in parallel

2018

2019
- Clinical stage company
- 2nd clinical candidate at IND enabling studies
- 3rd clinical candidate announced
- Several prospects for candidates 4th, 5th and 6th
- Pharma collaboration

2020
- CTX-471 Efficacy Data
- BCMA x NKp30 Phase 1
- TAA#2 x NKp30 IND
- Next-Gen checkpoint blocking bispecific