High-Specificity OmniAb Antibodies for Bispecific Applications

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VP of Antibody Technologies

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The OmniAb Technology Suite

The only platform leveraging four-species

Robust solutions for bispecific antibodies

Human frameworks with ultralong CDR-H3s

Industry’s most diverse offering

Proven success
Antibody Repertoires and Bispecific Antibodies

Combining sources provides partners even more diverse repertoires and new target access.

Common light chain techs being used for flexibility and bispecific program optionality.
# Approved and Clinical Partner Bispecific Pipeline

**ONE APPROVED PRODUCT AND 10 ACTIVE CLINICAL OMNIAB- Derived Antibodies**

<table>
<thead>
<tr>
<th>Partner</th>
<th>Program</th>
<th>Source Animal</th>
<th>Area</th>
<th>Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janssen</td>
<td>TECVAYLI®</td>
<td>OmniRat</td>
<td>Oncology</td>
<td>BCMA x CD3</td>
</tr>
<tr>
<td>Genmab</td>
<td>GEN1046</td>
<td>OmniRat</td>
<td>Oncology</td>
<td>PD-L1 x 4-1BB</td>
</tr>
<tr>
<td>Aptevo</td>
<td>APVO436</td>
<td>OmniMouse</td>
<td>Oncology</td>
<td>CD123 x CD3</td>
</tr>
<tr>
<td>Janssen</td>
<td>JNJ-67371244</td>
<td>OmniMouse</td>
<td>Oncology</td>
<td>CD33 x CD3</td>
</tr>
<tr>
<td>Janssen</td>
<td>JNJ-70218902</td>
<td>OmniRat</td>
<td>Oncology</td>
<td>Undisclosed</td>
</tr>
<tr>
<td>Janssen</td>
<td>JNJ-78306358</td>
<td>OmniRat</td>
<td>Oncology</td>
<td>HLA-G x CD3</td>
</tr>
<tr>
<td>Genmab</td>
<td>GEN1047</td>
<td>OmniRat</td>
<td>Oncology</td>
<td>B7H4 x CD3</td>
</tr>
<tr>
<td>Abbvie</td>
<td>TNB-383B</td>
<td>OmniFlic</td>
<td>Oncology</td>
<td>BCMA x CD3</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>TNB-486</td>
<td>OmniFlic</td>
<td>Oncology</td>
<td>CD19 x CD3</td>
</tr>
<tr>
<td>AMGEN</td>
<td>AMG 340</td>
<td>OmniFlic</td>
<td>Oncology</td>
<td>PSMA x CD3</td>
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<tr>
<td>Undisclosed</td>
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† Programs discovered by Tenebio

TECVAYLI® granted conditional marketing authorization (CMA) by the EMA. [Janssen Marks First Approval Worldwide for TECVAYLI® (teclistamab) with EC Authorisation of First-in-Class Bispecific Antibody for the Treatment of Patients with Multiple Myeloma | Johnson & Johnson (jnj.com)]
Rodent Platforms

- Endogenous Ig genes inactivated
- Expression of full human V gene diversity
- Streamlined conversion into fully human molecule

Well-validated transgene design utilizes rodent constant regions for robust immune responses from the B-cell repertoire
OmniChicken Platform

POWERED BY EVOLUTION

Greater evolutionary distance yields greater immunogenicity and more antibody diversity
Engineering of Ig Loci
ADAPTATION TO CHICKEN GENE CONVERSION PROCESS

Gene conversion

Engineered locus

Diversified B-cells

Germline VH3-23
VK3-15 or VL1-44

CDR-focused diversity

Human V’s selected for:

• High expression level, stability, ubiquity
• High sequence diversity in CDRs
• Low sequence diversity in FWs

Gene conversion
Common Light Chain Platforms

STANDARD IGG FORMAT TO DE-RISK DOWNSTREAM DEVELOPMENT\(^1\) OF BISPECIFIC MABS

\[\text{Rearranged human VK3-15 light chain combined with diversifying heavy chain}\]

\[\text{"Germlining" human VK3-15 light chain combined with diversifying heavy chain}\]

\[\text{Simple reformatting from monospecific into bispecific for efficient production}\]

\[\text{Common light chain for OmniFlic and OmniClic allows interchangeability between the platforms}\]

\(^1\)The Evolution of Bispecific Antibodies, Nimish Gera
https://doi.org/10.1080/14712598.2022.2040987
OmnidAb™: Heavy Chain Only Transgenic Chickens

HCO STRATEGY USING TRUNCATED LIGHT CHAIN (TLC)

- Normal chicken heavy chain can express as VH alone
- VHH transgene in development
Ultralong CDRH3s Create Novel Binding Domains

UNIQUE STRUCTURAL FEATURES OF ULTRALONG H3 ANTIBODIES

- Novel structure may enable targeting epitopes unreachable by standard antibodies
- Long H3 domains can be expressed on human VH framework, or alone as ~5kD Picobodies™

Picobodies™ as Building Blocks for Novel Therapeutics

regular IgG

different knob paratopes

knobs

bispecific formats

cocktails

multispecific formats
# OmniAb Antibody Repertoires

## OPTIONS AVAILABLE TO ADDRESS DIVERSE PARTNER OBJECTIVES

<table>
<thead>
<tr>
<th>Host</th>
<th>V genes</th>
<th>Structural and immunological features</th>
<th>Benefits for therapeutics discovery and development</th>
</tr>
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<tbody>
<tr>
<td>OmniMouse</td>
<td>Full human V gene diversity Choice of light chain isotype</td>
<td>Diverse V gene usage and mixed genetic backgrounds</td>
<td>Widely accessible and flexible workflows</td>
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<tr>
<td>OmniRat</td>
<td>Full human V gene diversity Choice of light chain isotype</td>
<td>Diverse V gene usage and mixed genetic backgrounds</td>
<td>Industry standard</td>
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<td>OmniChicken</td>
<td>Single framework VH3/VK3 or VH3/VL1</td>
<td>Evolutionarily divergent host system for robust immune responses</td>
<td>Widely accessible and flexible workflows, Extensive track record</td>
</tr>
<tr>
<td>OmniFlic</td>
<td>Full human VH gene diversity with non-diversifying VK3</td>
<td>Fixed light chain for bispecific applications</td>
<td>Bispecific applications leveraging standard IgG format</td>
</tr>
<tr>
<td>OmniClic</td>
<td>Single framework VH3/non-diversifying VK3</td>
<td>Fixed light chain for bispecific applications</td>
<td>Diverse epitope coverage, Excellent physical properties, Ease of manufacturing</td>
</tr>
<tr>
<td>Omni dAb</td>
<td>Single camelized human VH framework with truncated LC</td>
<td>Domain antibody of the “VHH” type</td>
<td>Diverse and new epitope coverage from human single-domain format, 12-15kD Building blocks for multispecific molecules</td>
</tr>
<tr>
<td>Omni Taur</td>
<td>Single framework VH4/VL1</td>
<td>Ultralong CDR-H3's for enormous structural diversity</td>
<td>Access cryptic epitopes, Unique modalities (picobodies™), Building blocks for multispecific molecules</td>
</tr>
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</table>
Screening Technology: xPloration®

1 | Loading

- Unique through-hole format
- Workflows for OmniAb B-cells

1.5 million, 40 µm
6 million, 20 µm

2 | Assay + Machine Vision

- Bright Field
- Enzymatic Reactions
- Fluorescent Antibodies

- Label-free
- Enzyme Inhibitions
- Cell Surface Binding

- GFP Reporter
- Immune Activation

- cAMP Signaling 20 hr
- Primary Cells 24-72 hr

- AI-driven hit detection

3 | Recovery & Single-Cell NGS

- Precise laser-based recovery
- 1 cell/sec (single-cell mode), single-cell barcoding
Leveraging Biological Intelligence with Computational Tools

### Biological Intelligence

- **OmniRat**
- **OmniChicken**
- **OmniMouse**
- **OmniTaur**
- **OmniFlic**
- **OmniClic**

Differentiated sources of antibody sequences

### Model-aided optimization

- Antibody homology modeling
- Computational antibody optimization

### In silico developability

- Sequence liability assessment
- Comparison to clinical antibodies
- Structure-based calculations

### Sequence databases and ML

- Customized cloud-based antibody sequence databases
- Machine learning classification
The OmniAb Platform

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<th>Create Diverse Antibody Pools</th>
<th>Screen Antibody Candidates</th>
<th>Identify the Right Antibody</th>
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<tr>
<td>Create Diverse Pools of High-Quality Naturally Optimized Antibodies</td>
<td>Screen Millions of Cells to Find Potential Therapeutic Candidates</td>
<td>Further Characterize, Select &amp; Optimize the Right Antibody</td>
</tr>
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</table>

OmniAb Technologies

- **OmniRat**
  - Robust Antibodies for Any Target
- **OmniMouse**
  - Computational Antigen Design & Proprietary Reagents
- **OmniChicken**
  - xPoration High-Throughput Single Cell Screening
- **OmniFlic**
  - Bispecific Antibody Generation
- **OmniClic**
  - Cow-inspired Antibodies for Difficult Targets
- **OmniTaur**
  - Gel Encapsulated Microenvironment (GEM) Single Cell Screening

Technology offering addresses the most critical challenges of antibody discovery
THANK YOU TO THE OMNIAB TEAM!

www.OmniAb.com