NOV1501

Fully human antibody therapeutics
- Currently at preclinical phase (GLP)
- Mechanism: Inhibition of DLL4/Notch and VEGF/VEGFR2 Interaction
- Proposed Indications: Gastric cancers and the other DLL4 positive solid tumors
- Dosage regimen: Every 2 week, IV infusion
- Competition: Demcizumab (Phase I)
- Patent expiration: ~2034

Key features

-Dual targeting (VEGF, DLL4)
-First Best in class

NOV1501 (ABL001)

bispecific antibody with better anti-cancer activity than Avastin

VEGF is a key inducer of angiogenesis in cancer, forms new blood vessels and results in tumor growth beyond a certain size. Anti-VEGF therapy has been widely used in patients with various tumor types, but the effects are variable and resistance is frequently encountered. VEGF induces DLL4 expression in endothelial tip cells. VEGF-induced expression of DLL4 in vascular endothelium leads to the activation of Notch signaling. Blocking the Notch/DLL4 signaling results tumor growth due to the formation of immature and poorly functional vessels that result in reduced tumor perfusion. Blockade of DLL4 can have potent inhibition effects on tumor growth that are resistant to anti-VEGF therapies. Furthermore, the simultaneous targeting of DLL4 and VEGF has produced additive of synergistic anti-tumor effects compared to single agents in a number of tumor models. NOV1501 is an anti-DLL4/anti-VEGF bispecific monoclonal antibody. It inhibits both DLL4/Notch and VEGF/VEGFR2 interactions in nanomolar level. It shows greater anti-cancer effects in various animal models in comparison to anti-DLL4 or anti-VEGF agents. NOV1501’s unique design of the bispecific antibody helps simpler purification and higher anti-cancer efficacy.

Current Status

End of Pre-Clinical stage (preparation of IND for FIH trial)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Pre-C</th>
<th>Ph 1</th>
<th>Ph 2a</th>
<th>Ph 2b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid tumors (gastric, colon, ovarian cancer)</td>
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Applicability and Market Dynamics

- NOV1501 is applicable to the following DLL4 positive cancers:

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<tbody>
<tr>
<td>Case number</td>
<td>318,660(1)</td>
<td>119,657(2)</td>
<td>55,801(3)</td>
<td>824,856(4)</td>
</tr>
<tr>
<td>DLL4 positivity</td>
<td>48% in tumor &amp; 22% in cancer stroma</td>
<td>72% in tumor/endothelial cells of cancer</td>
<td>30-80%, depends on grade of glioma</td>
<td>71% in endothelial cells of cancer</td>
</tr>
</tbody>
</table>

Advantages:

Antibody Combination vs. bispecific NOV1501 (ABL001)

Economic view
- Increased Cost
- Difficult to have both antibody epitopes

BD’s view
- No geometrical benefit targeting tumor-vascularity in tumors
- Potential for further combo therapy with other agents
- Frequent injection

Scientific view
- Lower manufacturing cost
- Potential attraction to both antibody epitopes
- Geometrical benefit targeting tumor-vascularity in tumors
- Potential for further combo therapy with other agents
- Improve patient compliance by reduced injection frequency

Patients’ view
- Increased Cost
- Difficult to have both antibody epitopes

<NOV1501 (ABL001)>
NOV1501

Project Leader: National OncoVenture
Originator: ABLBio Inc.

About National OncoVenture
http://nov.ncc.re.kr

National OncoVenture (NOV) has founded in 2011 to support Korean new drug R&D researchers for their cancer drug development. NOV’s cancer drug development experts lead the R&D program of selected pre-clinical candidates from the Korean drug R&D institutions and develop through human phase 2 clinical trials in global standards.

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Contact:
Mina Lee
Director, Business Development
E-mail: minalee@ncc.re.kr
Phone: 82-31-920-2772

Young-Whan Park, Ph D
Sr. Vice President, Business Development
E-mail: parkyo@ncc.re.kr
Phone: 82-31-920-2780

All BD people
E-mail: bd.nov@ncc.re.kr

Non-Clinical studies

**Efficacy**

**In vitro:**
- High binding affinity, competitive inhibition of ligands/receptors
- Inhibition of signaling pathway and various cell responses induced by VEGF or Dll4

**In vivo:**
- Better efficacy compared to antibodies targeting VEGF or Dll4 alone
- SCH, SNU16 gastric, A549 lung, Ovarian cancer patient-derived xenograft models

**CMC**
- Master cell bank (MCB)/Cultivation process (1 g/L) & purification process (65% yield & 95% purity)
- Analytical methods for quality control of ABL001

Non-Clinical Studies
- No significant adverse effects/NOAEL (no-observed-adverse-effect level): 10 mg/kg
- Similar PK profiles compared to general IgG antibody in cynomolgus monkeys

Clinical Study Plan: IND (First in human) in preparation

A Phase I Study to Assess the Safety, Tolerability and Pharmacokinetics of NOV1501
+ Parallel study for the possibility of DLL4 as a patient selection biomarker

Development Plan

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<tbody>
<tr>
<td>Solid tumors-Gastric Ca</td>
<td>QLP</td>
<td>IND</td>
<td>Ph 1</td>
<td>Ph 2</td>
<td>Ph 3</td>
<td>Ph 4</td>
<td>Ph 5</td>
<td>Ph 6</td>
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<tr>
<td>Solid tumors-Ovarian, CR, NSCLC</td>
<td>QLP</td>
<td>IND</td>
<td>Ph 1</td>
<td>Ph 2</td>
<td>Ph 3</td>
<td>Ph 4</td>
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Ph 2a with individual indication

National OncoVenture, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do, 10408, Republic of Korea