



NOV1501 (ABL001)

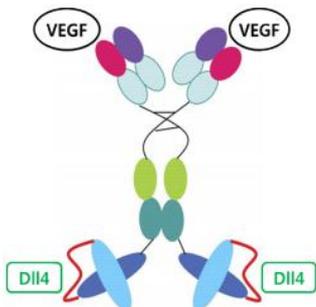
bispecific antibody with better anti-cancer activity than Avastin

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



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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 or 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)

Indication	Pre-C	Ph 1	Ph 2a	Ph 2b
Solid tumors (gastric, colon, ovarian cancer)				

Applicability and Market Dynamics

- NOV1501 is applicable to the following DLL4 positive cancers:

	Gastric cancer (2015E, 8MM)	Ovarian cancer (2015E, 11 MM)	GBM (2015E, 7MM)	Colon cancer (2015E, 8MM)
Case number	318,660 ⁽¹⁾	119,657 ⁽²⁾	55,801 ⁽³⁾	824,856 ⁽⁴⁾
DLL4 positivity	48% in tumor & 22% in cancer stroma	72% in tumor /endothelial cells of cancer	30-80%, depends on grade of glioma	71% in endothelial cells of cancer

(1). Incidence: GlobalData PharmaEtrack DB, 8 MM: France, Germany, Italy, Japan, Sapin, UK, US, China.

(2). Prevalence: GlobalData PharmaEtrack DB, 11 major market (MM): Brazil, China, France, Germany, India, Italy, Japan, Russia, Sapin, UK, US

(3). Incidence: GlobalData PharmaEtrack DB, 7 MM: France, Germany, Italy, Japan, Sapin, UK, US.

Advantages:

Antibody Combination vs. bispecific NOV1501 (ABL001)

	Combination Cocktail	VS	NOV1501(ABL001) Bispecific Ab
Economic view	-Increased Cost		-Lower manufacturing cost
BD's view	-Difficult to have both antibody pipelines		-Potential attraction to big pharmaceuticals
Scientific view	-No geometrical benefit -Difficulty in further combo therapy with other chemo/immuno-oncology agents		-Geometrical benefit targeting tumor vessels in tumors -Potential for further combo therapy with other agents
Patients' view	-Frequent injection		-Improve patient compliance by reduced injection frequency



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.

Supported by the Ministry of the Health and Welfare

Contact:

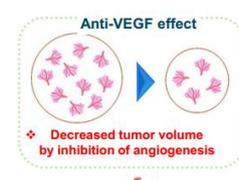
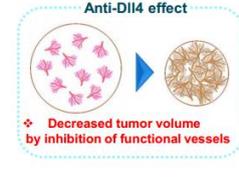
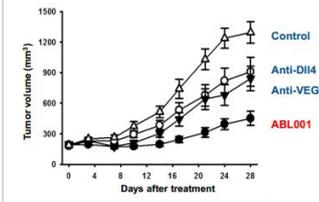
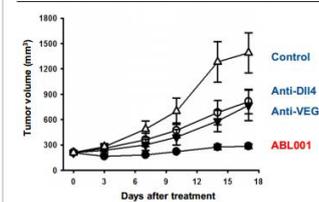
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Non-Clinical studies

Efficacy

In vitro:	<ul style="list-style-type: none"> High binding affinity, competitive inhibition of ligands/receptors Inhibition of signaling pathway and various cell responses induced by VEGF or DLL4
In vivo:	<ul style="list-style-type: none"> Better efficacy compared to antibodies targeting VEGF or DLL4 alone SCH, SNU16 gastric, A549 lung, Ovarian cancer patient-derived xenograft models <div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; padding: 5px;"> <p style="text-align: center;">Combination effect of ABL001</p> <p style="text-align: center;">Anti-VEGF effect</p>  <p style="text-align: center;">Anti-DLL4 effect</p>  </div> <div style="border: 1px solid black; padding: 5px;"> <p style="text-align: center;">Tumor growth in A549 lung cancer model</p>  <p style="text-align: center;">Tumor growth in SCH gastric cancer model</p>  </div> </div>

CMC

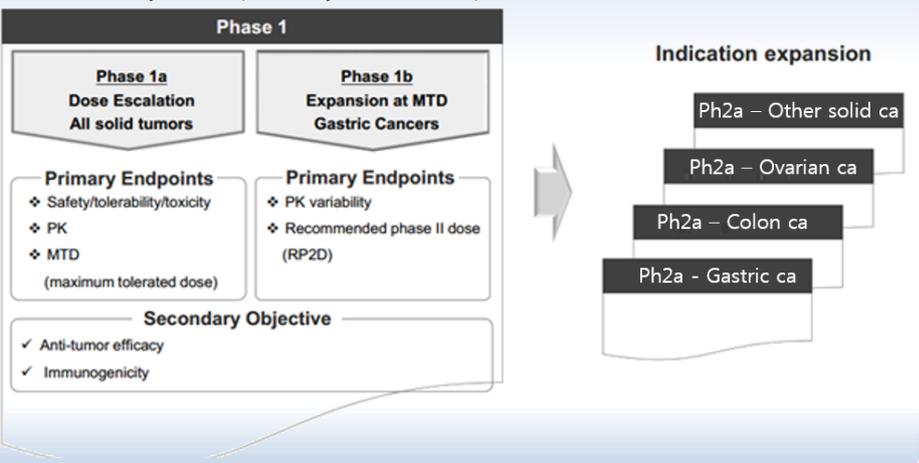
- Master cell bank (MCB)/Cultivation process (1 g/L) & purification process (65% yield & 95% purity)
- Analytical methods for quality control of ABL001

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

Indication	2015	2016	2017	2018	2019	2020	2021	2022
Solid tumor -Gastric ca		GLP	IND Ph 1		Ph1 expansion			
Solid tumor-Ovarian, CRC, NSCLC							Ph 2a with individual indication	