

Intelligent Ecosystem: Fast Development Track of ActRII Antibody for Obesity Treatment

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Abstract

Great Bay Bio (GBB) used the antibody sequence generation platform, AlfaBody, obtaining five potential Hit antibody candidates out of 260 anti-ActRII AI-generated sequences. Within 6 weeks, the three antibody candidates were obtained with 50-115 fold improvement of affinity by using the antibody molecule optimization platform, AlfaDAX. The stable cell line was obtained within 1.5 months through AlfaCell, the site-specific integration platform for cell line development. The poster will present that with GBB's intelligent ecosystem, the antibody can be developed into a preclinical asset within 7-9 months.

Materials & Methods

♦ Great Bay Bio Intelligent Ecosystem

Table 1 The affinity data for the 5 potential Hit antibody candidates targeting ActRII.

Sample ID	KD (M)	ka (1/Ms)	kdis (1/s)
B134	1.13E-08	1.78E+06	2.02E-02
B141	1.06E-08	1.35E+06	1.43E-02
B149	1.10E-08	8.66E+05	9.55E-03
B150	1.57E-08	1.19E+06	1.87E-02
B151	1.28E-08	9.25E+05	1.18E-02

2. Affinity maturation of the Hit antibody molecule B149 was performed over 2 rounds, taking a total of 6 weeks.





Fig.1 Intelligent ecosystem for improving biologics development from drug discovery to CMC within 7 months.

Fig.4 Octet binding profile of antibody molecules after affinity maturation.

Table 2 The affinity data for targeting ActRII.

Sample ID	Affinity Fold	KD (M)	ka (1/Ms)	kdis (1/s)
B149	1	5.02E-09	1.66E+06	8.33E-03
BTH39BTL25	53	9.41E-11	1.79E+06	1.69E-04
BTH38BTL25	66	7.57E-11	1.83E+06	1.39E-04
BTH41BTL25	115	4.38E-11	2.12E+06	9.28E-05



Binding Affinity Assay

> AlfaBodY: Antibody Molecule Generation Platform

- AlfaDAX: Antibody Molecule Design and Optimization Platform
- AlfaCell: Site-specific Integration Cell Line Development Platform
- > AlfaMedX: Cell Culture Media Development Platform
- > AlfaOPA: No-screening Cell Culture Media Optimization Platform
- ♦ Great Bay Bio Antibody Discovery Process



Fig.2 The process of antibody discovery.

- The AlfaBodY platform generates Hit antibody molecules that bind to antigens based on AI structure prediction.
- > Rapid druggability prediction of Hit molecules is performed through the AlfaDAX platform.
- Simultaneously conducts a "3-in-1" optimization process that includes humanization, affinity maturation, and druggability.

Protein Conc.(ng/ml)

	BTH41BTL25	BTH39BTL25	BTH38BTL25	Benchmark
EC50	8.215	11.62	11.83	7.894

Fig.5 ELISA data of antibody molecules after affinity maturation.

✓ With transient expression, 20 antibody sequences per round, 40 sequences in total.
 ✓ 3 antibodies showed a 50-fold increase, with the highest showing an increase of 115-fold.
 ✓ ELISA verified binding affinity assay.

 Table 3 AlfaDAX assessed the druggability of affinity-matured antibodies, with scores meeting requirements, thus reducing the risk of process development.

Sample ID	Humanization (≥0.2)	Stable (≤-15)	Aggregation (≤1)	Viscosity (≤1)	Nonspecific Binding (≤1)
BTH38BTL25	0.78	-17.12	0.4	0.4	0.62
BTH39BTL25	0.78	-15.6	0.43	0.45	0.44
BTH41BTL25	0.78	-15.14	0.43	0.43	0.46
Benchmark	0.67	-14.14	0.55	0.49	0.63

• Great Bay Bio SSI Cell Line Development Process



Results & Discussion

1. AlfaBodY, using a structure-based design, generated 260 antibody sequences targeting ActRII.





Fig.3 Octet binding profile of Hit antibody candidates.

6 weeks to complete RCB construction

Fig.6 The site-specific integration cell line development platform, AlfaCell, completed the generation of stable cell lines for antibody production within 6 weeks.

Results & Discussion

GBB's intelligent ecosystem has successfully streamlined the process from designing and optimizing antibody sequences to generating stable cell lines for commercial production. The antibody expression level meets the needs of *in vivo* efficacy evaluation. The candidate antibody monoclonal cell line generated by the AlfaCell platform can be used for commercial production, thus ensuring consistency in antibody quality (including glycosylation modifications) between the antibody discovery and process development stages, minimizing development risks.

<sup>BTH41BTL25
BTH39BTL25
BTH38BTL25</sup>

Benchmark