

(51) International Patent Classification:

C07K 16/28 (2006.01) C12N 15/62 (2006.01)
C07K 14/705 (2006.01) A61K 39/00 (2006.01)

(21) International Application Number:

PCT/US2024/045653

(22) International Filing Date:

06 September 2024 (06.09.2024)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/537,382 08 September 2023 (08.09.2023) US
63/639,356 26 April 2024 (26.04.2024) US

(71) Applicant: **MLAB BIOSCIENCES, INC.** [US/US]; 117 Kendrick Street, Suite 400, Needham, Massachusetts 02494 (US).

(72) Inventors: **ZHU, Yunxiang**; c/o MLAB Biosciences, Inc., 117 Kendrick Street, Suite 400, Needham, Massachusetts 02494 (US). **CHEN, Yangde**; c/o MLAB Biosciences, Inc., 117 Kendrick Street, Suite 400, Needham, Massachusetts 02494 (US). **ZHOU, Yanfeng**; c/o MLAB Biosciences, Inc., 117 Kendrick Street, Suite 400, Needham, Massachusetts 02494 (US).

(74) Agent: **XIAO, Jian** et al.; Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, California 94304-1018 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

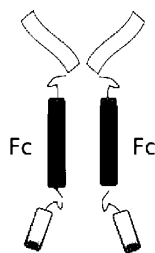
(88) Date of publication of the international search report:

17 April 2025 (17.04.2025)

(54) Title: BIFUNCTIONAL PROTEINS AND USES THEREOF

FIG. 1E

Notch Ligand ECD



Muscle-targeting scFv

(57) Abstract: Provided herein are compositions and methods of treating muscular dystrophies by administering an effective amount of a composition comprising a bifunctional protein comprising a first binding moiety that binds to muscle-specific molecules and a second functional domain that activates Notch signaling, thereby spatiotemporally activating Notch signaling in muscle tissues to boost satellite cell renewal in situ, and thus enhancing muscle repair/regeneration to improve muscle function as a treatment of various muscular dystrophies and sarcopenia. Also provided are engineered DLL4 extracellular domains and protein constructs comprising thereof.