

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization

International Bureau

(43) International Publication Date  
21 November 2024 (21.11.2024)



(10) International Publication Number  
**WO 2024/238807 A3**

(51) International Patent Classification:  
C07K 14/015 (2006.01) C12N 15/864 (2006.01)

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).

(21) International Application Number:  
PCT/US2024/029714

**Published:**

(22) International Filing Date:  
16 May 2024 (16.05.2024)

- 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))

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
63/502,595 16 May 2023 (16.05.2023) US  
PCT/US2023/072424

(88) Date of publication of the international search report:  
26 December 2024 (26.12.2024)

17 August 2023 (17.08.2023) US  
63/625,790 26 January 2024 (26.01.2024) US  
63/643,890 07 May 2024 (07.05.2024) US

(71) Applicant: **AFFINIA THERAPEUTICS INC.** [US/US];  
43 Foundry Ave., Suite 120, Waltham, MA 02453 (US).

(72) Inventors: **ALBRIGHT, Charles, Francis**; c/o Affinia Therapeutics Inc., 43 Foundry Ave., Suite 120, Waltham, MA 02453 (US). **OLIVIERI, Kevin, C.**; c/o Affinia Therapeutics Inc., 43 Foundry Ave., Suite 120, Waltham, MA 02453 (US). **CAO, Xiaohong**; c/o Affinia Therapeutics Inc., 43 Foundry Ave., Suite 120, Waltham, MA 02453 (US). **TAN, Jie**; c/o Affinia Therapeutics Inc., 43 Foundry Ave., Suite 120, Waltham, MA 02453 (US).

(74) Agent: **BECKER, Daniel, M.** et al.; Fenwick & West LLP,  
801 California Street, Mountain View, CA 94041 (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,

(54) Title: RECOMBINANT AAVS WITH IMPROVED TROPISM AND SPECIFICITY

(57) Abstract: The present disclosure provides a modified AAV capsid protein comprising a targeting peptide in variable region VIII (VR VIII) and/or a peptide segment in variable region I (VR I). The modified AAV capsid protein can form an rAAV, which has a preferred tropism, specificity or biodistribution *in vivo* or *in vitro*. The rAAV of the present disclosure can be used for gene therapies targeted at a specific tissue.

WO 2024/238807 A3