



(51) International Patent Classification:

A61K 39/13 (2006.01) *A61K 39/12* (2006.01)
C12N 7/00 (2006.01)

(21) International Application Number:

PCT/EP2015/063489

(22) International Filing Date:

16 June 2015 (16.06.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/013,379 17 June 2014 (17.06.2014) US
14176071.0 8 July 2014 (08.07.2014) EP

(71) Applicant: **CRUCCELL HOLLAND B.V.** [NL/NL];
Archimedesweg 4, NL-2333 CN Leiden (NL).

(72) Inventors: **SANDERS, Barbara, Petronella**;
Archimedesweg 4-6, NL-2333 CN Leiden (NL).
CUSTERS, Jérôme H.H.V.; Archimedesweg 4-6, NL-
2333 CN Leiden (NL). **EDO-MATAS, Diana**;
Archimedesweg 4-6, NL-2333 CN Leiden (NL). **UIL,**
Taco, Gilles; Archimedesweg 4-6, NL-2333 CN Leiden
(NL). **LEWIS, John, Alfred**; 270 West Main Road, Little
Compton, RI 2837 (US).

(74) Agents: **MANTEN, Annemieke** et al.; Archimedesweg 4-
6, NL-2333 CN Leiden (NL).

(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, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, 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, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, 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, 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).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

(54) Title: COLD-ADAPTED-VIRAL-ATTENUATION (CAVA) AND NOVEL ATTENUATED POLIOVIRUS STRAINS

(57) Abstract: A poliovirus (PV) strain was attenuated by a novel method of Cold-Adapted-Viral-Attenuation (CAVA). The resulting recombinant attenuated PV, CAVA-PV, shows wild-type replication at 30°C, but no substantial replication at 37°C. The inability to replicate at 37°C is defined by an inability to quantify virus during infection at this temperature by titration (infectious units), qPCR (viral RNA) or Electron Microscopy (visual signs of infection). CAVA-PV is genetically stable under production conditions and shows utility for use as the backbone to produce attenuated strains with the same antigenic profile as conventional vaccines by replacing the sequence coding for the capsid of CAVA-PV with sequences coding for capsids of different PV strains. Furthermore, mutations identified in CAVA-PV can be engineered into different, even wild-type and neurovirulent poliovirus background strains to obtain additional CAVA-PV strains.



WO 2015/193324 A1