

(19) World Intellectual Property
Organization
International Bureau



(10) International Publication Number
WO 2015/158317 A8

(43) International Publication Date
22 October 2015 (22.10.2015)

- (51) International Patent Classification:
C07F 9/6521 (2006.01) C07F 9/6558 (2006.01)
- (21) International Application Number:
PCT/CZ2015/000037
- (22) International Filing Date:
15 April 2015 (15.04.2015)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
PV 2014-259 15 April 2014 (15.04.2014) CZ
- (71) Applicant: ZENTIVA, K.S. [CZ/CZ]; U Kabelovny 130,
102 37 Praha 10 (CZ).
- (72) Inventors: STEFKO, Martin; Cemysevskeho 15, 851 01
Bratislava (SK). MAN, Stanislav; Ke Kyselce 191, 687 32
Nezdenice (CZ). RADL, Stanislav; Ohnicova 127, 250 84
Kvetnice (CZ).
- (74) Agents: JIROTKOVA, Ivana et al.; ROTT, RUZICKA &
GUTTMANN, Vinohradska 37, 120 00 Praha 2 (CZ).
- (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))

Published:

- with international search report (Art. 21(3))

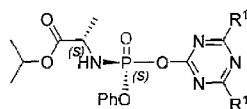
(48) Date of publication of this corrected version:

22 September 2016

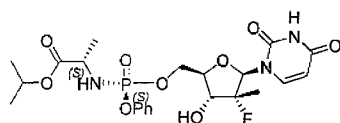
(15) Information about Correction:

see Notice of 22 September 2016

(54) Title: USE OF A 1,3,5-TRIAZIN-2-YL PHOSPHORAMIDATE COMPOUND IN THE SYNTHESIS OF SOFOSBUVIR



(I)



(II)

(57) Abstract: The present invention relates to a new type of 1,3,5-triazin-2-yl phosphoramidates of general formula I with the absolute configuration (S) at the phosphorus atom, an Sp diastereoisomer, wherein R¹ and R² can independently be H, a C1-C6 (un)branched alkyl, a C1-C6 (un)branched alkoxy group, a C1-C6 (un)branched alkylsulfanyl group, C1-C6 (un)branched monoalkylamino or dialkylamino group, including cyclic amino groups, e.g. pyrrolidino, piperidino or morpholino group; and to their use for the production of biologically active phosphoramidate prodrugs, especially sofosbuvir of formula II. Sofosbuvir II is a nucleotide inhibitor of the RNA polymerase, used for the treatment of hepatitis C in the form of a prodrug, releasing the active antiviral agent 2'-deoxy-2'-a-fluoro- P-C-methyluridine-5'-triphosphate in the organism.