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NATIONAL FORENSIC LABORATORY
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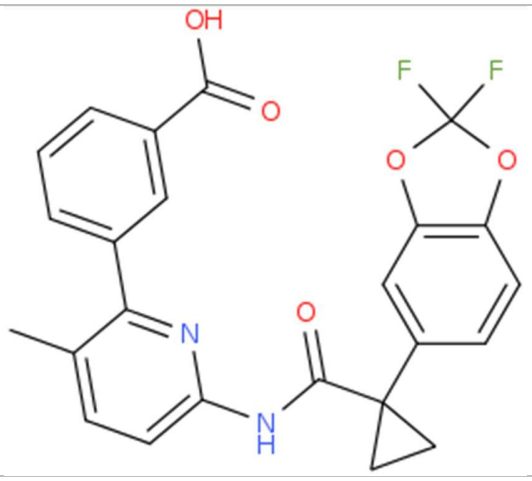
ANALYTICAL REPORT

VX-809 (C24H18F2N2O5)

3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid

Remark – other NPS detected: none

Sample ID:	1500-16
Sample description:	powder
Sample type:	test purchase /RESPONSE -purchasing
Date of entry (DD/MM/YYYY) into NFL database:	12/02/2016
Report updates (if any) will be published here:	http://www.policija.si/apps/nfl_response_web/seznam.php

Substance identified - structure[1] (base form)	
Systematic name	3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid
Other names	Lumacaftor
Formula (per base form)	C24H18F2N2O5
M_w (g/mol)	452,41
Salt form/anions detected	chloride (trace)
StdInChIKey (per base form)	UFSKUSARDNFIRC-UHFFFAOYSA-N
Other NPS detected	none
Additional info (purity..)	

[1] Created by OPSIN free tool: http://opsin.ch.cam.ac.uk/ **DOI:** 10.1021/ci100384d

Report updates

date	comments (explanation)

Instrumental methods (if applied) in NFL

1. GC-MS (Agilent): GC-method is RT locked to tetracosane (9.258 min). Injection volume 1 µl and split mode (1:50). Injector temperature: 280 0C. Chromatographic separation: on column HP1-MS (100% dimethylpolysiloxane), length 30 m, internal diameter 0.25 mm, film thickens 0.25 µm. Carrier gas He: flow-rate 1.2 ml/min. GC oven program: 170 ^{0}C for 1 min, followed by heating up to 190 ^{0}C at rate 8 ^{0}C/min, then heating up to 293 0C at a rate of 18 ^{0}C/min, hold for 6.1 min, then heating at 50 ^{0}C/min up to 325 ^{0}C and finally 9.1 min isothermal. MSD source EI = 70 eV. GC-MS transfer line T= 235^{0}C, source and quadropole temperatures 280^{0}C and 180^{0}C, respectively. Scan range m/z scan range: from 50 (30 until 6 min.) to 550 (300 until 6 min) amu.

2. HPLC-TOF (Agilent): 6230B TOF with Agilent 1260 Infinity HPLC with binary pump, column: Zorbax Eclipse XDB-C18, 50 x 4.6 mm, 1.8 micron. Mobile phases (A) 0.1% formic acid and 1mM ammonium formate in water; (B) 0.1% formic acid in methanol (B). Gradient: starting at 5% B, changing to 40% B over 4 min, then to 70% over 2 min and in 5 min to 100%, hold 1 min and back to 5%, equilibration for 1.7 min. The flow rate: 1.0 ml/min; Injection volume 1 µl. MS parameters: 2GHz, Extended Dynamic range mode to a maximum of 1700 amu, acquisition rate 1.30 spectra/sec. Sample ionisation: by Agilent Jet Stream technology (Dual AJS ESI). Ion source: positive ion scan mode with mass scanning from 82 to 1000 amu. Other TOF parameters: drying gas (N2) and sheath temperature 325 °C; drying gas flow rate 6 l/min; sheath gas flow rate 8 l/min; nebulizer 25 psig; Vcap. 4000 V; nozzle 2000 V; skimmer 65 V; fragmentor 175 V and Octopole RF 750 V.

3.FTIR-ATR (Perkin Elmer): scan range 4000-400 cm-1; resolution 4cm-1

4. GC- (MS)-IR solid phase (GC-MS (Agilent) & IR (Spectra analyses-Danny)
GC-method: Injection volume 1 µl and split mode (1:5). Injector temperature 280 ^{0}C. Chromatographic separation as above **(1).**
Split MS : IR = 1: 9.
MSD source EI = 70 eV. GC-MS transfer line T= 235^{0}C, source and quadropole temperatures 280^{0}C and 180^{0}C, respectively. Scan range m/z scan range: from 50 (30 until 6 min.) to 550 (300) amu.
IR (condesed (solid) phase): IR scan range 4000 to 650, resolution 4 cm^{-1} .

5. **IC** (anions) (Thermo Scientific, Dionex ICS 2100), Column: IonPac AS19, 2 x 250mm; Eluent: 10mM KOH from 0 to 10 min, 10-58 mM from 10 to 40min; Flow rate: 0.25 ml/min; Temperature: 30˚C; Suppressor: AERS 500 2mm, suppressor current 13mA; Inj. Volume: 25 µl

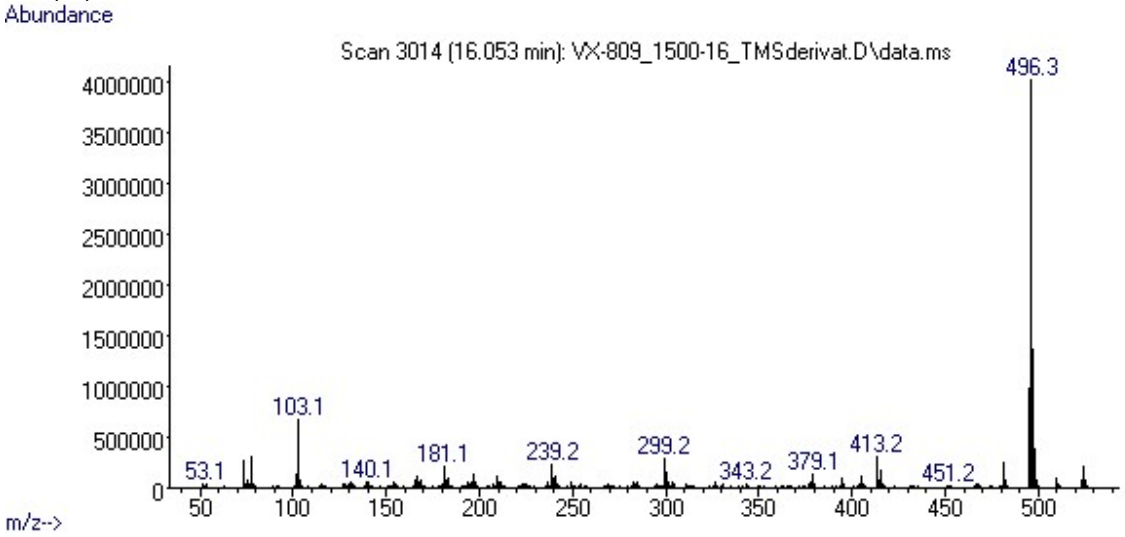
Supporting information

Solubility in	result/remark
CH_2Cl_2	low (bad)
MeOH	soluble
H_2O	low (bad)

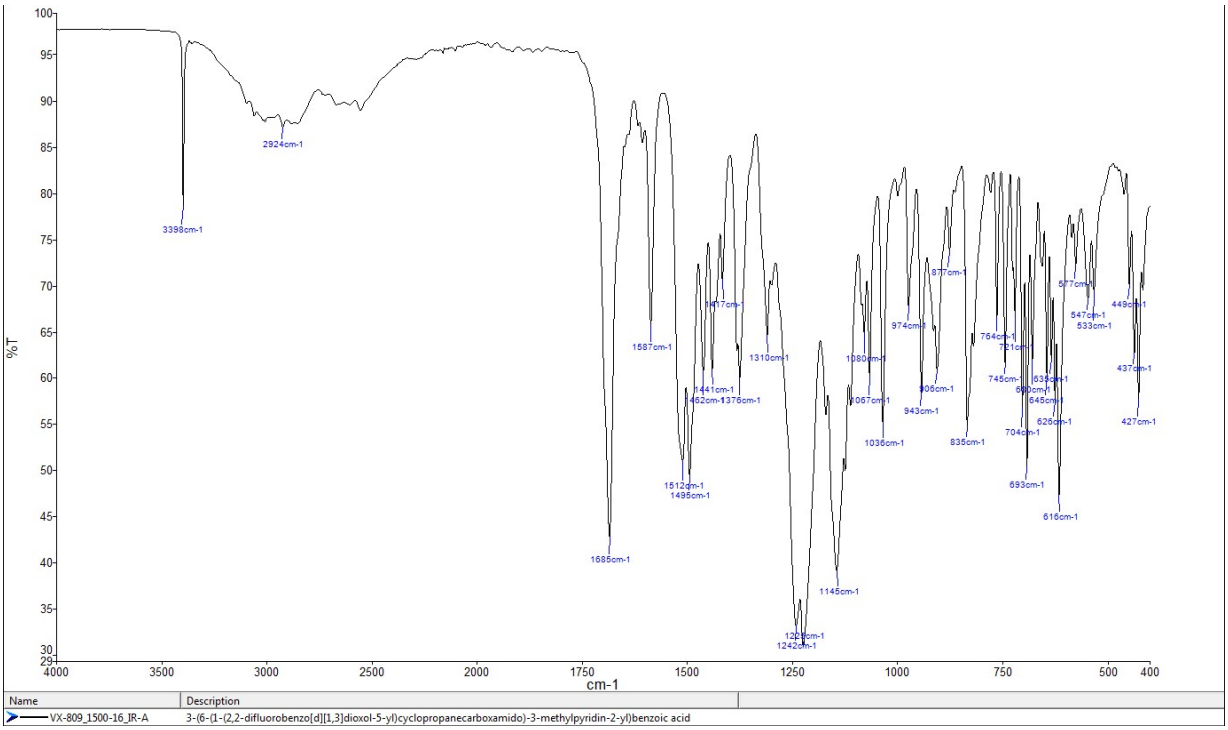
Analytical technique:	applied	remarks
GC-MS (EI ionization)	+	NFL GC-RT (min): 16,05 BP(1): 496; BP(2): 497,BP(3) :495, **RT and peaks refer to TMS derivative of substance**
HPLC-TOF	+	Exact mass (theoretical): 452,1184; measured value Δppm:0,43; formula:C24H18F2N2O5
FTIR-ATR	+	direct measurement (sample as received)
FTIR (solid phase) always as base form		
IC (anions)	+	
NMR (in FKKT)		
validation		
other		

ANALYTICAL RESULTS

MS (EI)



FTIR-ATR - direct measurement (sample as received)



TOF REPORT

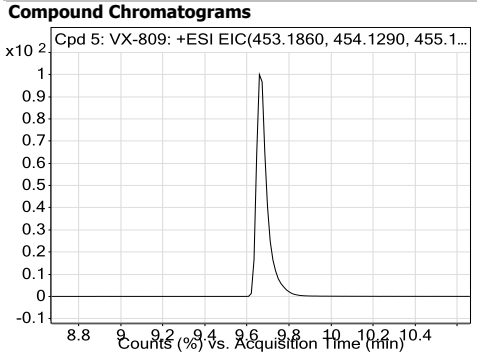
Data File	VX-809_1500-16_TOF.d	**Sample Name**	ID_1500-16
Sample Type	Sample	**Position**	P1-F7
Instrument Name	6230B TOF LC-MS	**User Name**	TG
Acq Method	general-1512015-XDB-C18-ESI-poz-pod.m	**Acquired Time**	2/10/2016 8:14:00 AM
IRM Calibration Status	Success	**DA Method**	Drugs_NFL.m
Comment	extract in MeOH		

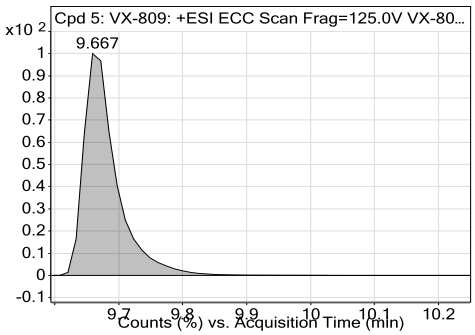
Compound Table

Label	Compound Name	MFG Formula	Obs. RT	Obs. Mass
Cpd 5: VX-809	VX-809	C24 H18 F2 N2 O5	9.667	452.1182

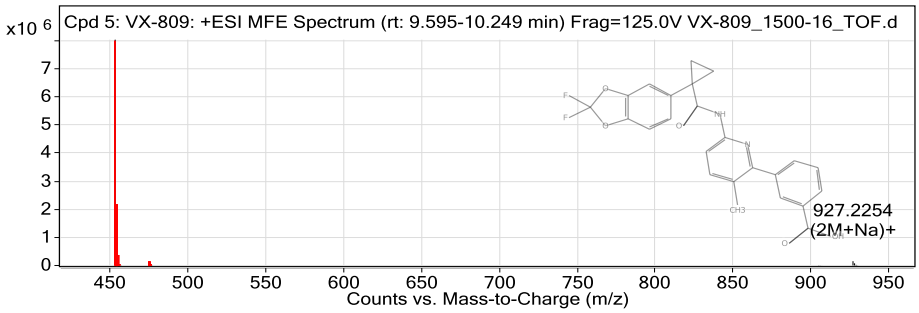
Name	*Obs. m/z*	Obs. RT	Obs. Mass	DB RT	DB Formula	DB Mass	DB Mass Error (ppm)
VX-809	453.1254	9.667	452.1182	9.67	C24 H18 F2 N2 O5	452.1184	0.43

Compound Chromatograms

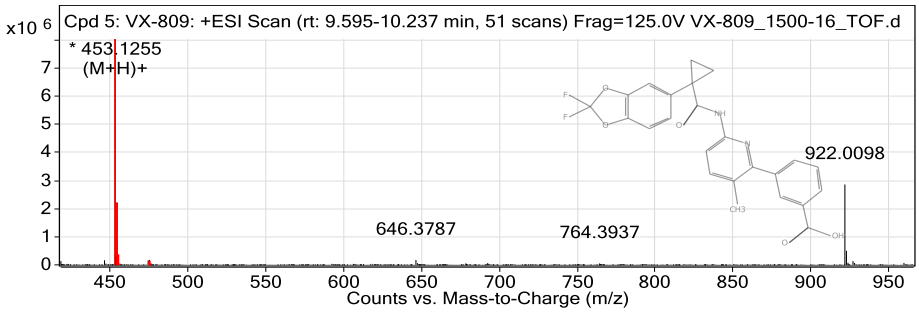




MFE MS Zoomed Spectrum



MS Zoomed Spectrum



MS Spectrum Peak List

Obs. m/z	Charge	Abund	Formula	Ion/Isotope
453.1254	1	8038577.5	C24 H18 F2 N2 O5	(M+H)+
454.1288	1	2157293.17	C24 H18 F2 N2 O5	(M+H)+
455.1319	1	328668.84	C24 H18 F2 N2 O5	(M+H)+
456.1339	1	38211.92	C24 H18 F2 N2 O5	(M+H)+
475.1072	1	119896.41	C24 H18 F2 N2 O5	(M+Na)+
476.1103	1	29844.21	C24 H18 F2 N2 O5	(M+Na)+
905.2429	1	7568.61		(2M+H)+
927.2254	1	152825.72		(2M+Na)+
928.2284	1	76936.19		(2M+Na)+
929.2309	1	21540.31		(2M+Na)+

--- End Of Report ---

Peak Integration Report

Sample Name:	**VX-809_1500-16_IC**	*Inj. Vol.:*	**25,00**
Injection Type:	**Unknown**	*Dilution Factor:*	**1,0000**
Program:	**ANIONI**	*Operator:*	**kemija**
Inj. Date / Time:	**09-feb-2016 / 14:23**	*Run Time:*	**42,00**

No.	Time min	Peak Name	Peak Type	Area µS*min	Height µS	Amount mg/L
1,00	8,61	**Chloride**	BMB	0,53	2,33	n.a.
		TOTAL:		0,53	2,33	0,00