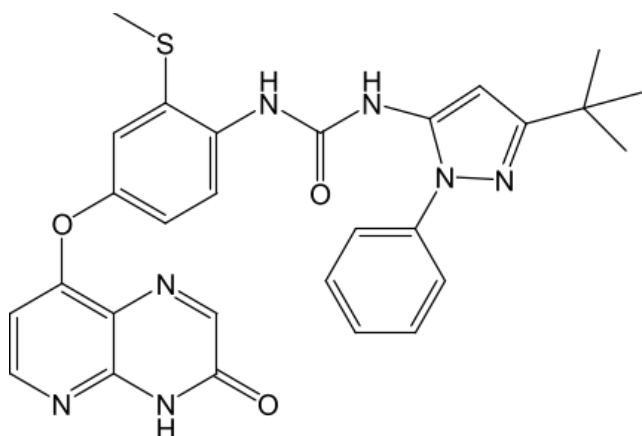


RGNCY-0023 (CTT241161)

Rev 1.0 – August 13, 2015



Systematic Name: 1-(3-(tert-butyl)-1-phenyl-1H-pyrazol-5-yl)-3-(2-(methylthio)-4-((3-oxo-3,4-dihydropyrido[2,3-b]pyrazin-8-yl)oxy)phenyl)urea

Pub Med 25500121
Ref.

Molecular Weight: 541.63

Molecular Formula: C₂₈H₂₇N₇O₃S

SMILES: CC(C)(C)C1=NN(C2=CC=CC=C2)C(NC(NC(C(SC)=C3)=CC=C3OC4=C5C(NC(C=N5)=O)=NC=C4)=O)=C1

Purity: 98%

CAS No: 1163719-91-2

Description

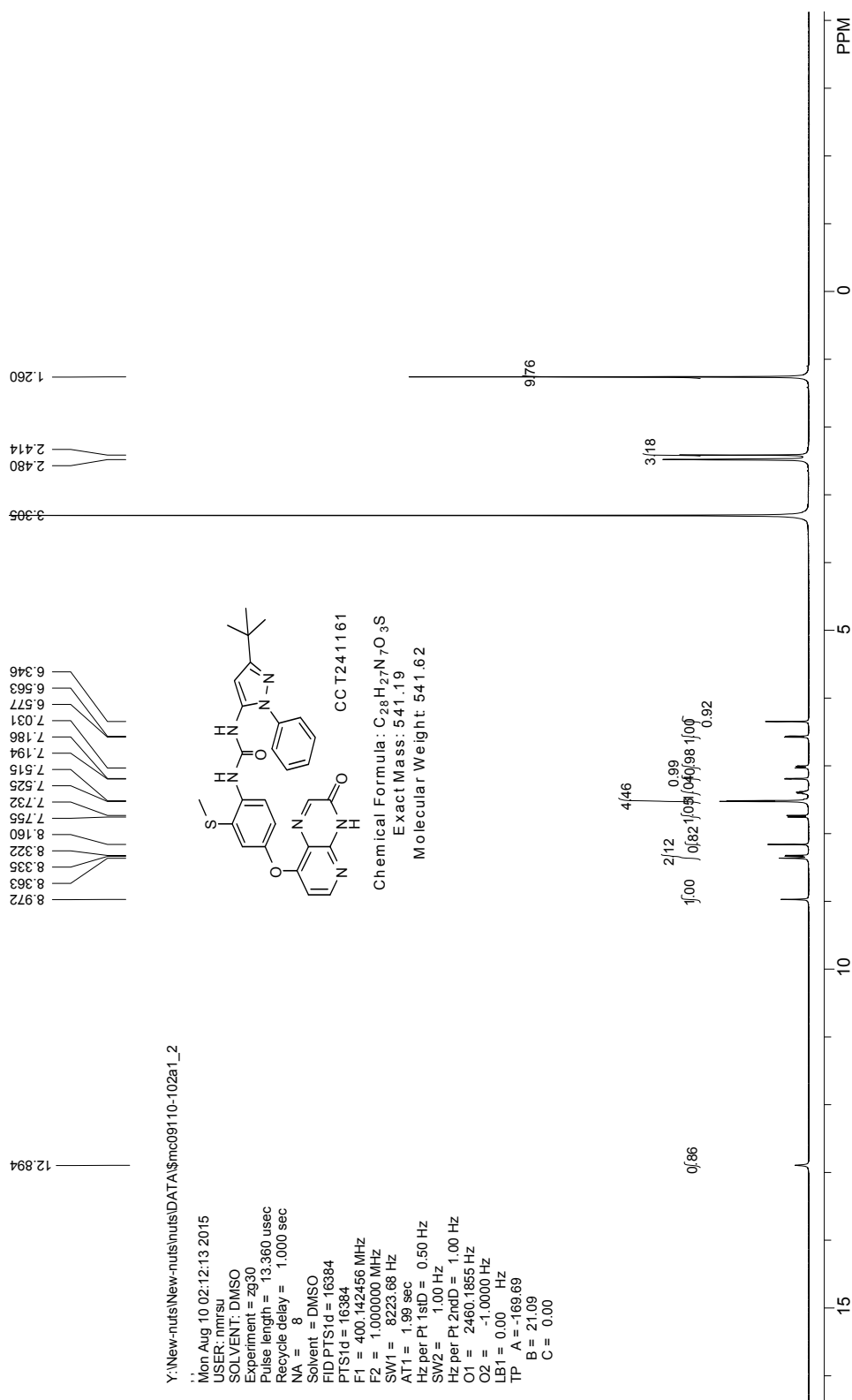
Another member of the series of orally available pan-RAF/SFK inhibitor is active against treatment-naïve BRAF and NRAS mutant tumors. It is active in tumors from patients who developed resistance to BRAF-selective inhibitors and a BRAF plus MEK inhibitor

combination. This compound series could provide a first-line therapy for treatment naïve patients and a second-line therapy for a range of patients with relapsed melanoma. Phase 1 clinical trials will commence in 2015 with this series of compounds. IC_{50} 0.03 μ M and 0.01 μ M for BRAF kinase and SRC kinase respectively.

References

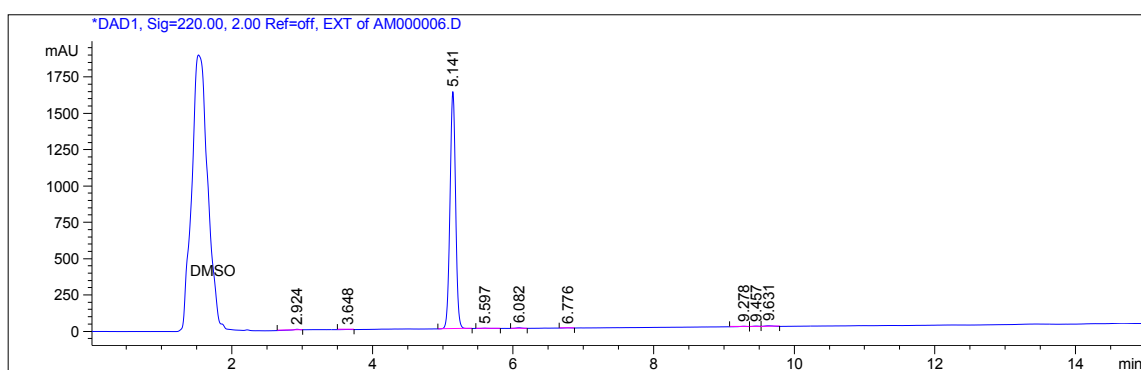
Girotti, Maria Romina, et al. "Paradox-Breaking RAF Inhibitors that Also Target SRC Are Effective in Drug-Resistant BRAF Mutant Melanoma." *Cancer cell* 27.1 (2015): 85-96.

Analytical Data



Data File D:\CHEM32\DATA\2015\150810\2015-08-10\AM000006.D
Sample Name: MC09110-102A1

```
=====
Acq. Operator   : XXYAN                      Seq. Line :    6
                                           Location : Vial 36
Injection Date  : 10-Aug-15, 10:54:21        Inj       :    1
                                           Inj Volume: 1 µl
                                           Actual Inj Volume: 4 µl
Different Inj Volume from Sequence !
Acq. Method     : M-A50B50.M
Analysis Method  : D:\CHEM32\METHOD\WAITING-C8.M
Last changed    : 8/10/2015 11:09:49 AM by XXYAN
                  (modified after loading)
Method Info     : Velch Ultimate XB-C18,5um,150*4.6mm
                  A:0.1 % FA in H2O B:0.1% FA in ACN
=====
```



Area Percent Report

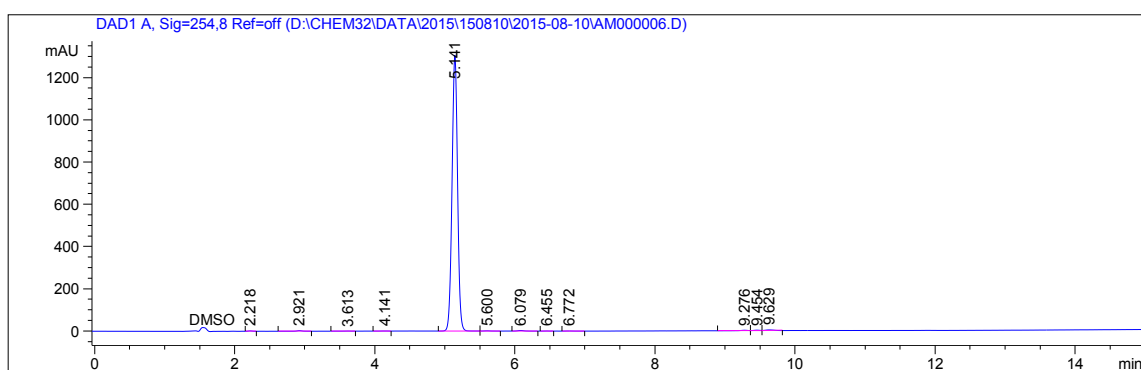
```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: DAD1, Sig=220.00, 2.00 Ref=off, EXT
Signal has been modified after loading from rawdata file!

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.924	BB	0.0849	25.53939	4.45236	0.2794
2	3.648	BB	0.1003	5.45876	8.57333e-1	0.0597
3	5.141	BB	0.0863	8990.24414	1632.04309	98.3553
4	5.597	BB	0.0947	9.25261	1.48581	0.1012
5	6.082	BB	0.0881	21.35851	3.89011	0.2337
6	6.776	BB	0.0904	8.44040	1.39855	0.0923
7	9.278	BV	0.1020	20.12952	2.93403	0.2202
8	9.457	VV	0.0971	20.89904	3.33473	0.2286
9	9.631	VB	0.1370	39.25801	4.53480	0.4295

Data File D:\CHEM32\DATA\2015\150810\2015-08-10\AM000006.D
Sample Name: MC09110-102A1

```
=====
Acq. Operator   : XXYAN                      Seq. Line :    6
                                           Location  : Vial 36
Injection Date  : 10-Aug-15, 10:54:21        Inj       :    1
                                           Inj Volume: 1 µl
                                           Actual Inj Volume: 4 µl
Different Inj Volume from Sequence !
Acq. Method     : M-A50B50.M
Analysis Method  : D:\CHEM32\METHOD\WAITING-C8.M
Last changed    : 8/10/2015 11:08:46 AM by XXYAN
                  (modified after loading)
Method Info     : Velch Ultimate XB-C18,5um,150*4.6mm
                  A:0.1 % FA in H2O B:0.1% FA in ACN
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: DAD1 A, Sig=254,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.218	BB	0.0593	6.20232	1.67054	0.0857
2	2.921	BB	0.0742	13.26609	2.75180	0.1832
3	3.613	BB	0.0862	1.96939	3.57624e-1	0.0272
4	4.141	BB	0.0881	2.32942	4.11354e-1	0.0322
5	5.141	BV	0.0856	7132.38281	1307.88208	98.5029
6	5.600	VB	0.0945	6.94018	1.11739	0.0958
7	6.079	BB	0.0931	16.92028	2.77711	0.2337
8	6.455	BB	0.0774	1.67313	3.40235e-1	0.0231
9	6.772	BB	0.0892	2.56672	4.45697e-1	0.0354
10	9.276	BV	0.1054	14.65565	2.09968	0.2024