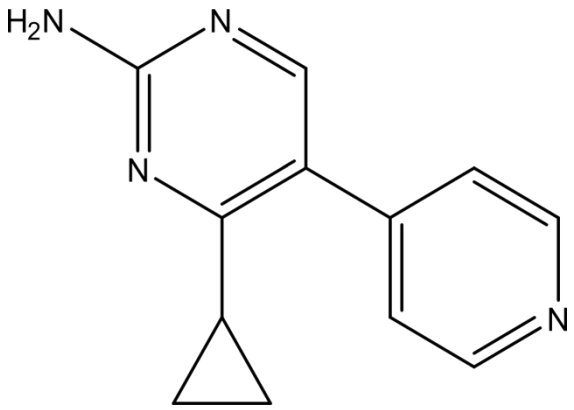
RGNCY-0013 (Glucocorticoid Resistance Inhibitor J9)



Systematic Name:
4-cyclopropyl-5-(pyridin-4-yl)pyrimidin-2-amine

Molecular Weight: 212.26

Molecular Formula: $C_{12}H_{12}N_4$

SMILES:
NC1=NC(C2CC2)=C(C3=CC=NC=C3)C=N1

Purity: 99.9%

Batch No: R13-1-15

Description

This compound (J9) was selected for its lead-like properties at restoring sensitivity to glucocorticoid resistant T-ALL cells (CUTLL1 cell line) through the upregulation of the glucocorticoid receptor. Patients can develop glucocorticoid resistance rendering the treatment ineffective. This compound and its mechanism of action provides a useful strategy for overcoming this resistance. The EC_{50} of J9 in combination with destramethasone is 28 μM.

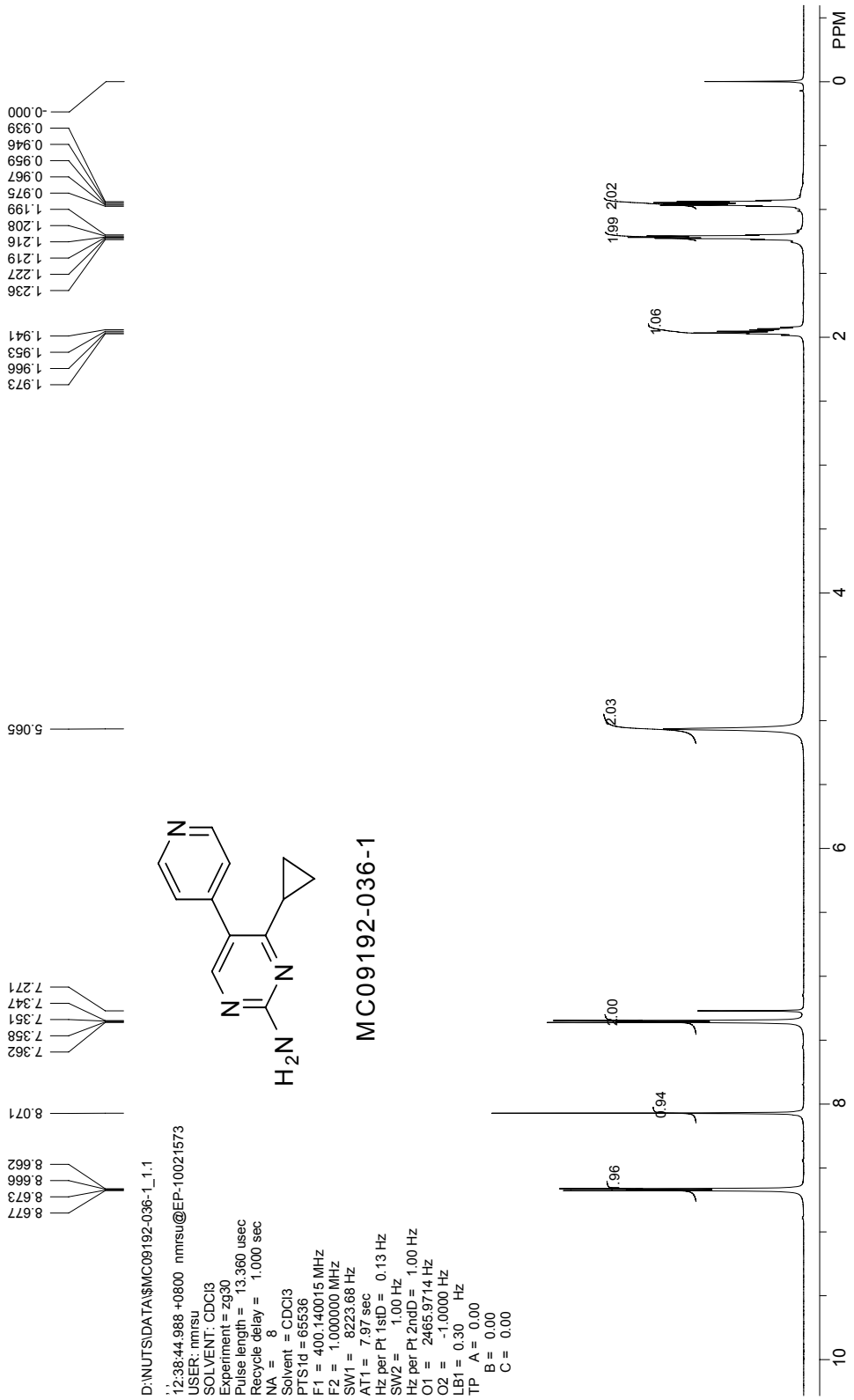
References

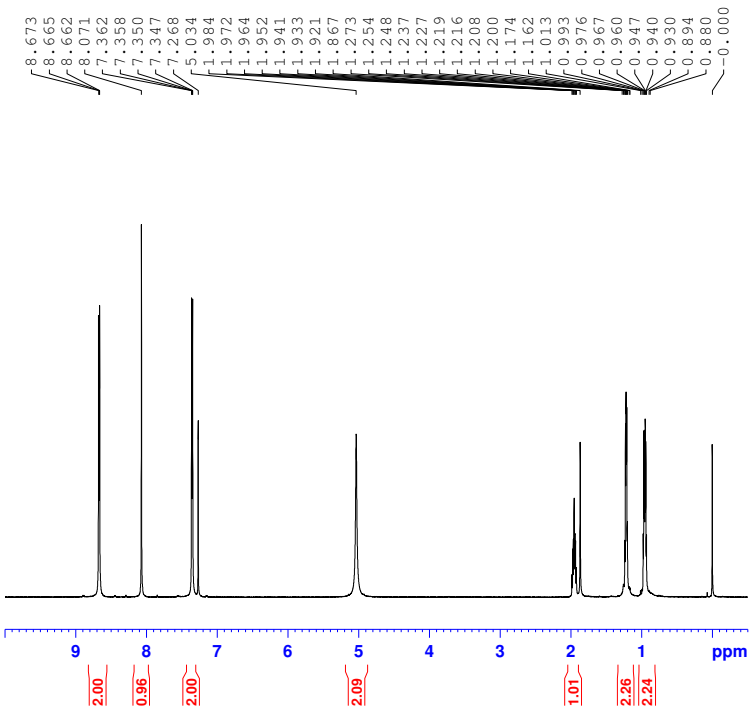
Alexandra M. Cantley, Matthew Welsch, Alberto Ambesi-Impiombato, Marta Sanchez-Martin, Mi-Yeon Kim, Andras Bauer, Adolfo Ferrando, and Brent R. Stockwell. "Small Molecule that Reverses Dexamethasone Resistance in T-cell Acute Lymphoblastic Leukemia (T-ALL)." *ACS Medicinal Chemistry Letters* 5.7 (2014): 754-759

*Compound J9

Analytical Data

PO Box 9242, South Yarra, VIC, 3141, Australia +61 0431091329 www.reagency.co



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Current Data Parameters
NAME      QC-MC09192-036-1
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_              20141223
Time                 16.46
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              8223.685 Hz
FIDRES           0.250967 Hz
AQ               1.9923444 sec
RG                    128
DW                 60.800 usec
DE                  6.50 usec
TE                 295.5 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 13.36 usec
PLW1         15.00000000 W
SFO1         400.1424710 MHz

F2 - Processing parameters
SI                  65536
SF           400.1400060 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
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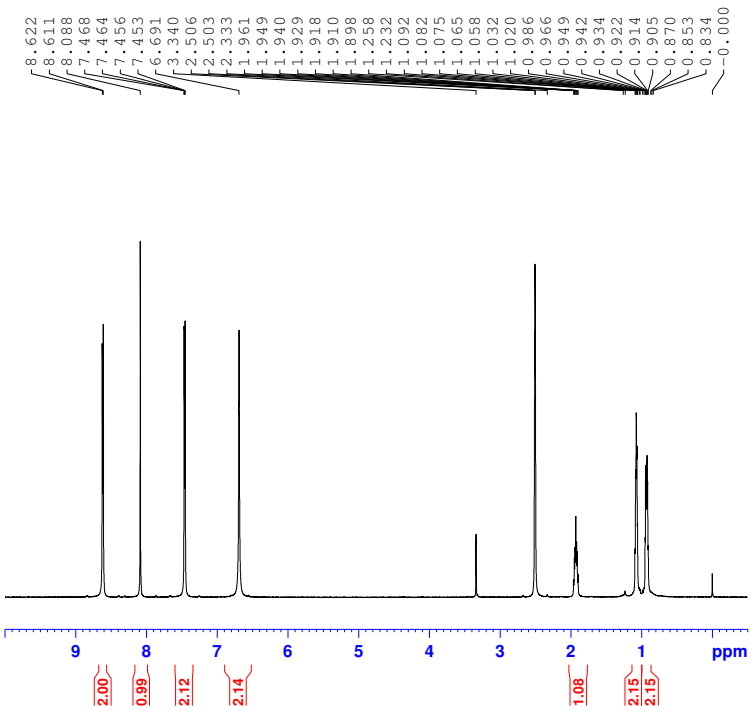

BRUKER

```
Current Data Parameters
NAME      QC-MC09192-036-1-DMSO
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_           20141224
Time              14.42
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG            zg30
TD                32768
SOLVENT            DMSO
NS                    8
DS                    2
SWH            8223.685 Hz
FIDRES         0.250967 Hz
AQ             1.9923444 sec
RG                  114
DW                60.800 usec
DE                 6.50 usec
TE                295.7 K
D1            1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1                13.36 usec
PLW1        15.00000000 W
SFO1        400.1424710 MHz

F2 - Processing parameters
SI                65536
SF          400.1400006 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
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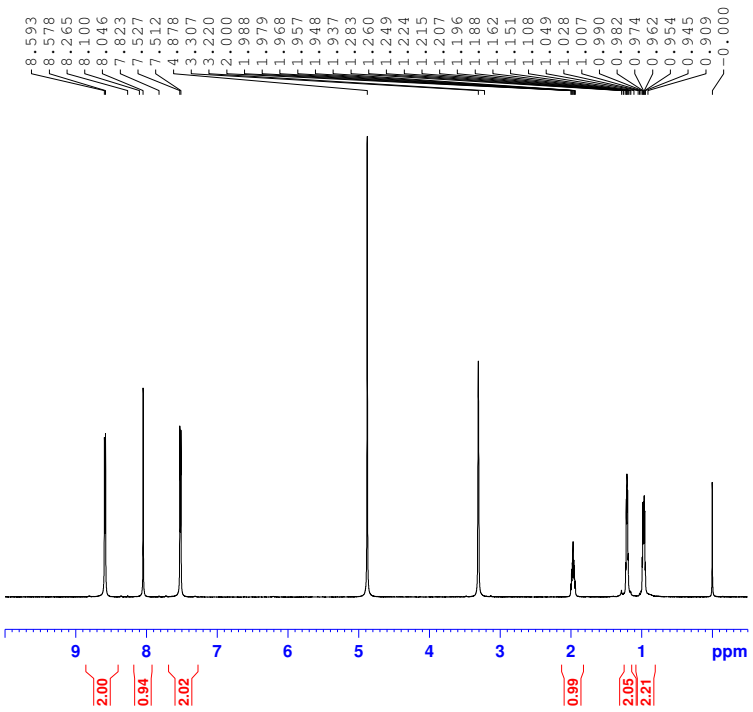


BRUKER

```
Current Data Parameters
NAME      QC-MC09192-036-1-MeOD
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_           20141224
Time              14.46
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                32768
SOLVENT            MeOD
NS                    8
DS                    2
SWH            8223.685 Hz
FIDRES         0.250967 Hz
AQ             1.9923444 sec
RG                  128
DW                60.800 usec
DE                 6.50 usec
TE                295.7 K
D1            1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1                13.36 usec
PLW1        15.00000000 W
SFO1        400.1424710 MHz

F2 - Processing parameters
SI                65536
SF          400.1400085 MHz
WDW                 EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

Shimadzu MS Report

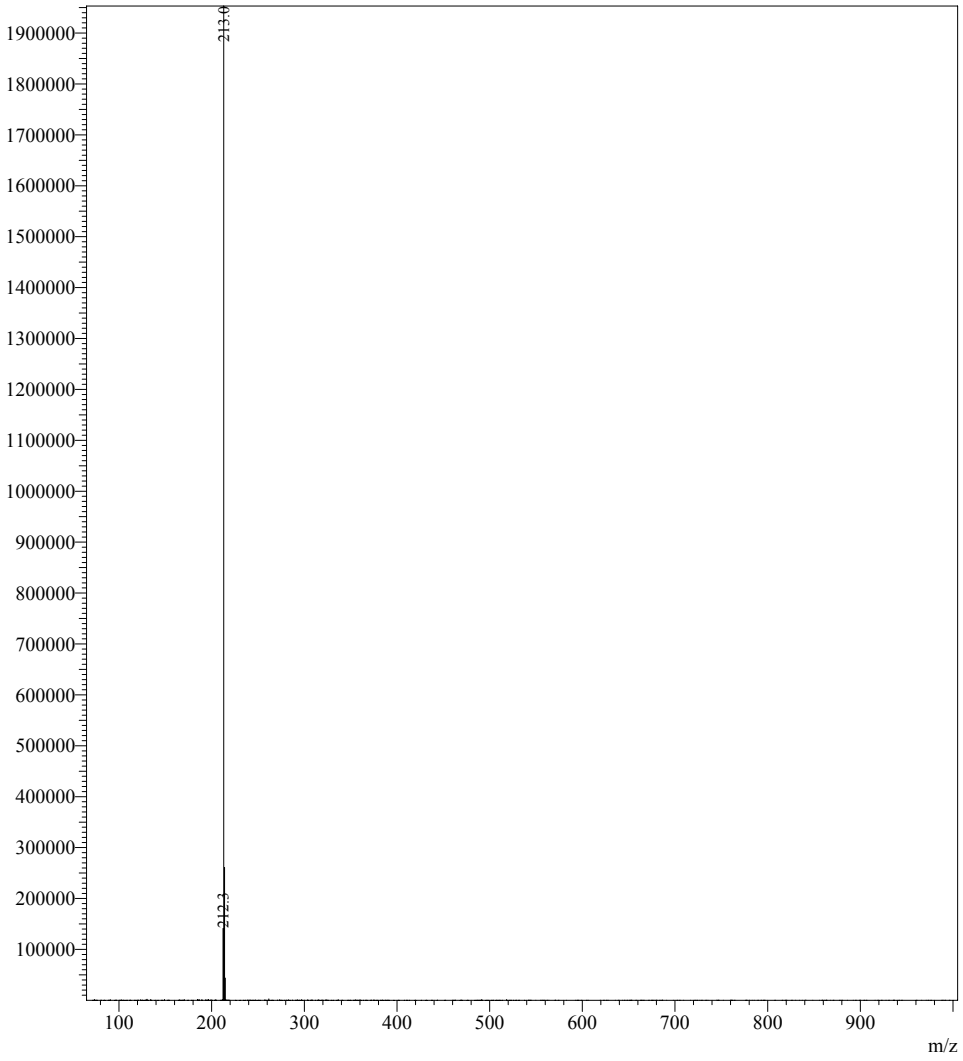
Sample Information

MS

Data File	: MC09192-036-1.lcd	Date Acquired	: 12/23/2014 10:53:03 AM
Injection Volume	: 2	Tray#	: 1
Vial#	: 23	Method File	: A90B10+-.lcm

Mass Spectrum

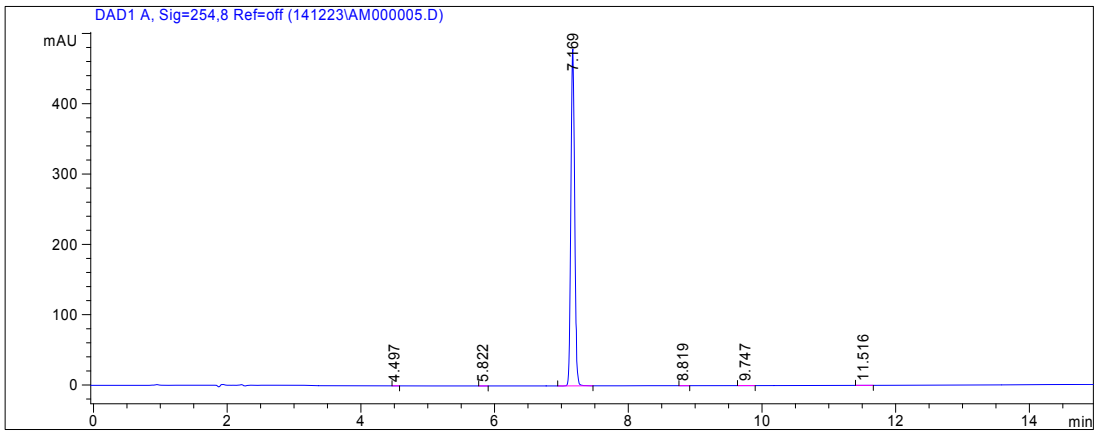
Rt=0.447min Positive



D:\Data\user\MC09192-036-1.lcd

Data File E:\CHEM32\DATA\2014\141223\AM000005.D
Sample Name: QC-MC09192-036-1

```
==========================================================================
Acq. Operator   : xxyan                          Seq. Line :   5
Acq. Instrument : Instrument 1                    Location : Vial 43
Injection Date  : 12/23/2014 4:59:13 PM                Inj :   1
                                                 Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 0.5 µl
Acq. Method     : E:\CHEM32\METHODS\M-A90B10.M
Last changed    : 12/23/2014 4:44:02 PM by xxyan
                  (modified after loading)
Analysis Method : E:\CHEM32\METHODS\WAITING-N.M
Last changed    : 12/23/2014 5:17:10 PM by xxyan
                  (modified after loading)
Method Info     : Phenomenenex Gemini C18 5µm,150x4.6 mm Column,
                  Mobile phase:B:  0.1%NH3.H2O in ACN,   A:  0.1%NH3.H2O in H2O
```




```
==========================================================================
                          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

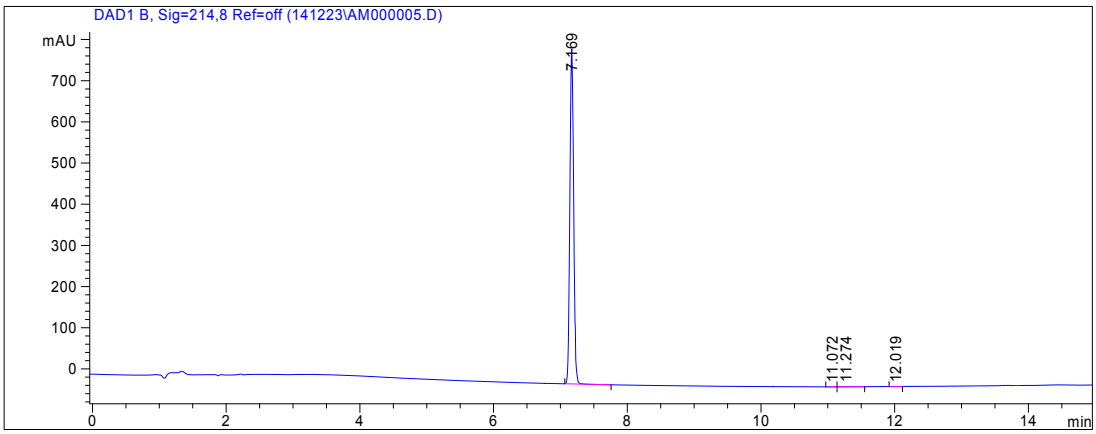
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.497 BB    0.0395 8.02582e-2 3.40582e-2 4.252e-3
   2   5.822 BB    0.0581 2.06424e-1 5.22605e-2   0.0109
   3   7.169 BB    0.0617 1885.47498  481.23981  99.9019
   4   8.819 BB    0.0666 2.01874e-1 4.47573e-2   0.0107
   5   9.747 BB    0.0771 3.43788e-1 6.56858e-2   0.0182
   6  11.516 BB    0.1161    1.01974 1.26449e-1   0.0540

Totals :                  1887.32706  481.56302

==========================================================================
                          *** End of Report ***
```

Data File E:\CHEM32\DATA\2014\141223\AM000005.D
Sample Name: QC-MC09192-036-1

```
======================================================================
Acq. Operator   : xxyan                          Seq. Line :   5
Acq. Instrument : Instrument 1                    Location : Vial 43
Injection Date  : 12/23/2014 4:59:13 PM                Inj :   1
                                                 Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 0.5 µl
Acq. Method     : E:\CHEM32\METHODS\M-A90B10.M
Last changed    : 12/23/2014 4:44:02 PM by xxyan
                  (modified after loading)
Analysis Method : E:\CHEM32\METHODS\WAITING-N.M
Last changed    : 12/23/2014 5:18:13 PM by xxyan
                  (modified after loading)
Method Info     : Phenomenenex Gemini C18 5µm,150x4.6 mm Column,
                  Mobile phase:B:  0.1%NH3.H2O in ACN,   A:  0.1%NH3.H2O in H2O
```




```
======================================================================
                        Area Percent Report
======================================================================

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


Signal 1: DAD1 B, Sig=214,8 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.169 BB    0.0617 3204.43921  817.26477  99.7854
   2  11.072 BV    0.0567 5.87892e-1 1.77378e-1   0.0183
   3  11.274 VB    0.1289    3.93030 3.92202e-1   0.1224
   4  12.019 BV    0.0924    2.37444 3.93721e-1   0.0739

Totals :                  3211.33184  818.22807


======================================================================
                        *** End of Report ***
```