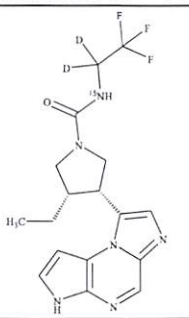
Certificate of Analysis

Certificate No.: **20221215022**

Date: December 15, 2022 Retest date: December 12, 2025

Compound Name:	**Upadacitinib-^{15}N-d_2**
Synonyms:	(3S,4R)-3-ethyl-4-(3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazin-8-yl)-*N*-(2,2,2-trifluoroethyl-1,1-d_2)pyrrolidine-1-carboxamide-*N*-^{15}N
TLC Catalogue Number:	U-103020
CAS Number:	1310726-60-3 (non-labelled)
Molecular Weight:	383.38
Molecular Formula:	$C_{17}H_{17}D_2F_3N_5{}^{15}NO$
Source:	TLC Pharmaceutical Standards
Source Lot No.:	4941-047A5
Storage Conditions:	Store at 2-8 °C
Solubility:	Methanol, DMSO



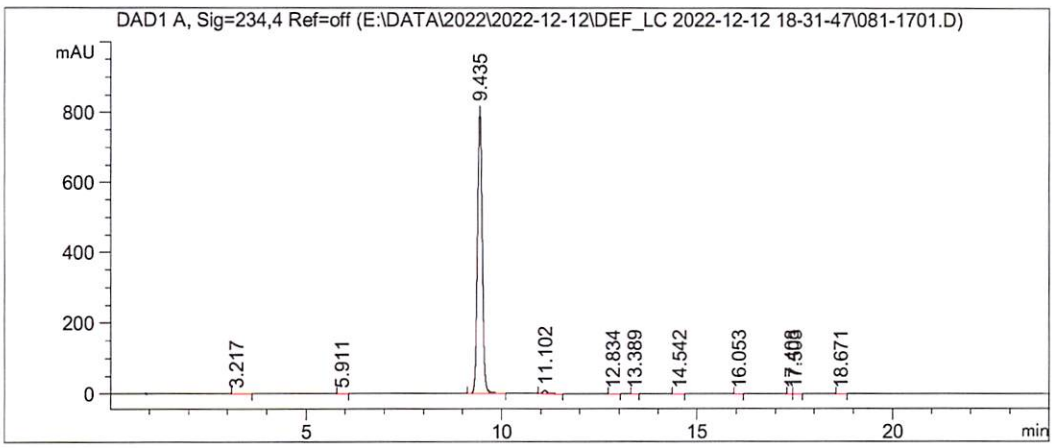
Test Description	**Specifications**	**Results**
Visual Description	Pale yellow solid	**Conforms**
Identification **IR** **MS** **^{1}H NMR**	 Conforms to structure Conforms to structure Conforms to structure	 **Conforms** **Conforms** **Conforms**
Purity (HPLC)	Not less than 95.0%	**98.9%**
Impurity (HPLC)	RT 11.10, 0.91%	
Isotopic Enrichment	Not less than 98.0%	**99.0% D; 98.0% ^{15}N**
Optical Rotation	N/A	$[\alpha]_D^{25.0}$(c=0.47, CH_3OH): **-283.8°**
Residual Solvents (NMR)	1.5% methanol	
Assay (qNMR)	Not less than 90.0%	**96.3%**
Recommendation:	**Release.**	

Name	**Department**	**Signature**	**Date**
Reviewed and approved by:	Quality Control	Kelvin Zhu	12/16/2022
Approved by:	Quality Assurance	Kanli	12/16/2022

Attachments: HPLC, IR, MS and NMR spectra.

Data File E:\DATA\2022\2022-12-12\DEF_LC 2022-12-12 18-31-47\081-1701.D
Sample Name: 4941-047A5

```
==========================================================================
Acq. Operator    : Qi Zhou                          Seq. Line :  17
Acq. Instrument  : LC-1260_2                         Location : Vial 81
Injection Date   : 12/13/2022 1:10:47 AM                Inj :   1
                                                   Inj Volume : 1.000 µl
Acq. Method      : E:\DATA\2022\2022-12-12\DEF_LC 2022-12-12 18-31-47\17.M
Last changed     : 12/12/2022 6:31:48 PM by Qi Zhou
Analysis Method  : C:\CHEM32\1\METHODS\2.M
Last changed     : 12/13/2022 9:23:20 AM by Qi Zhou
                   (modified after loading)
Sample Info      : Poroshell HPH-C18 (4.6*100mm,2.7um); F=1.0mL/min; T=30 degree;
                   CH3OH/10mmol/L CH3COONH4+0.03% TEA=39/61(0-6min),39/61-65/35(6-18min),65/35
                   (after 18min)
                   ~1.2mg in 0.5mL CH3OH
```




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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=234,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   3.217 BB    0.0842    3.75134 6.60692e-1   0.0546
   2   5.911 BBA   0.1070    2.04563 2.31636e-1   0.0297
   3   9.435 BBA   0.1292 6798.35400  816.28107  98.8677
   4  11.102 BB    0.1114   62.22810    8.70432   0.9050
   5  12.834 BB    0.0828    1.32658 1.96358e-1   0.0193
   6  13.389 BB    0.0777 9.10427e-1 1.48212e-1   0.0132
   7  14.542 BB    0.1086    1.46655 1.84689e-1   0.0213
   8  16.053 BBA   0.0974    1.15982 1.62296e-1   0.0169
   9  17.408 BV    0.0622    1.29065 2.67839e-1   0.0188
  10  17.503 VBA   0.0939    2.41630 3.28017e-1   0.0351
  11  18.671 BB    0.0995    1.26084 1.57330e-1   0.0183
```

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Totals :	6876.21024	827.32245

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*** End of Report ***

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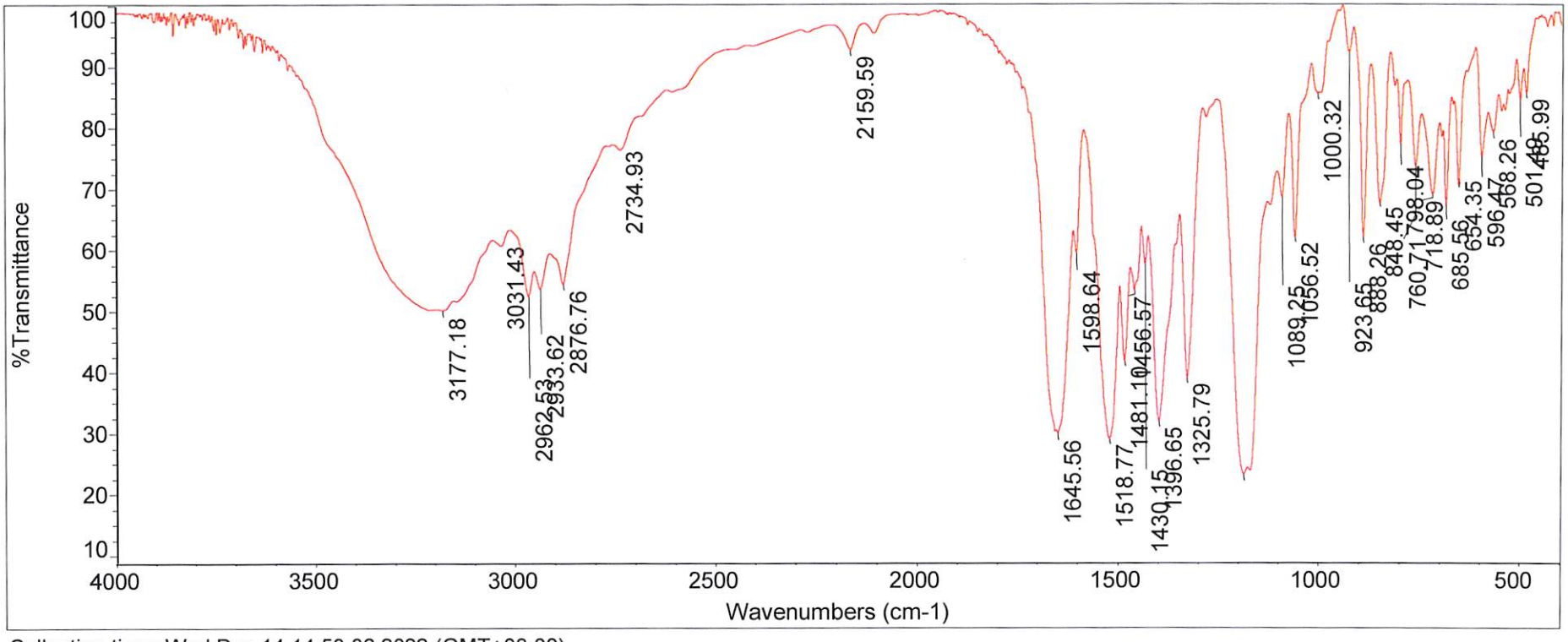
4941-047A5



Collection time: Wed Dec 14 14:53:36 2022 (GMT+08:00)

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Wed Dec 14 15:21:57 2022 (GMT+08:00)
FIND PEAKS:
Spectrum: 4941-047A5
Region: 4000.00 400.00
Absolute threshold: 94.671
Sensitivity: 50
Peak list:

Position:	485.99	Intensity:	85.714
Position:	501.49	Intensity:	84.690
Position:	568.26	Intensity:	79.358
Position:	596.47	Intensity:	75.372
Position:	654.35	Intensity:	70.636
Position:	685.56	Intensity:	67.181
Position:	718.89	Intensity:	69.079
Position:	760.71	Intensity:	73.757
Position:	798.04	Intensity:	77.460
Position:	848.45	Intensity:	67.652
Position:	888.26	Intensity:	62.094
Position:	923.65	Intensity:	92.436
Position:	1000.32	Intensity:	85.550
Position:	1056.52	Intensity:	61.943
Position:	1089.25	Intensity:	68.636
Position:	1184.98	Intensity:	23.191
Position:	1325.79	Intensity:	38.943
Position:	1396.65	Intensity:	31.864
Position:	1430.15	Intensity:	57.576
Position:	1456.57	Intensity:	53.276
Position:	1481.10	Intensity:	41.739
Position:	1518.77	Intensity:	28.965
Position:	1598.64	Intensity:	59.477
Position:	1645.56	Intensity:	29.858
Position:	2159.59	Intensity:	92.726
Position:	2876.76	Intensity:	54.411
Position:	2933.62	Intensity:	53.634
Position:	2962.53	Intensity:	52.459
Position:	3177.18	Intensity:	50.068

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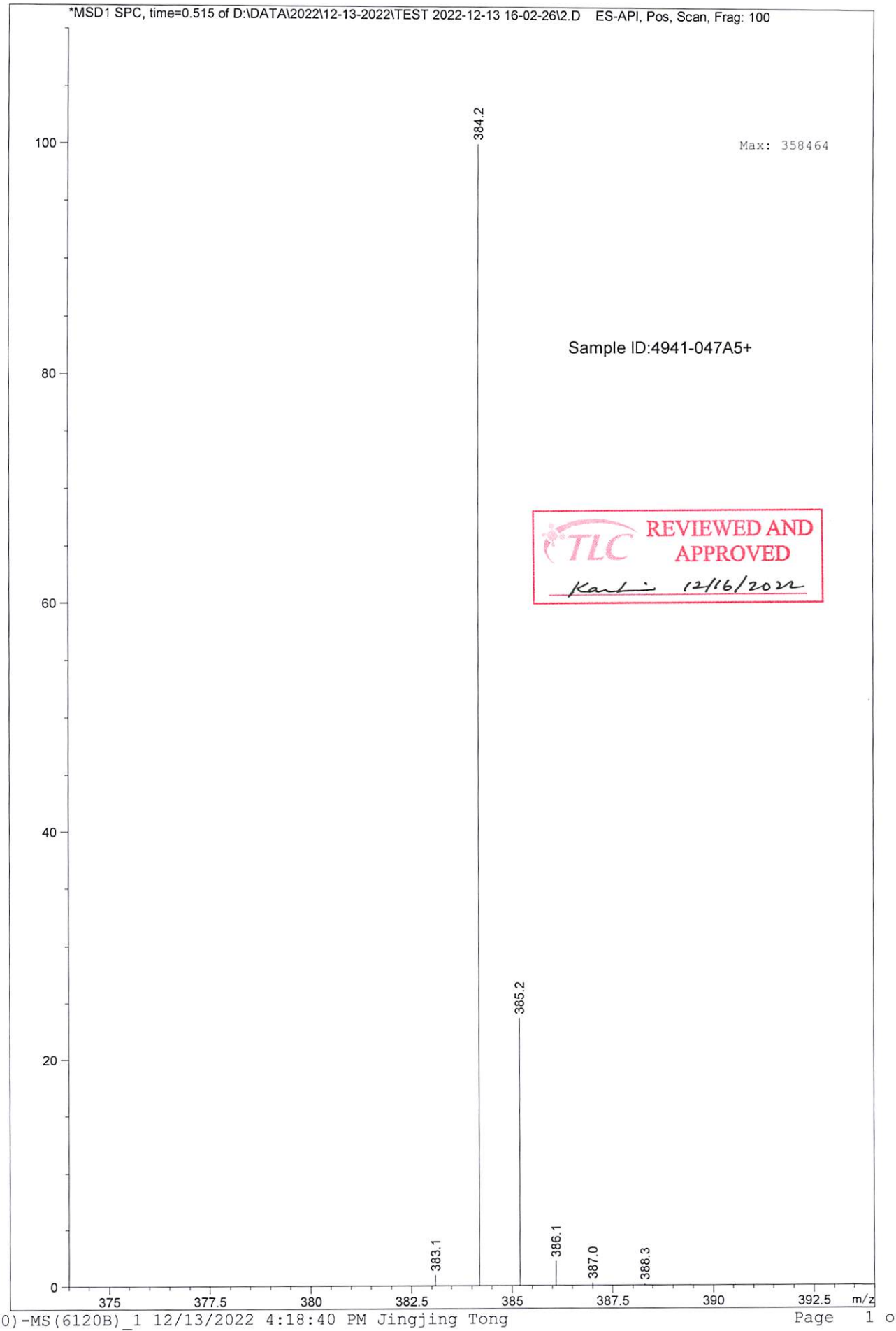
Signature: Xuewei Sheng, 12-14-2022 15:22:22 (GMT+08:00), Authorship - signifies ownership
4941-047A5

MS Spectrum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Max: 358464
384.2
385.2
383.1
386.1
387.0
388.3
Sample ID:4941-047A5+
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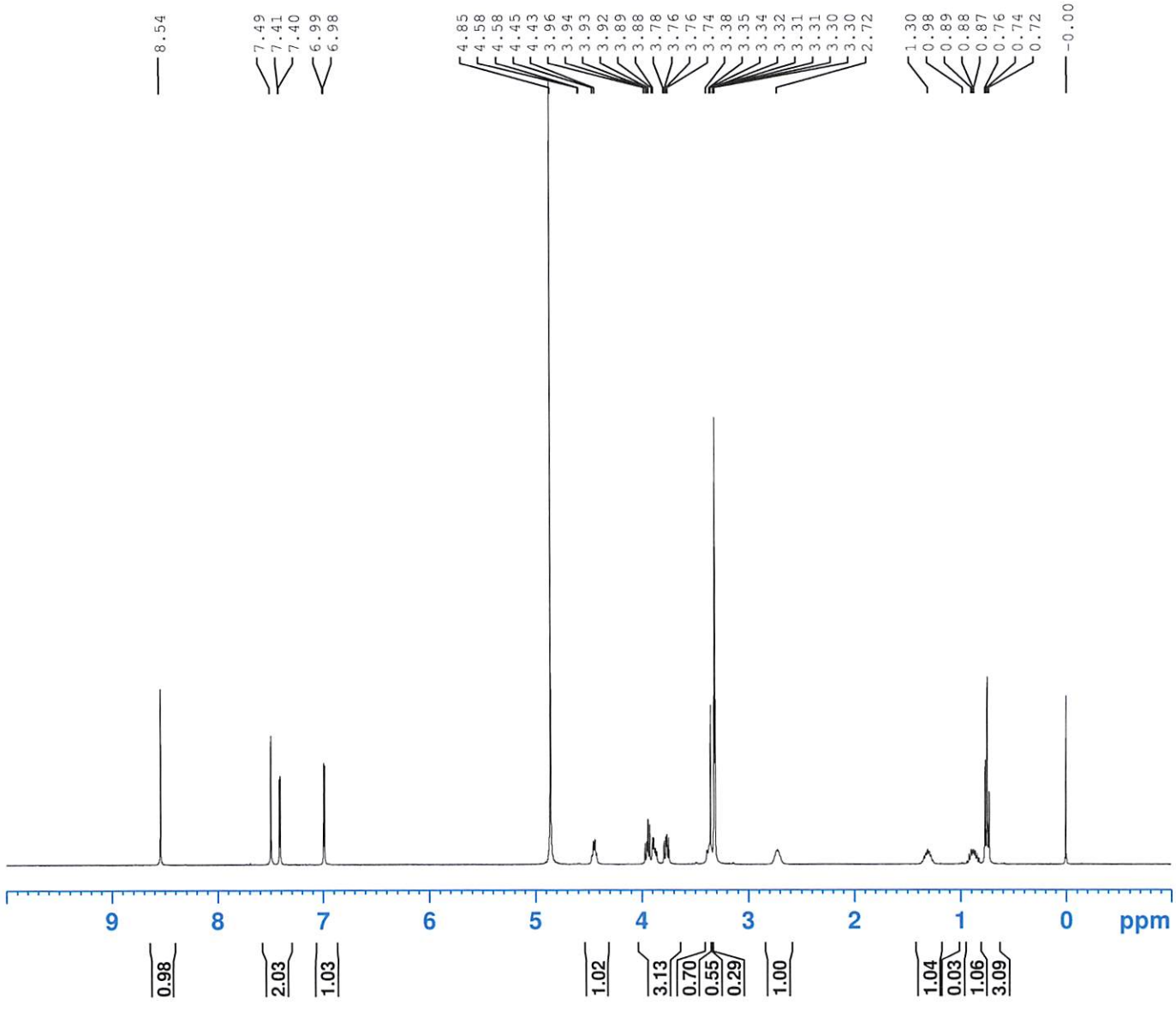
100
80
60
40
20
0
375
377.5
380
382.5
385
387.5
390
392.5
m/z

4941-047A5 1H NMR in CD3OD



BRUKER

Current Data Parameters
NAME 2022-12-12(NMR-400_2)
EXPNO 43
PROCNO 1

F2 - Acquisition Parameters
Date_ 20221212
Time 11.13 h
INSTRUM spect
PROBHD Z116098_0656 (
PULPROG zg30
TD 65536
SOLVENT CD3OD
NS 4
DS 0
SWH 9615.385 Hz
FIDRES 0.293438 Hz
AQ 3.4078720 sec
RG 71.77
DW 52.000 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1836016 MHz
NUC1 1H
P1 9.70 usec
PLW1 19.54100037 W

F2 - Processing parameters
SI 65536
SF 400.1800081 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 0.50

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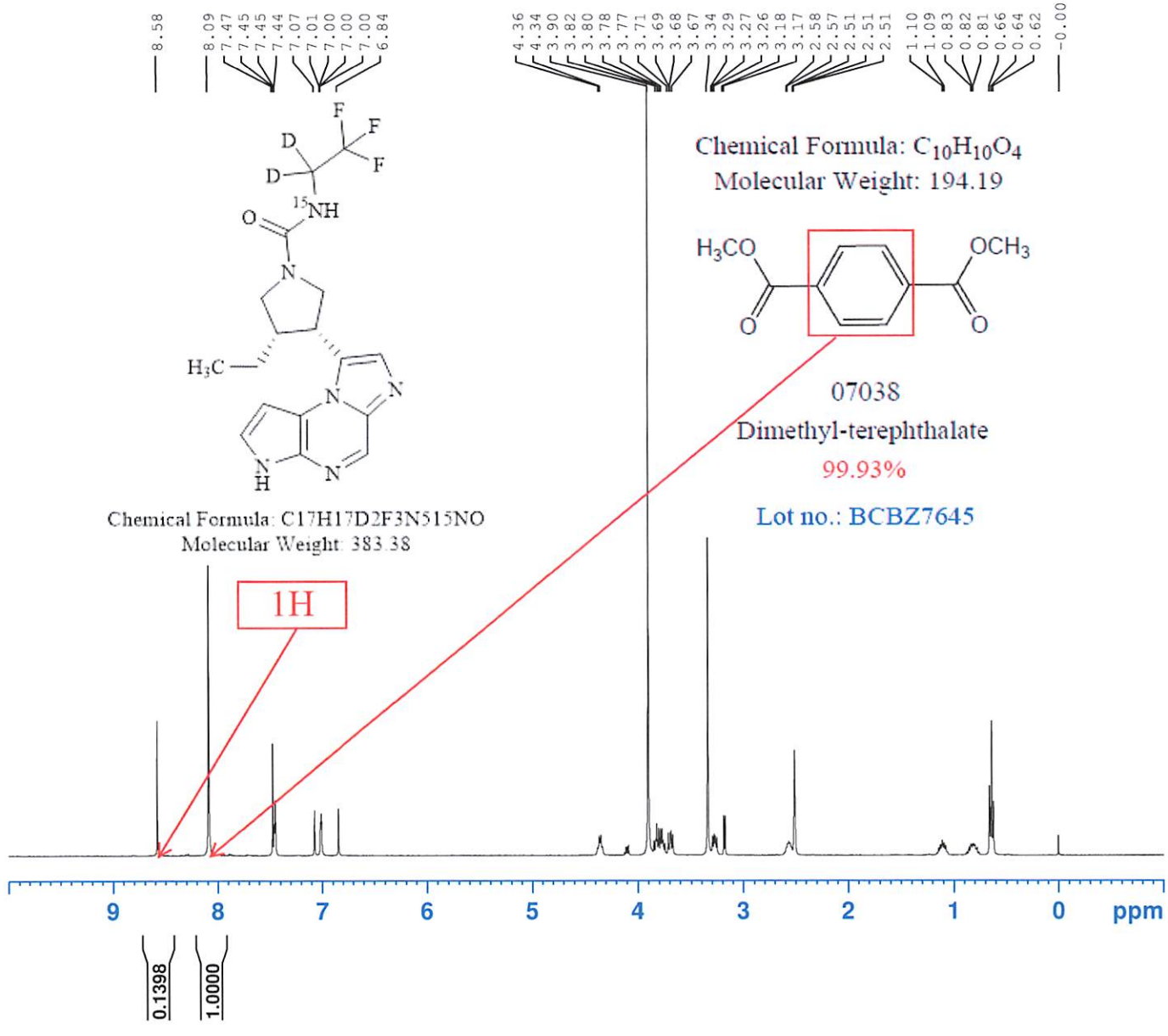
4941-047A5(6.045mg) and 07038(5.279mg) 1H NMR in DMSO-d6



Current Data Parameters
NAME 2022-12-14(NMR-400_1)
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
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Time 9.58 h
INSTRUM spect
PROBHD Z116098_0293 (
PULPROG zg30
TD 65536
SOLVENT DMSO-d6
NS 8
DS 0
SWH 4807.692 Hz
FIDRES 0.146719 Hz
AQ 6.8157439 sec
RG 80.36
DW 104.000 usec
DE 6.50 usec
TE 298.0 K
D1 60.00000000 sec
TD0 1
SFO1 400.1320007 MHz
NUC1 1H
P1 9.63 usec
PLW1 17.45800018 W

F2 - Processing parameters
SI 65536
SF 400.1299995 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

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