Supporting Information:

GNE-886: A Potent and Selective Inhibitor of the Cat Eye Syndrome Chromosome Region Candidate 2 Bromodomain

Terry D. Crawford,[†] James E. Audia,[‡] Steve Bellon,[‡] Daniel J. Burdick,[†] Archana Bommi-Reddy,[‡] Alexandre Côté,[‡] Richard T. Cummings,[‡] Martin Duplessis,[‡] E. Megan Flynn,[†] Michael Hewitt,[‡] Hon-Ren Huang,[‡] Hariharan Jayaran,[‡] Ying Jiang,[§] Shivangi Joshi,[‡] James R. Kiefer,[†] Jeremy Murray,[†] Christopher G. Nasveschuk,[‡] Arianne Neiss,[‡] Eneida Pardo,[‡] F. Anthony Romero,[†] Peter Sandy,[‡] Robert J. Sims III,[‡] Yong Tang,[‡] Alexander M. Taylor,[‡] Vickie Tsui,[†] Jian Wang,[§] Shumei Wang,[†] Yongyun Wang,[§] Zhaowu Xu,[§] Laura Zawadzke,[‡] Xiaoqin Zhu,[§] Brian K. Albrecht,[‡] Steven R. Magnuson,[†] Andrea G. Cochran[†]*

[†]Genentech Inc., 1 DNA Way, South San Francisco, CA 94080

[‡]Constellation Pharmaceuticals, 215 First Street, Suite 200, Cambridge, MA 02142

[§]Wuxi Apptec Co., Ltd., 288 Fute Zhong Road, Waigaoqiao Free Trade Zone, Shanghai 200131, People's Republic of China

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Protein expression and purification methods

Production of bromodomain proteins was carried out as previously described[1]. TR-FRET assay conditions have been reported previously.[2, 3]

Synthesis of biotinylated probes for TR-FRET assays. The synthesis and characterization of biotinylated probe molecules has been previously reported.[2]

Cell-based assay

The bromodomain chromatin-release ("dot") assay has been described previously for the CBP bromodomain.[4] Briefly, a cell line derived from U2OS, U2OS-C433, expressing a ZsGreen fluorescence tag fused to a nuclear localization signal sequence (MDPKKKRKVDPKKRKVDPKKKRKV) followed by CECR2 bromodomain (M404–H515), was used to visualize the localization of the bromodomain. In the absence of target engagement, the fluorescence signal is seen in the nucleus and is diffuse. Addition of inhibitor results in the formation of large nuclear puncta ("dots") that are quantified and converted to compound EC_{50} values as previously described.[4]

Crystallography methods

Crystals of the CECR2 ligand complex were grown by vapor diffusion with a precipitant solution of 1.5 M lithium sulfate and 0.1 M Tris-HCl pH 8.5 combined with protein solution at a ratio of 4:3. Protein concentration was 21.5 mg/mL with final ligand concentration at 2 mM. Crystals grew after 3–4 weeks of incubation at 4 °C. Data were collected at the Advanced Photon Source (APS beamline: SER-CAT 22BM) at a wavelength of 1.00 Å. Crystals were dipped in a 1:1 mixture of paratone and paraffin oil prior to flash cooling in liquid nitrogen. The data were integrated and scaled to 2.7 Å resolution with HKL2000[5] and determined to be of space group I222 (Table 1). The initial structure was determined by the molecular replacement method using PHASER[6], using an internal bromodomain structure as a search

model. The model was adjusted using COOT[7], and the final refinement was performed with BUSTER[8,9] to an R_{free} value of 22.2% and included four protein molecules per asymmetric unit.

Table S1. Crystallographic data collection and refinement statistics for Compound 6 bound to CECR2 [PDB 5V84].

Data Collection	
Wavelength (Å)	1.0
Resolution range*	50.0 - 2.70 (2.8 - 2.7)
Space group	I222
Unit cell (a,b,c,α,β,γ)	101.18 116.49 132.93 90 90 90
Total reflections	133,846
Unique reflections	21,604 (2117)
Multiplicity	6.2 (6.2)
Completeness (%)	99 (100)
Mean I/sigma(I)	16.3 (2.4)
Wilson B-factor	72.8
R_{merge}	0.07 (0.52)
Refinement	
Resolution	43.8 – 2.7 (2.83 – 2.7)
Reflections used in refinement	21,595 (1,900)
R_{work}/ R_{free} (%)	20.6/22.2 (24.4/25.7)
Number of non-hydrogen atoms	3,521
macromolecules	3,359
ligands	138
solvent	24
Protein residues	406
RMS(bonds)	0.010
RMS(angles)	0.96
Ramachandran favored (%)	97
Ramachandran allowed (%)	2.5
Ramachandran outliers (%)	0
Rotamer outliers (%)	6.4
Clashscore	13.70
Average B-factor	84.34
macromolecules	78.30
ligands	78.49
solvent	61.95
Number of TLS groups	16

*Statistics for the highest-resolution shell are shown in parentheses.

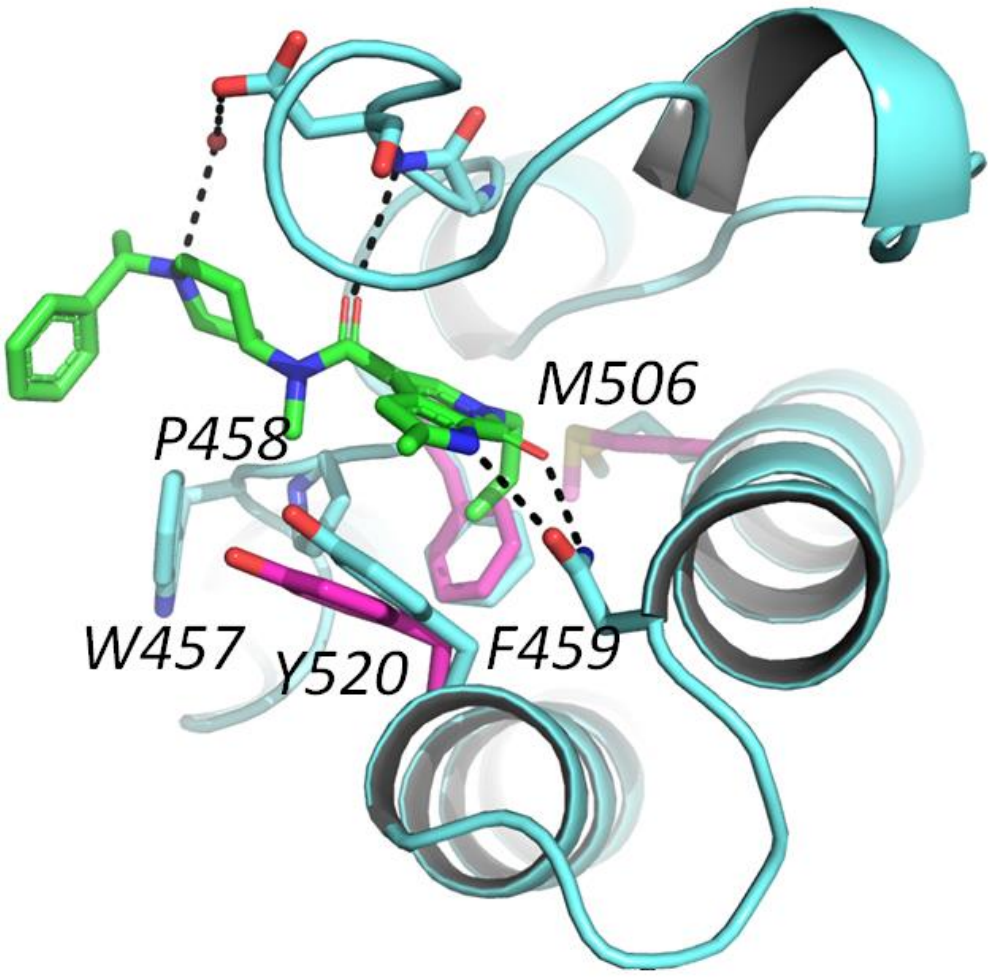


Figure S1. Comparison of the Compound **6** structure with Apo structure residues Phe459, Tyr520, Met506 in red. Compound **6** is shown as green sticks and H-bond interactions are represented as black dashes.

Table S2. TR-FRET assay data for compounds Tables 1 and 2 including standard deviations.

Compound	CECR2	BRD4(1)	BRD4(2)	BRD9	TAF1(2)
			IC_{50} (uM)		
2	0.78 ± 0.3	>20	17.2 ± 0.7	>20	6.1 ± 0.6
3	0.50 ± 0.04	>20	19.2 ± 0.4	17.8 ± 2	8.4 ± 0.2
4	0.33 ± 0.06	>20	6.1 ± 0.5	11 ± 1	3.6 ± 0.5
5	0.50 ± 0.01	>20	>20	>20	16.1 ± 0.3
6	0.20 ± 0.02	>20	>20	3.5 ± 0.0	16.5 ± 0.4
7	0.19 ± 0.02	>20	>20	4.4 ± 0.1	11.9 ± 2

Compound	CECR2	BRD4(1)	BRD9	TAF1(2)
			IC_{50} (uM)	
8	0.24 ± 0.1	>20	5 ± 0.3	2.1 ± 0.6
9	0.2 ± 0.06	>20	11.4 ± 0.3	3.4 ± 0.8
10	0.13 ± 0.02	>20	8.5 ± 0.2	2.8 ± 0.5
11	0.083 ±0.02	>20	6.1 ± 0.7	1.8 ± 0.2
12	0.055 ± 0.004	>20	5.7 ± 0.8	2.8 ± 0.3
13	0.071 ± 0.01	>20	5.8 ± 1	2.7 ± 0.3
14	0.093 ± 0.02	>20	7.6 ± 0.7	5.1 ± 0.5
15	0.052 ± 0.001	>20	3.5 ± 0.2	3.3 ± 0.3
16	0.059 ± 0.002	>20	6.9 ± 1	3.4 ± 0.4
17	0.045 ± 0.02	>20	3.3 ± 0.3	2.5 ± 0.6
18	0.046 ± 0.001	>20	1.7 ± 0.2	2.4 ± 0.4
19	0.044 ± 0.02	>20	1.5 ± 0.2	2.5 ± 0.8
20	0.045 ± 0.01	>20	2.6 ± 0.4	2.6 ± 0.4
21	0.016 ± 0.002	>20	1.6 ± 0.1	1.4 ± 0.1

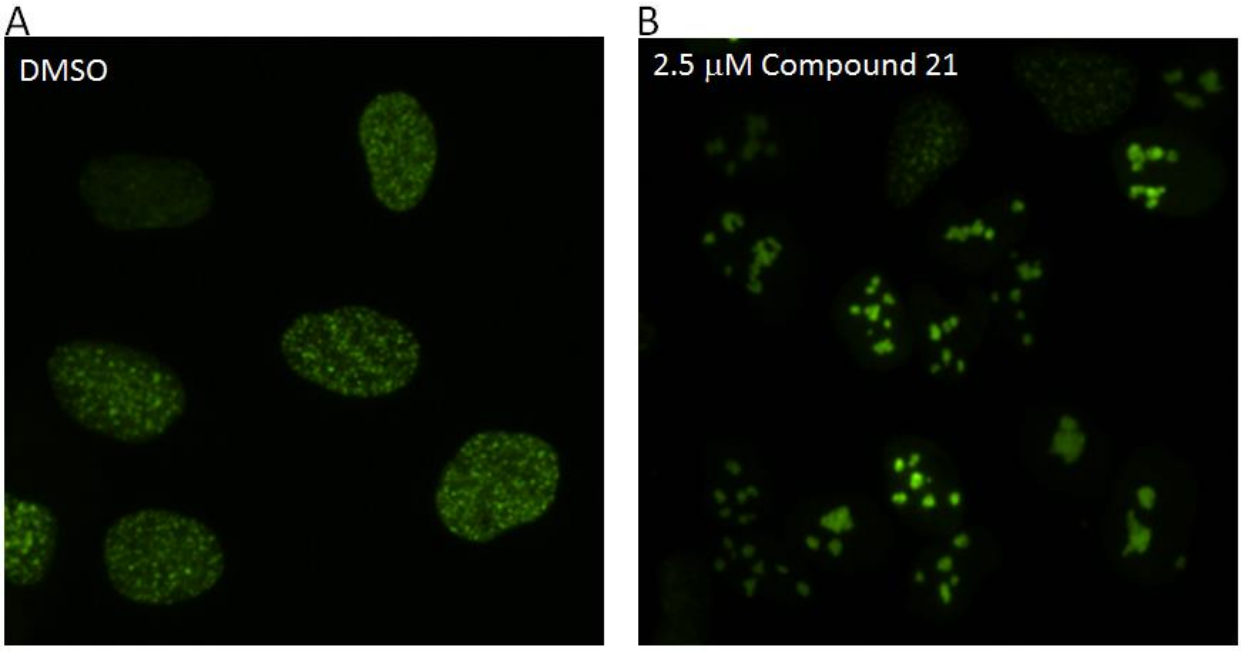


Figure S2. Displacement of a CECR2 ZsGreen fusion protein from chromatin. Control cells in DMSO in Figure S1A, and aggregate dots resulting from displacement highlighted in Figure S1B.

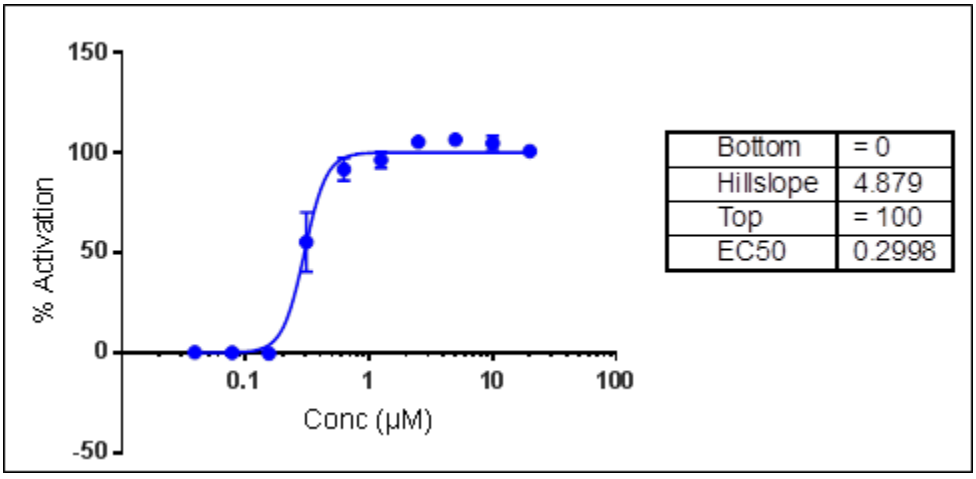


Figure S3. Representative dose-response curve for compound **21** in CECR2 dot assay.

Table S3. CECR2 dot assay data for 6 replicate experiments (A-F), measuring the percent activation observed at 10 concentrations for compound **21** (EC_{50} = 370 nM).

	Percent activation					
Conc (μM) of compd **21**	**A**	**B**	**C**	**D**	**E**	**F**
40	100.1	96.2	99.9	88.0	100.0	101.4
20	111.0	106.9	97.6	91.8	102.2	107.1
10	97.7	89.6	87.6	92.3	106.5	
5	102.0	108.5	102.4	99.3	105.1	105.5
2.5	99.2	99.2	86.4	87.5	93.3	99.2
1.25	74.4	81.4	74.4	86.6	95.6	87.7
0.625	63.2	62.9	56.3	62.7	44.8	65.8
0.315	48.0	45.5	6.1	-1.9	-0.3	-0.4
0.16	9.7	10.6	-5.1	-7.7	-0.2	0.2
0.08	0.4	-0.4	0.1	-2.5	-0.3	0.7

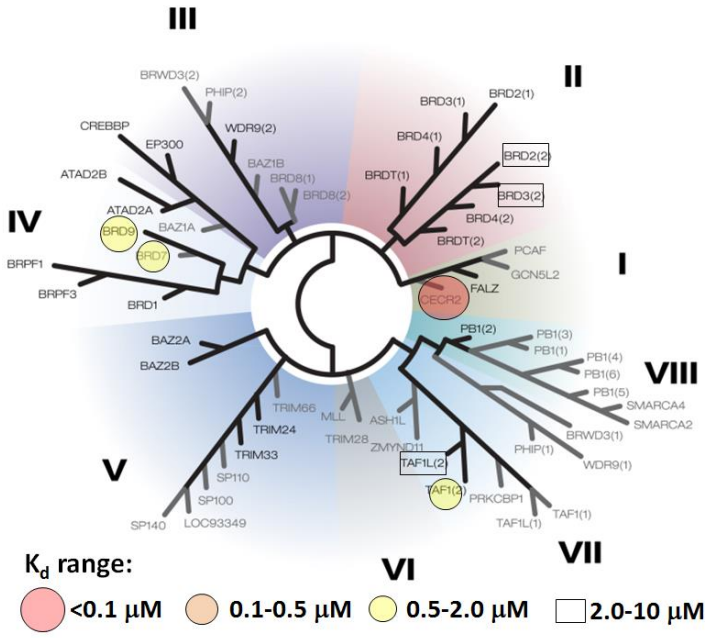


Figure S4. BROMOscan data for GNE-886. Kd values are the average of 2 independent experiments.

Table S3. BROMO*scan*® bromodomain selectivity data for compound **21** (GNE-886) provided by DiscoveRx Corp., Fremont, CA, USA, http://www.discoverx.com. This screen measured binding competition against immobilized ligands for 40 DNA-tagged bromodomains. Compound Kd values are an average of 2 independent experiments.

Target	GNE-886	Target	GNE-886	Target	GNE-886
Gene Symbol	Kd (nM)	BRD4(2)	>10000	FALZ	>10000
ATAD2A	>10000	BRD4(full-length,short-iso.)	>10000	GCN5L2	>10000
ATAD2B	>10000	BRD7	1100	PBRM1(2)	>10000
BAZ2A	>10000	BRD8(1)	>10000	PBRM1(5)	>10000
BAZ2B	>10000	BRD8(2)	>10000	PCAF	>10000
BRD1	>10000	BRD9	2000	SMARCA2	>10000
BRD2(1)	>10000	BRDT(1)	>10000	SMARCA4	>10000
BRD2(1,2)	>10000	BRDT(1,2)	>10000	TAF1(2)	620
BRD2(2)	5300	BRDT(2)	>10000	TAF1L(2)	2400
BRD3(1)	>10000	BRPF1	>10000	TRIM24(Bromo.)	>10000
BRD3(1,2)	>10000	BRPF3	>10000	TRIM24(PHD,Bromo.)	>10000
BRD3(2)	4900	CECR2	42	TRIM33(PHD,Bromo.)	>10000
BRD4(1)	>10000	CREBBP	>10000	WDR9(2)	>10000
BRD4(1,2)	>10000	EP300	>10000		

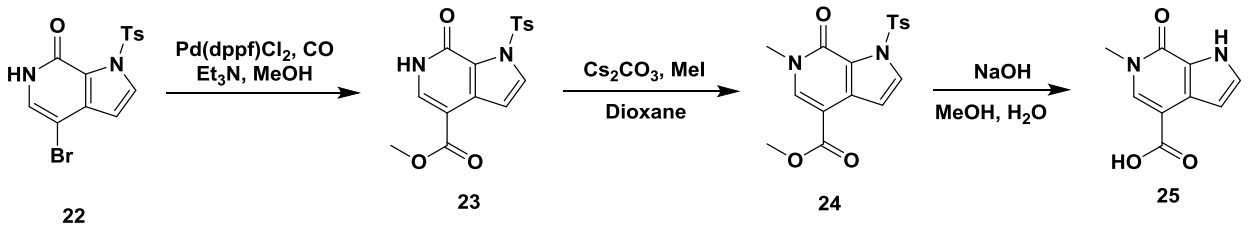
Table S4: Kinase selectivity data for Compound **21** (GNE-886). Invitrogen panel of 35 kinases, percent inhibition at 1.0 μM.

Kinase	GNE-886 @1.0uM	Kinase	GNE-886 @1.0uM
AKT1	2.5	MAP4K4	6.5
Abl	9	MEK1	3.5
Aurora_B	1	MST3	3
CDK2/cyclinA	0.5	MYLK3(caMLCK)	1.5
CDK5/p25	-1.5	Mink1	10
CHK1	10.5	MuSK	1.5
CLK2	6.5	PIM1	2.5
CSF1R	6	PKA	1.5
DMPK	0.5	PLK1	-2
EphA1	3.5	RIPK2	-0.5
Flt3	2.5	RSK3	4.5
GSK3_beta	3.5	Ret	1
IRAK4	11.5	SIK2	0.5
InsR	3.5	Src	3
JAK1	-5	TGFBR1	3
JNK1_alpha1	9.5	TrkA	11.5
Lck	18.5	Yes	4
		p38_alpha(direct)	3

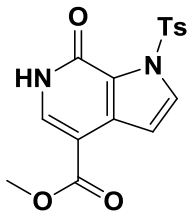
Chemistry Methods. All solvents and reagents were used as obtained. NMR analysis performed in a deuterated solvent with a Varian Avance 300-MHz or Bruker Avance 400- or 500-MHz NMR spectrometers, referenced to trimethylsilane (TMS). Chemical shifts are expressed as δ units using TMS as the external standard (in NMR description, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad peak). All coupling constants (*J*) are reported in Hertz. Mass spectra were measured with a Finnigan SSQ710C spectrometer using an ESI source coupled to a Waters 600MS high performance liquid chromatography (HPLC) system operating in reverse-phase mode with an X-bridge Phenyl column of dimensions 150 mm by 2.6 mm, with 5 μm sized particles. Preparatory-scale silica gel chromatography was performed using medium-pressure liquid chromatography (MPLC) on a CombiFlash Companion (Teledyne ISCO) with RediSep normal phase silica gel (35−60 μm) columns and UV detection at 254 nm. Reverse-phase (HPLC) was used to purify compounds as needed by elution from a Phenomenex Gemini-NX C18 column (20.2 x 50 mm, 5 μm) as stationary phase using mobile phase indicated, and operating at a 35 mL/min flow rate on a Waters 3100 mass-directed prep instrument. Chiral separation was performed on a Thar 80 prep SFC with ChiralCel OD-H column (250 x 30 mm, 5 μm) as stationary phase using mobile phase as indicated, and operating at a 40 mL/min flow rate. Chemical purities were >95% for all final compounds as assessed by LC/MS analysis. The following analytical methods were used to determine chemical purity of final compounds: 1) HPLC-Agilent 1200, water with 0.05% TFA, acetonitrile with 0.05% TFA (buffer B), Agilent SB-C18, 1.8 μM, 2.1 x 30 mm, 25 ºC, 3–95% buffer B in 8.5 min, 95% in 2.5 min, 400 μL/min, 220 nm and 254 nm, equipped with Agilent quadrupole 6140, ESI positive, 90-1300 amu. 2) Chrial SFC, ChiralCel AD-H column, 150 x 4.6 mm, 5 μm, CO_2 mobile phase

A, with methanol with 0.05% diethylamine (mobile phase buffer B), 40 ºC, 40% buffer B 2.35 mL/min.

Scheme S1. Synthesis of carboxylic acid Intermediate **25.**

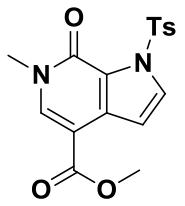


Compound 23. methyl 7-oxo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridine-4-carboxylate



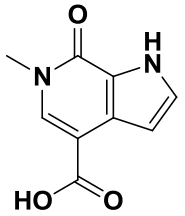
[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride (5.0 g, 8.5 mmol) was added to a mixture of 4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one[1](10.0 g, 27.3 mmol), Et_3N (20.0 mL, 143.5 mmol) in methanol (1 L). After addition, the mixture was stirred under CO atmosphere (50 psi) at 80 °C for 24 h, at which time TLC (petroleum ether :ethyl acetate=1:1) showed the completion of the reaction. The resulting mixture was concentrated under reduced pressure and the residue was purified by flash column (petroleum ether : ethyl acetate=5:1 to 3:1) to give the title compound (Intermediate B) (7.5 g, 79.5% yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.79 (s, 1 H), 8.03 (d, *J* = 3.6 Hz, 1 H), 7.88 (d, *J* = 8.4 Hz, 2 H), 7.80 (s, 1 H),7.37 (d, *J* = 8.0 Hz, 2 H), 7.05 (d, *J* = 3.2 Hz, 1 H), 3.77 (s, 3 H), 2.33 (s, 3 H).

Compound 24. methyl 6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylate



Methyl iodide (18.1 g, 127.24 mmol) was added dropwise to a stirred solution of methyl 7-oxo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridine-4-carboxylate (11.6 g, 33.49 mmol) and Cs_2CO_3 (13.1 g, 40.18 mmol) in dioxane (230 mL). After addition, the resulting mixture was stirred at room temperature for 4 hr, at which time TLC indicated the reaction was completed. The solid was removed by filtration and the filtrate was concentrated. The residue was dissolved in ethyl acetate (250 mL) and washed with water (50 mL x 2). The organic layer was dried over sodium sulfate and concentrated under reduced pressure to give the title compound (11.0 g, 91.1% yield) as a white solid. This crude was used into next step without further purification. LCMS *m/z* (M+H) 360.9.

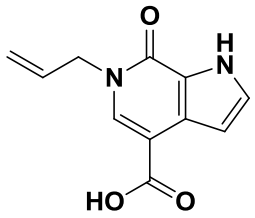
Intermediate 25. 6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid



Sodium hydroxide (6.0 g, 150.0 mmol) was added in portions to a stirred solution of methyl 6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylate (12.0 g, 33.3 mmol) in methanol/water (260/30 mL). After addition, the mixture was stirred at 80 °C for 2 h, at which time LCMS indicated the reaction had gone to completion. After cooling, the mixture was

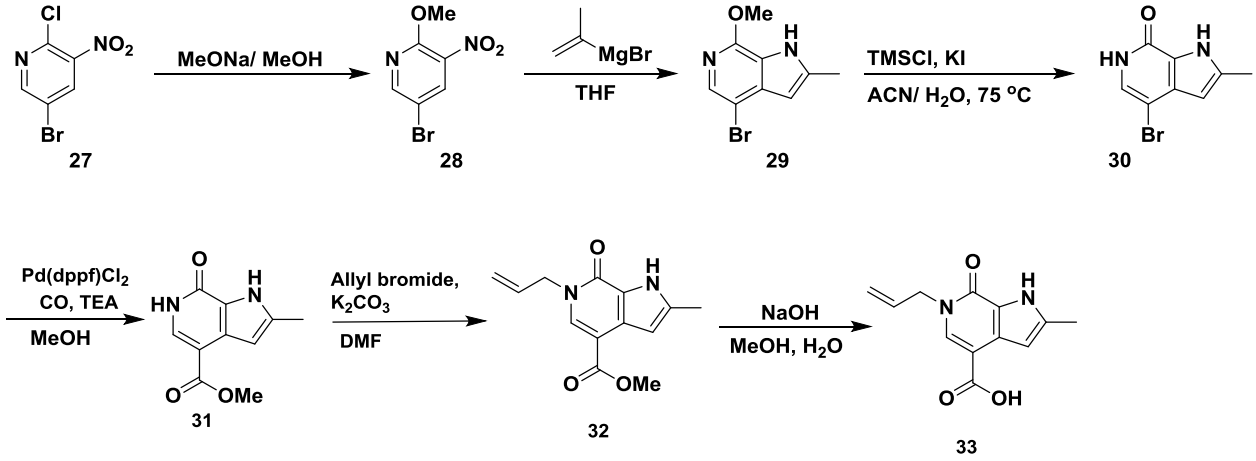
concentrated under reduced pressure. The residue was dissolved in water (30 mL) and the aqueous solution was acidified to pH 3-4 using 5 N hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and dried under reduced pressure to give the title compound (Intermediate C) (4.3 g, 67.2% yield) as a brown solid. This crude material was used in the next step without further treatment. LCMS *m/z* (M+H) 192.8.

Intermediate 26. 6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid

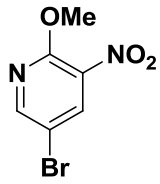


Intermediate **26** was prepared in a similar fashion as Intermediate **25**, utilizing allyl bromide as alkylating agent and potassium carbonate as base, (4.04 g, 91% yield over 2 steps). LCMS *m/z* (M+H) 240.1, 219.3

Scheme S2. Synthesis of carboxylic acid Intermediate **33**.

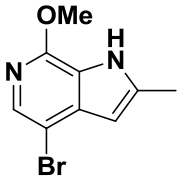


Compound 28. 5-bromo-2-methoxy-3-nitropyridine



Sodium methoxide (17.2 g, 318.4 mmol) was added to a stirred solution of 5-bromo-2-chloro-3-nitropyridine (15.0 g, 64.2 mmol) in methanol (125 mL). After addition, the reaction mixture was heated at reflux for 2 h. The mixture was concentrated under reduced pressure, and the residue was diluted with water (200 mL). The resulting precipitate was collected by filtration, washed with water, and dried under reduced pressure to give the title compound (12.0 g, 81.5% yield) as a brown solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 8.43 (d, *J* = 2.4 Hz, 1 H), 8.38 (d, *J* = 2.0 Hz, 1 H), 4.09 (s, 3 H).

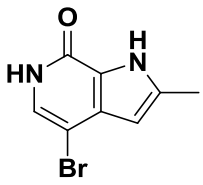
Compound 29. 4-bromo-7-methoxy-2-methyl-1H-pyrrolo[2,3-c]pyridine



Isopropenyl magnesium bromide (0.5 M in THF, 105.0 mL, 55.0 mmol) was added dropwise to a stirred and cooled (-78^{o}C) solution of 5-bromo-2-methoxy-3-nitropyridine (4.0 g, 17.1 mmol) in THF (40 mL). After addition, the resulting mixture was allowed to warm to room temperature gradually and stirred for an additional 3 h. The reaction mixture was quenched by addition of 1 M aqueous ammonium chloride (150 mL), and then extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether : ethyl acetate

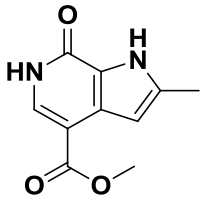
= 10:1) to give the title compound (1.65 g, 39.9% yield) as brown oil. LCMS *m/z* (M+H) 240.1, 242.1.

Compound 30. 4-bromo-2-methyl-1,6-dihydropyrrolo[2,3-c]pyridin-7-one



Hydrogen bromide (40% aqueous, 20 mL) was added to a solution of 4-bromo-7-methoxy-2-methyl-1H-pyrrolo[2,3-c]pyridine (1.65 g, 6.8 mmol) in ethanol (10 mL). After addition, the reaction mixture was heated at 90^{o}C for 15 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled to 0 °C and the resulting solid was collected by filtration. This solid was washed with water and dried to give title compound (Intermediate B, 0.9 g, 57.9% yield) as a brown solid. ^{1}H NMR (400MHz, DMSO-*d6*): δ 12.06 (s, 1 H), 11.00 (s, 1 H), 7.03 (s, 1 H), 5.97 (s, 1 H), 2.29 (s, 3 H). LCMS *m/z* (M+H) 226.8, 228.8

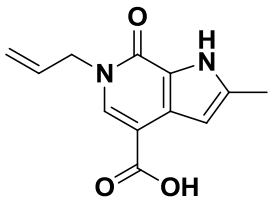
Compound 31. Methyl 2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylate



A mixture of 4-bromo-2-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (Intermediate E) (9.0 g, 39.6 mmol), Et_3N (15 ml, 107.6 mmol) and $Pd(dppf)Cl_2$ (2.4 g, 3.3 mmol) in methanol (1.0 L) was heated at 80 °C under CO atmosphere (50 psi) for 18 h, at which time LCMS showed the completion of the reaction. After cooled, the solvent was evaporated under reduced pressure.

The residue was diluted with water (150 mL) and the resulting precipitate was collected by filtration. The solid was washed with water (10 mL x 2), isopropanol (10 mL x 2) and dried to give the title compound (5.0 g, 61% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1 H), 11.32 (s, 1 H), 7.63 (d, *J* = 6.4, 1 H), 6.44 (s, 1 H), 3.76 (s, 3 H), 2.30 (s, 3 H). LCMS *m/z* (M+H) 207.0.

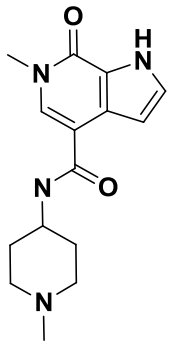
Intermediate 33. 6-allyl-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid



To a solution of methyl 2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4- carboxylate (10.0 g, 48.5 mmol) in DMF (100 mL) was added K_2CO_3 (20.1 g, 145.0 mmol) and allyl bromide (5.9 g, 48.5 mmol). After addition, the mixture was stirred at ambient temperature for 12 h, at which time LCMS showed the completion of the reaction. The reaction mixture was diluted with ice-water (200 mL). The resulting precipitate was collected by filtration, washed with water and dried.

A suspension of the above crude product in methanol (150 mL) and was added KOH (10.9 g, 194 mmol) in water (50 mL). The mixture was heated at 50 °C for 4 h, at which time LCMS showed the completion of the reaction. Methanol was evaporated under reduced pressure, and the aqueous solution was acidified by adding 2M HCl to pH 2. The resulting precipitate was collected by filtration and dried to give the title compound (10.2 g, 91% yield) as a grey solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.51 (s, 1H), 12.04-11.89 (m, 1H), 7.93 (s, 1H), 6.48 (dd, *J* = 2.4 Hz, 1H), 5.98 (ddt, *J* = 17.2, 10.6, 5.4 Hz, 1H), 5.23 – 5.13 (m, 1H), 5.07 (ddt, *J* = 17.1, 1.7, 1.7 Hz , 1H), 4.68 (dt, *J* = 5.7, 1.7 Hz, 2H), 2.34 (s, 3H). LCMS *m/z* (M+H) 233.3

Compound 1. 6-methyl-N-(1-methyl-4-piperidyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



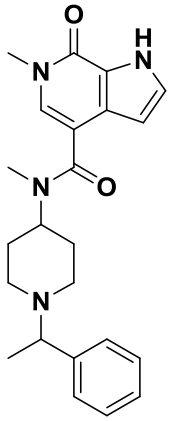
To a solution of 6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (30 mg, 0.156 mmol, 1.0 equiv) in DMF (1.0 mL) was added N1,N1-dimethylcyclohexane-1,4-diamine dihydrochloride (18.7 mg, 0.187 mmol, 1.2 equiv), HATU (78 mg, 0.203 mmol, 1.3 equiv) and N,N-diisopropylethylamine (110 uL, 0.624 mmol, 4.0 equiv). Reaction was stirred at room temperature for 16 hr. The reaction mixture was concentrated under vacuum and the crude product was purified by Prep-HPLC (Column, Gemini C18 100x30 mm; mobile phase, CH3CN:NH4OH/H2O (10 mmol/L) = 5%-85%, 10min; flow rate, 70 mL/min; Detector, UV 254 nm) to give 21.7 mg (44%) of N-[4-(dimethylamino)cyclohexyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide as an off white solid. ^{1}H NMR (400 MHz, DMSO-d6) δ 12.03 (s, 1H), 7.81 (s, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.30 (s, 1H), 6.68 (dd, *J* = 2.9, 1.2 Hz, 1H), 3.77 – 3.63 (m, 1H), 3.55 (s, 3H), 2.75 (d, *J* = 11.7 Hz, 2H), 2.16 (s, 3H), 2.00 – 1.89 (m, 2H), 1.78 (d, *J* = 12.5 Hz, 2H), 1.62 – 1.47 (m, 2H). LCMS *m/z* (M+H) 289

The following compounds were prepared in a similar manner as compound 1.

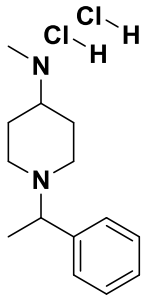
Compound 2. N,6-dimethyl-N-(1-methyl-4-piperidyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide, 13 mg (30%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.36 (s, 1H), 7.31 (d, *J* = 2.6 Hz, 1H), 6.18 (d, *J* = 2.7 Hz, 1H), 3.95 (s, 1H), 3.52 (s, 3H), 2.84 – 2.76 (m, 5H), 2.12 (s, 3H), 1.85 – 1.73 (m, 4H), 1.61 – 1.54 (m, 2H). LCMS *m/z* (M+H) 303.2

Compound 3. N-(1-isopropyl-4-piperidyl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide, 21 mg (41% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.11 (s, 1H), 7.36 (s, 1H), 7.32 (t, *J* = 2.7 Hz, 1H), 6.21 – 6.15 (m, 1H), 3.93 (s, 1H), 3.52 (s, 3H), 2.85 – 2.77 (m, 5H), 2.66 (p, *J* = 6.6 Hz, 1H), 2.10 – 2.02 (m, 2H), 1.81 – 1.66 (m, 2H), 1.65 – 1.57 (m, 2H), 0.92 (d, *J* = 6.5 Hz, 6H). LCMS *m/z* (M+H) 331.2

Compound 4. N,6-dimethyl-7-oxo-N-[1-(1-phenylethyl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide

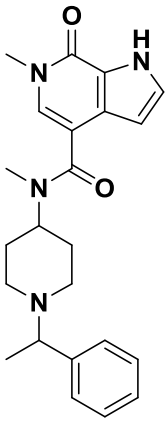


Step 1: N-methyl-1-(1-phenylethyl)piperidin-4-amine dihydrochloride



To a 40 mL vial was added 1-bromoethylbenzene (475 mg, 2.6 mmol) tert-butyl N-methyl-N-(4-piperidyl)carbamate (500 mg, 2.3 mmol), acetonitrile (4 mL), and *N*,*N*-diisopropylethylamine (1.2 mL 7.0 mmol). The reaction was capped and shaken at 80°C overnight. The reaction was cooled to room temperature, then extracted with ethyl acetate/water. The organic phase was concentrated under reduced pressure. The crude product was then taken up in 10 mL methanol, and 10 mL of 4M HCl in dioxane was added. The reaction was stirred for 1h. The resulting precipitate was collected by filtration, and washed 2x with ethyl acetate, yielding desired product as a white solid (510 mg, 75% over two steps). LCMS *m/z* (M+H) 219.3

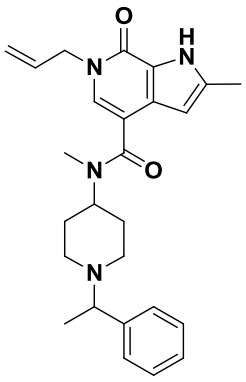
Step 2: N,6-dimethyl-7-oxo-N-[1-(1-phenylethyl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



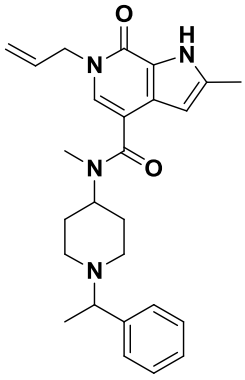
Compound **4** was prepared in a similar manner to compound 1, utilizing Int **25** and *N*-methyl-1-(1-phenylethyl)piperidin-4-amine dihydrochloride from step 1, 71 mg (53% yield). LCMS *m/z* (M+H) 393.3

Compound **5** was prepared in a similar manner to compound 1, utilizing Int **26** and *N*-methyl-1-(1-phenylethyl)piperidin-4-amine dihydrochloride from step 1, 87 mg (60% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 7.41 – 7.12 (m, 7H), 6.16 (d, *J* = 2.7 Hz, 1H), 3.51 (s, 3H), 3.48 – 3.37 (m, 1H), 3.09 – 2.59 (m, 4H), 1.94 – 1.59 (m, 6H), 1.33 – 1.23 (m, 3H). LCMS *m/z* (M+H) 419.4

Compounds 6 & 7.



Compound 6
Peak 1



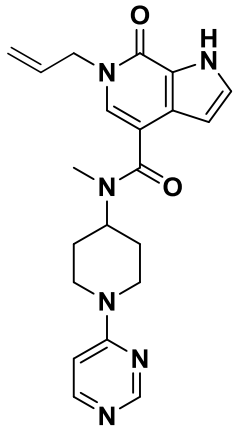
Compound 7
Peak 2

The racemic mixture was prepared in a similar manner to compound 1, utilizing Int **33** and *N*-methyl-1-(1-phenylethyl)piperidin-4-amine dihydrochloride from step 1. The racemate was then separated by SFC (SFC80; Chiralpak OD 250 X 30 mm I.D., 5um; Supercritical CO_2 / MeOH+NH_3.H_2O= 60/40; 40 ml/min, 100 bars, 40 ^{o}C) to give yield purified enantiomers:

Compound 6 (Peak 1): 6-allyl-N,2-dimethyl-7-oxo-N-(1-(1-phenylethyl)piperidin-4-yl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (19.2 mg, 7%) as white solid. ^{1}H NMR (400 MHz, 340K, DMSO-d_6) δ 11.67 (s, 1H), 7.35 – 7.25 (m, 4H), 7.25 – 7.17 (m, 1H), 7.12 (s, 1H), 6.01 – 5.86 (m, 2H), 5.11 (ddt, *J* = 10.3, 1.5, 1.5 Hz, 1H), 5.02 (ddt, *J* = 17.1, 1.6, 1.6 Hz, 1H), 4.58 (dt, *J* = 5.5, 1.6 Hz, 2H), 3.91 – 3.86 (m, 1H), 3.52 – 3.47 (m, 1H), 3.05 – 2.97 (m, 1H), 2.86 – 2.77 (m, 4H), 2.30 (s, 3H), 2.00 – 1.66 (m, 4H), 1.65 – 1.50 (m, 2H), 1.28 (d, *J* = 6.8 Hz, 3H). LCMS *m/z* (M+H): 433. Retention time, 6.77 minutes. Enatiomeric ratio: 97:3.

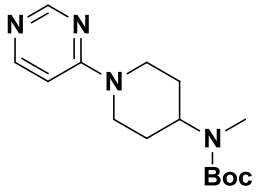
Compound 7 (Peak 2): 6-allyl-N,2-dimethyl-7-oxo-N-(1-(1-phenylethyl)piperidin-4-yl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (37.4 mg, 13%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.69 (s, 1H), 7.34 – 7.26 (m, 4H), 7.25 – 7.17 (m, 1H), 7.12 (s, 1H), 6.00 – 5.87 (m, 2H), 5.10 (ddt, *J* = 10.3, 1.6, 1.6 Hz, 1H), 5.02 (ddt, *J* = 17.2, 1.7, 1.7 Hz, 1H), 4.58 (dd, *J* = 5.6, 1.8 Hz, 2H), 3.90 – 3.85 (m, 1H), 3.50 – 3.41 (m, 1H), 3.04 – 2.94 (m, 1H), 2.90 – 2.75 (m, 4H), 2.31 (s, 3H), 1.95 – 1.65 (m, 4H), 1.65 – 1.48 (m, 2H), 1.27 (d, *J* = 6.8 Hz, 3H). LCMS [M+H]: 433. Retention time 12.25 minutes. Enantiomeric ratio >99:1.

Compound 8: 6-allyl-N-methyl-7-oxo-N-(1-pyrimidin-4-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

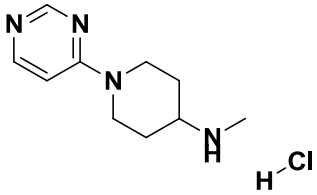
tert-butyl methyl(1-(pyrimidin-4-yl)piperidin-4-yl)carbamate



A mixture of tert-butyl methyl(piperidin-4-yl)carbamate (500 mg, 2.3 mmol), cesium carbonate (836 mg, 2.6 mmol) and 4-chloropyrimidine (294 mg, 2.6 mmol) in DMF (10 mL) was heated at 80 °C for 3 h, at which time LCMS indicated full conversion of starting material. The reaction mixture was poured into ice water (10 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure to give the title compound (450 mg, 66.0% yield) as a yellow solid. This crude material was used in the next step without further purification.

Step 2:

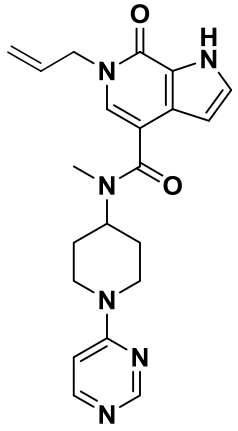
N-methyl-1-(pyrimidin-4-yl)piperidin-4-amine hydrochloride



To a cooled (0 °C) solution of tert-butyl methyl(1-(pyrimidin-4-yl)piperidin-4-yl)carbamate (300 mg, 1.0 mmol) in ethyl acetate (50 mL) was added hydrogen chloride (2M in ethyl acetate, 10 mL). After addition, the reaction mixture was stirred at 25 °C for 3 h. The solvent was evaporated under reduced pressure to give the crude title compound (165 mg, 72% yield) as a yellow solid.

Step 3:

N,6-dimethyl-7-oxo-N-(1-pyrimidin-4-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



A mixture of Intermediate **26** (50 mg, 0.23 mmol), triethylamine (93 mg, 0.92 mmol), HATU (94 mg, 0.24 mmol) and 1-(pyrimidin-4-yl)piperidin-4-amine hydrochloride (62 mg, 0.27 mmol) in DMF (1 mL) was stirred at 25 °C overnight. The reaction was then diluted with DCM, washed with water, and the organic phase concentrated under reduced pressure. The residue was purified by preparative HPLC, acetonitrile : water (10 nM ammonia) : 32%-62%, to give the title compound. 6-allyl-N-methyl-7-oxo-N-(1-pyrimidin-4-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (32 mg, 35% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.14 (s, 1H), 8.47 (d, *J* = 1.2 Hz, 1H), 8.15 (d, *J* = 6.2 Hz, 1H), 7.43 – 7.25 (m, 2H), 6.85 (dd, *J* = 6.4, 1.3 Hz, 1H), 6.24

(t, *J* = 2.3 Hz, 1H), 5.99 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H), 5.17 (ddt, *J* = 10.3, 1.4 , 1.4 Hz, 1H), 5.13 – 5.01 (m, 1H), 4.72 – 4.58 (m, 2H), 4.51 (d, *J* = 13.1 Hz, 2H), 4.33 (s, 1H), 2.79 (s, 5H), 1.72 (td, *J* = 11.4, 10.2, 3.8 Hz, 4H). LCMS *m/z* (M+H) 393.2

Compound 9: 6-allyl-N-methyl-7-oxo-N-[1-[6-(trifluoromethyl)pyrimidin-4-yl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (49% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 8.61 (d, *J* = 1.1 Hz, 1H), 7.38 – 7.27 (m, 3H), 6.25 (d, *J* = 2.7 Hz, 1H), 6.06 – 5.92 (m, 1H), 5.22 – 5.13 (m, 1H), 5.12 – 5.02 (m, 1H), 4.68 – 4.60 (m, 2H), 4.41 – 4.36 (m, 1H), 3.35 – 3.23 (m, 2H), 2.96 (s, 2H), 2.79 (s, 3H), 1.79 – 1.72 (m, 4H). LCMS *m/z* (M+H) 461.2

Compound 10: 6-allyl-N-[1-(6-methoxypyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (31% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.23 (d, *J* = 0.8 Hz, 1H), 7.34 (d, *J* = 2.8 Hz, 1H), 7.30 (s, 1H), 6.24 (d, *J* = 2.7 Hz, 1H), 6.10 (d, *J* = 0.9 Hz, 1H), 6.06 – 5.91 (m, 1H), 5.21 – 5.12 (m, 1H), 5.12 – 5.01 (m, 1H), 4.64 (dt, *J* = 5.5, 1.5 Hz, 2H), 4.45 (d, *J* = 13.1 Hz, 2H), 4.30 (s, 1H), 3.81 (s, 3H), 3.37 – 3.25 (m, 1H), 2.78 (s, 5H), 1.74 – 1.62 (m, 4H). LCMS *m/z* (M+H) 423.2.

Compound 11: 6-allyl-N-[1-(6-cyclopropylpyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (34% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 8.30 (d, *J* = 1.0 Hz, 1H), 7.38 – 7.28 (m, 2H), 6.79 (d, *J* = 1.2 Hz, 1H), 6.24 (dd, *J* = 2.9, 1.4 Hz, 1H), 6.06 – 5.91 (m, 1H), 5.21 – 5.13 (m, 1H), 5.12 – 5.01 (m, 1H), 4.67 – 4.60 (m, 2H), 4.51 (d, *J* = 13.2 Hz, 2H), 4.44 – 4.18 (m, 1H), 3.37 – 3.23 (m, 22H), 2.91 – 2.72 (m, 5H), 1.95 – 1.84 (m, 1H), 1.76 – 1.63 (m, 4H), 0.98 – 0.84 (m, 4H). LCMS *m/z* (M+H) 433.2

Compound 12: 6-allyl-N-[1-(6-tert-butylpyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (11% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.14 (d, *J* = 6.1 Hz, 1H), 7.32 (d, *J* = 19.9 Hz, 2H), 6.63 (d, *J* = 6.2 Hz, 1H), 6.24 (d, *J* = 2.8

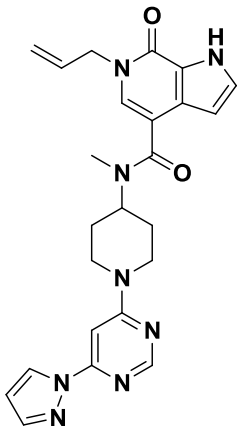
Hz, 1H), 5.99 (ddt, *J* = 17.0, 10.4, 5.4 Hz, 1H), 5.17 (ddt, *J* = 10.2, 1.3, 1.3 Hz, 1H), 5.07 (ddt, *J* = 17.3, 1.6, 1.6 Hz, 1H), 4.64 (dt, *J* = 5.8, 1.6 Hz, 2H), 4.55 (s, 1H), 2.79 (s, 5H), 1.73 (td, *J* = 11.4, 10.2, 4.0 Hz, 4H), 1.27 (s, 9H). LCMS *m/z* (M+H) 449.2G0

Compound 13: 6-allyl-N-[1-(6-methoxy-2-methyl-pyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (32 % yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 7.37 – 7.27 (m, 2H), 6.23 (d, *J* = 2.7 Hz, 1H), 6.06 – 5.88 (m, 2H), 5.17 (d, *J* = 10.2 Hz, 1H), 5.11 – 5.02 (m, 1H), 4.63 (d, *J* = 5.4 Hz, 2H), 4.45 (d, *J* = 13.0 Hz, 2H), 4.29 (s, 0H), 3.79 (s, 3H), 2.93 – 2.68 (m, 5H), 2.31 (s, 3H), 1.69 (t, *J* = 5.9 Hz, 4H). LCMS *m/z* (M+H) 437.2

Compound 14: 6-allyl-N-[1-(2,6-dimethylpyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (36% yield). 1H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 7.38 – 7.27 (m, 2H), 6.53 (s, 1H), 6.28 – 6.21 (m, 1H), 6.06 – 5.91 (m, 1H), 5.21 – 5.13 (m, 1H), 5.12 – 5.01 (m, 1H), 4.64 (dt, J = 5.4, 1.6 Hz, 2H), 4.51 (d, J = 13.1 Hz, 2H), 4.31 (s, 1H), 2.81 – 2.76 (m, 5H), 2.31 (s, 3H), 2.20 (s, 3H), 1.75 – 1.61 (m, 4H). LCMS *m/z* (M+H) 421.2

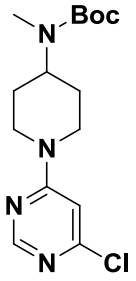
Compound 15: 6-allyl-N-[1-(6-cyclopropyl-2-methyl-pyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (11%). 1H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 7.38 – 7.27 (m, 2H), 6.57 (s, 1H), 6.24 (d, J = 2.6 Hz, 1H), 5.99 (ddt, J = 15.9, 10.3, 5.3 Hz, 1H), 5.17 (d, J = 10.2 Hz, 1H), 5.07 (d, J = 17.2 Hz, 1H), 4.64 (d, J = 5.4 Hz, 2H), 4.51 (d, J = 13.0 Hz, 2H), 4.31 (s, 1H), 2.78 (s, 5H), 2.27 (s, 3H), 1.85 (tt, J = 8.7, 5.1 Hz, 1H), 1.68 (d, J = 18.8 Hz, 4H), 0.95 – 0.80 (m, 4H). LCMS *m/z* (M+H) 447.2

Compound 16: 6-allyl-*N*-methyl-7-oxo-*N*-[1-(6-pyrazol-1-ylpyrimidin-4-yl)-4-piperidyl]-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



Step 1

tert-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl)carbamate

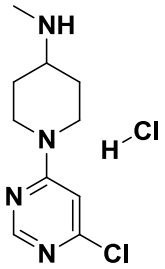


To a solution of 4,6-dichloropyrimidine (5.2 g, 35.00 mmol) in DMF (100 mL) were added *tert*-butyl methyl(piperidin-4-yl)carbamate (5.0 g, 23.33 mmol) and cesium carbonate (15.2 g, 46.66 mmol). After addition, the reaction mixture was heated at 80 ^{o}C for 16 h, at which time LCMS indicated the reaction had gone to completion. The solution was poured into ice water, and

extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by silica gel chromatography column (Hexanes/ethyl acetate = 5:1) to give the title compound (7.0 g, 92% yield) as a colorless oil.

Step 2

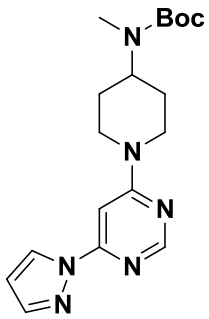
1-(6-chloropyrimidin-4-yl)-N-methylpiperidin-4-amine hydrochloride



To a solution of *tert*-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl) carbamate (7.0 g, 21.42 mmol) in ethyl acetate (25 mL) was added a solution of hydrogen chloride (2 in ethyl acetate, 10 mL). After addition, the mixture was stirred at room temperature for 3 h, at which time LCMS indicated the reaction had gone to completion. The solution was concentrated under reduced pressure to give the crude title compound (4.5 g, 80% yield) as a yellow oil.

Step 3

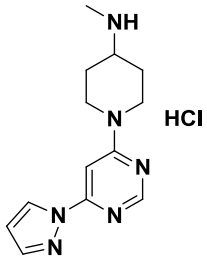
tert-butyl (1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)piperidin-4-yl)(methyl)carbamate



To a solution of *tert*-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl) carbamate (600 mg, 1.84 mmol) in DMF (10 mL) was added 1*H*-pyrazole (150 mg, 2.20 mmol) and cesium carbonate (1.2 g, 3.67 mmol). After addition, the reaction mixture was heated at 80 °C for 12 h, at which time LCMS indicated the reaction had gone to completion. After cooled, the solid was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (50 mL), washed with water (2 x 30 mL), dried over sodium sulfate and concentrated to give the crude title compound (500 mg, 76 % yield) as a yellow solid.

Step 4

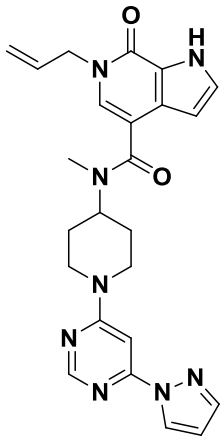
1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)-N-methylpiperidin-4-amine hydrochloride



To a solution of *tert*-butyl (1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)piperidin-4-yl)(methyl) carbamate (500 mg, 1.39 mmol) in ethyl acetate (10 mL) was added hydrogen chloride (2M in ethyl acetate, 10 mL) at 0 ^{o}C. After addition, the mixture was stirred at ambient temperature for 2 h, at which time LCMS indicated the reaction had gone to completion. The solution was concentrated under reduced pressure to give the crude title compound (400 mg, 97% yield) as a white solid.

Step 5

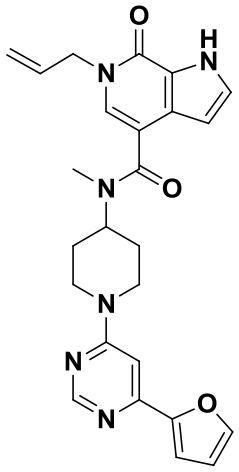
6-allyl-*N*-methyl-7-oxo-*N*-[1-(6-pyrazol-1-ylpyrimidin-4-yl)-4-piperidyl]-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



To a solution of 1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)-*N*-methylpiperidin-4-amine hydrochloride (216 mg, 0.73 mmol) in DMF (4 mL) was added 6-allyl-7-oxo -6,7-dihydro-1*H*-pyrrolo[2,3-c]pyridine-4-carboxylic acid (80 mg, 0.37 mmol), *N*-ethyl-*N*-isopropylpropan-2-amine (142 mg, 1.1 mmol) and HATU (181 mg, 0.48 mmol). After addition, the mixture was stirred at ambient temperature for 1.5 h, at which time LCMS indicated that the reaction had gone to completion. The solvent was removed under reduce pressure. The residue was dissolved in ethyl acetate (20 mL), washed with brine (2 x 15 mL) and concentrated. The crude product was purified by reverse phase chromatography (acetonitrile 40% / 0.1% NH_4OH in water) to

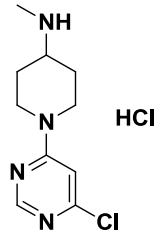
give the title compound (12.8 mg, 8% yield) as a yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.19 (s, 1 H), 8.68 (s, 1 H), 8.49 (s, 1 H), 7.91 (s, 1 H), 7.34 (d, *J* = 11.6 Hz, 2 H), 7.24 (s, 1 H), 6.63 (s, 1 H), 6.24 (s, 1 H), 5.99-5.94 (m, 1 H), 5.16 (d, *J* = 10.0 Hz, 1 H), 5.06 (d, *J* = 17.2 Hz, 1 H), 4.64-4.40 (m, 5 H), 3.03 (s, 2 H), 2.78 (s, 3 H), 1.79 (s, 4 H). LCMS *m/z* (M+H) 459.1.

Compound 17: 6-allyl-N-(1-(6-(furan-2-yl)pyrimidin-4-yl)piperidin-4-yl)-N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

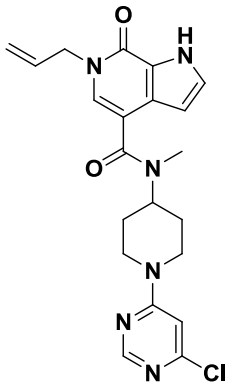
1-(6-chloropyrimidin-4-yl)-N-methylpiperidin-4-amine hydrochloride



To a solution of *tert*-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl)carbamate (7.0 g, 21.5 mmol) in ethyl acetate (50 mL) was added hydrogen chloride (2M in ethyl acetate, 50 mL). The reaction mixture was stirred at ambient temperature for 3 hours and then concentrated under reduced pressure to give the crude title compound as hydrogen chloride salt (5.5 g, 98%). This material was used directly in the next step without purification.

Step 2:

6-allyl-N-(1-(6-chloropyrimidin-4-yl)piperidin-4-yl)-N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide

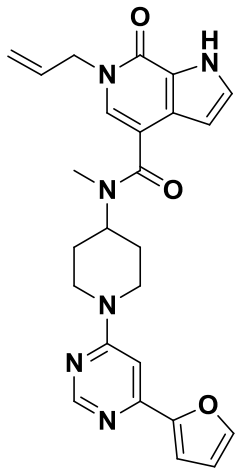


To a solution of 6-allyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (2.8 g, 12.8 mmol), HATU (5.9 g, 15.4 mmol) and triethylamine (3.9 g, 38.5 mmol) in DMF (100 mL) was added 1-(6-chloropyrimidin-4-yl)-N-methylpiperidin-4-amine hydrochloride (4.4 g, 16.7 mmol). The mixture was stirred at 20 ^{o}C for 16 hours. The solution was poured into water (100 mL) and extracted with ethyl acetate (3 x 100 mL). The combined organic layers were

concentrated under reduced pressure and the residue was purified by silica gel chromatography (Hexanes/ethyl acetate=1:1) to give the title compound (2.8 g, 51%) as a yellow solid.

Step 3:

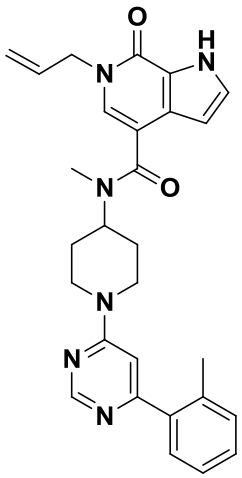
6-allyl-N-(1-(6-(furan-2-yl)pyrimidin-4-yl)piperidin-4-yl)-N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



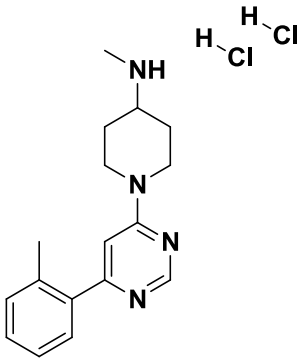
To a solution of 6-allyl-N-(1-(6-chloropyrimidin-4-yl)piperidin-4-yl)-N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (100 mg, 0.23 mmol) in dioxane / water (2.5/0.5 mL) was added furan-2-ylboronic acid (39 mg, 0.35 mmol), cesium carbonate (153 mg, 0.47 mmol) and Pd(dppf)Cl_2 (17 mg, 0.02 mmol). The mixture was stirred at 85 ^oC for 30 min by microwave under N_2. After cooled, the organic solution was concentrated under reduced pressure and the residue was purified by preparative HPLC (acetonitrile 20-50% / 0.1% NH4OH in water) to give 6-allyl-N-(1-(6-(furan-2-yl)pyrimidin-4-yl)piperidin-4-yl)-N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (16.9 mg, 16%) as a white solid. ^1H NMR (400 MHz, DMSO-d_6): δ 12.19 (br. s, 1H), 8.47 (s, 1 H), 7.88 (s, 1H), 7.36 – 7.32 (m, 2 H), 7.20

– 7.19 (m, 1 H), 7.05 (s, 1 H), 6.68 – 6.66 (m, 1H), 6.25 – 6.24 (m, 1H), 6.00 – 5.98 (m, 1 H), 5.18 – 5.15 (m, 1 H), 5.09 – 5.04 (m, 1 H), 4.65 – 4.50 (m, 4 H), 4.37 – 4.33 (m, 1H), 2.94 – 2.90 (m, 2 H), 2.79 (s, 3H), 1.78 – 1.73 (m, 4H). LCMS *m/z* (M+H) 459.1

Compound 18: 6-allyl-N-methyl-N-[1-[6-(o-tolyl)pyrimidin-4-yl]-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1: N-methyl-1-(6-o-tolylpyrimidin-4-yl)piperidin-4-amine dihydrochloride

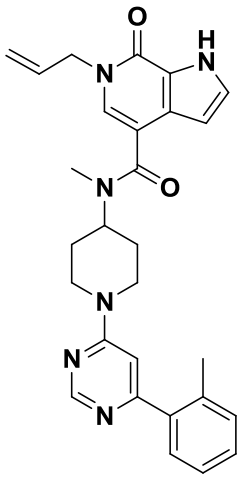


To an 8 mL vial was added tert-butyl N-[1-(6-chloropyrimidin-4-yl)-4-piperidyl]-N-methyl-carbamate (200 mg, 0.61 mmol), o-tolylboronic acid (166 mg, 1.22 mmol), XPhos (0.05 equiv.,

15 mg 0.03 mmol) XPhos Precatalyst (26 mg, 0.03 mmol), 1,4-dioxane (2 mL), and potassium phosphate tribasic 2M in water (0.92 mL, 1.836 mmol, 2.0 mol/L). The reaction was capped and shaken at 90°C for 1h. The reaction was cooled to room temperature then diluted with DCM and washed with water. The organic was then concentrated under reduced pressure. LCMS *m/z* (M+H) 383.3

The crude was taken up with 1 mL DCM, and 1 mL trifluoroacetic acid was added. The reaction was capped and shaken at room temperature for 1h, and was then concentrated under reduced pressure and carried directly on to the amide coupling step. LCMS *m/z* (M+H) 283.3

Step 2: 6-allyl-N-methyl-N-[1-[6-(o-tolyl)pyrimidin-4-yl]-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



The amide was prepared in a similar manner as Compound **1**. 6-allyl-N-methyl-N-[1-[6-(o-tolyl)pyrimidin-4-yl]-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (156 mg, 54 % yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.55 (d, *J* = 1.1 Hz, 1H), 7.42 – 7.22 (m, 6H), 6.90 (d, *J* = 1.3 Hz, 1H), 6.25 (d, *J* = 2.6 Hz, 1H), 5.99 (ddt, *J* = 17.0, 10.5, 5.4 Hz, 1H), 5.17 (ddt, *J* = 10.3, 1.4, 1.4 Hz, 1H), 5.07 (ddt, *J* = 17.2, 1.6, 1.6 Hz, 1H), 4.64 (dt, *J* = 5.6, 1.6

Hz, 3H), 4.34 (s, 1H), 2.88 (s, 1H), 2.80 (s, 3H), 2.34 (s, 3H), 1.75 (t, *J* = 6.5 Hz, 4H). LCMS *m/z* (M+H) 483.2

Compounds **19-20** were prepared in a manner similar to Compound 13

Compound 19: 6-allyl-N-(1-(6-(2-fluorophenyl)pyrimidin-4-yl)piperidin-4-yl)-N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (22 mg, 16% yield). ^{1}H NMR (400 MHz, CD_3OD): δ 8.74 (s, 1 H), 7.79-7.70 (m, 2 H), 7.45 – 7.36 (m, 5 H), 6.39 (s, 1 H), 6.08 – 6.00 (m, 1 H), 5.37 – 5.33 (m, 1 H), 5.25 – 5.21 (m, 2H), 4.73 - 4.74 (m, 2 H), 4.50 – 4.47 (m, 2 H), 3.36-3.34 (m, 1 H), 2.96 - 2.90 (m, 4 H), 2.20 - 1.99 (m, 4 H). LCMS *m/z* (M+H) 487

Compound 20: 6-allyl-N-(1-(6-(2-methoxyphenyl)pyrimidin-4-yl)piperidin-4-yl)-N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (20 mg, 17% yield). ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.19 (br. s, 1H), 8.56 (s, 1 H), 7.78 – 7.75 (m, 1 H), 7.42 – 7.40 (m, 1 H), 7.38 - 7.36 (m, 1 H), 7.30 (s, 1 H), 7.25 (s, 1H), 7.15 – 7.13 (m, 1H), 7.06 – 7.04 (m, 1H), 6.25 – 6.24 (m, 1 H), 5.99 – 5.95 (m, 1 H), 5.18 – 5.15 (m, 1 H), 5.08 – 5.06 (m, 1H), 5.04 – 5.03 (m, 2 H), 4.55 – 4.48 (m, 2 H), 4.35 – 4.30 (m, 1H), 3.84 (s, 3H), 2.96 – 2.90 (m, 2 H), 2.50 (s, 3H), 1.75 – 1.69 (m, 4H). LCMS *m/z* (M+H) 499

Compound 21: 6-allyl-N-[1-[6-(3-methoxyphenyl)pyrimidin-4-yl]-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide. Compound **21** was prepared in a similar manner to Compound **8**, starting from 4-chloro-6-(3-methoxyphenyl)pyrimidine. (165 mg, 33% yield). ^{1}H NMR (400 MHz, DMSO-δ6) δ 11.88 (s, 1H), 8.55 (d, *J* = 1.1 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 2.8 Hz, 1H), 7.27 – 7.21 (m, 2H), 7.03 (dd, *J* = 8.0, 2.6 Hz, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 5.99 (ddt, *J* = 17.2, 10.7, 5.5 Hz, 1H), 5.18 (ddt, *J* = 10.3, 1.5, 1.5 Hz, 1H), 5.12 (ddt, *J* = 17.2, 1.7 , 1.7 Hz, 1H), 4.70 – 4.58 (m, 4H), 4.35 (p, *J* = 8.5 Hz, 1H),

3.83 (s, 3H), 2.96 – 2.84 (m, 2H), 2.81 (s, 3H), 1.79 (td, *J* = 9.4, 8.3, 4.2 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-δ6, 360 K) δ 167.98, 162.60, 162.33, 160.26, 158.42, 154.17, 139.69, 134.73, 129.99, 128.60, 127.99, 127.85, 123.47, 119.75, 117.43, 116.30, 112.96, 111.73, 102.78, 99.06, 55.86, 54.26, 49.38, 43.69, 30.50, 28.95. HRMS: calcd for $C_{28}H_{31}N_6O_3$ *m/z* (M+H) 499.2452, found 499.2430.

Modeling Methods. The figures of crystal structures were created using MOE version 2014.09 (Chemical Computing Group, Inc.) with the exception of Figures 1 and 9, which were created using PyMol version 1.5.0.5 (Schrodinger, LLC). The Proasis water scores were computed using Proasis version 3 (Desert Scientific Software). The model of **3** bound to CECR2 was created in MOE, starting from a crystal structure of CECR2 with ethylene glycol bound in the Kac-binding pocket (PDB: 3NXB). Chain A of this structure was superimposed to the structure of **4** in BRD9, and **3** was manually built starting from the aligned small molecule **4**. Ethylene glycol and water were removed from the CECR2 pocket, resulting in a complex of **3** and the bromodomain of CECR2. This complex was minimized using the MMFFs force field with default minimization parameters but with protein residues other than those contacting **3** fixed. Residues in the pocket were tethered with default restraints, and no restraints were used on **3** during minimization.

Molecular Modeling Coordinates

```
ATOM      1  N   ASP B 438     -28.730 -13.743  -1.095  1.00 51.77           N1+
ATOM      2  CA  ASP B 438     -28.817 -12.255  -0.923  1.00 56.42           C
ATOM      3  C   ASP B 438     -27.465 -11.599  -1.185  1.00 62.16           C
ATOM      4  O   ASP B 438     -26.422 -12.251  -1.121  1.00 47.27           O
ATOM      5  CB  ASP B 438     -29.372 -11.842   0.468  1.00 57.46           C
ATOM      6  CG  ASP B 438     -28.395 -12.094   1.643  1.00 55.41           C
ATOM      7  OD1 ASP B 438     -28.704 -11.657   2.779  1.00 60.73           O
ATOM      8  OD2 ASP B 438     -27.340 -12.729   1.465  1.00 61.13           O1-
ATOM      9  N   ASP B 439     -27.504 -10.299  -1.456  1.00 57.94           N
ATOM     10  CA  ASP B 439     -26.325  -9.571  -1.894  1.00 50.16           C
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ATOM     22  CG  PHE B 440     -24.644  -9.657   4.148  1.00 46.28           C
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ATOM     41  CA  MET B 443     -20.515  -9.886  -1.591  1.00 25.42           C
ATOM     42  C   MET B 443     -19.475 -10.278  -0.545  1.00 25.07           C
ATOM     43  O   MET B 443     -18.280 -10.101  -0.747  1.00 23.13           O
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ATOM     45  CG  MET B 443     -21.777  -7.963  -2.725  1.00 29.20           C
ATOM     46  SD  MET B 443     -20.895  -8.103  -4.337  1.00 37.68           S
ATOM     47  CE  MET B 443     -21.521  -9.680  -5.010  1.00 31.72           C
ATOM     48  N   TYR B 444     -19.927 -10.841   0.568  1.00 27.93           N
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ATOM     50  C   TYR B 444     -18.164 -12.503   0.969  1.00 29.90           C
ATOM     51  O   TYR B 444     -16.964 -12.610   1.230  1.00 26.34           O
ATOM     52  CB  TYR B 444     -19.750 -11.810   2.837  1.00 33.90           C
ATOM     53  CG  TYR B 444     -19.017 -11.516   4.128  1.00 34.44           C
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ATOM     55  CD2 TYR B 444     -17.693 -11.921   4.318  1.00 40.69           C
ATOM     56  CE1 TYR B 444     -18.980 -10.556   6.336  1.00 45.25           C
ATOM     57  CE2 TYR B 444     -17.020 -11.657   5.513  1.00 44.74           C
ATOM     58  CZ  TYR B 444     -17.675 -10.970   6.519  1.00 35.53           C
ATOM     59  OH  TYR B 444     -17.031 -10.679   7.710  1.00 40.54           O
ATOM     60  N   LYS B 445     -18.799 -13.336   0.140  1.00 33.29           N
ATOM     61  CA  LYS B 445     -18.078 -14.416  -0.542  1.00 35.10           C
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ATOM     63  O   LYS B 445     -15.872 -14.371  -1.396  1.00 30.38           O
ATOM     64  CB  LYS B 445     -19.015 -15.343  -1.337  1.00 40.07           C
ATOM     65  CG  LYS B 445     -19.770 -16.328  -0.442  1.00 51.11           C
ATOM     66  CD  LYS B 445     -20.911 -17.052  -1.168  1.00 59.38           C
ATOM     67  CE  LYS B 445     -21.646 -18.000  -0.214  1.00 57.30           C
ATOM     68  NZ  LYS B 445     -22.890 -18.560  -0.796  1.00 63.95           N1+
ATOM     69  N   VAL B 446     -17.351 -12.847  -2.259  1.00 27.27           N
ATOM     70  CA  VAL B 446     -16.398 -12.121  -3.124  1.00 23.52           C
ATOM     71  C   VAL B 446     -15.226 -11.552  -2.318  1.00 27.64           C
ATOM     72  O   VAL B 446     -14.059 -11.675  -2.716  1.00 25.54           O
ATOM     73  CB  VAL B 446     -17.064 -10.969  -3.929  1.00 21.35           C
ATOM     74  CG1 VAL B 446     -15.985 -10.089  -4.677  1.00 19.09           C
ATOM     75  CG2 VAL B 446     -18.087 -11.532  -4.933  1.00 22.24           C
ATOM     76  N   LEU B 447     -15.537 -10.934  -1.177  1.00 23.48           N
ATOM     77  CA  LEU B 447     -14.512 -10.332  -0.339  1.00 26.08           C
ATOM     78  C   LEU B 447     -13.525 -11.381   0.213  1.00 22.38           C
ATOM     79  O   LEU B 447     -12.298 -11.167   0.190  1.00 23.70           O
ATOM     80  CB  LEU B 447     -15.152  -9.522   0.821  1.00 24.75           C
ATOM     81  CG  LEU B 447     -14.179  -8.542   1.485  1.00 31.18           C
ATOM     82  CD1 LEU B 447     -13.527  -7.605   0.448  1.00 40.46           C
ATOM     83  CD2 LEU B 447     -14.860  -7.725   2.561  1.00 29.83           C
ATOM     84  N   ASP B 448     -14.061 -12.486   0.728  1.00 26.25           N
ATOM     85  CA  ASP B 448     -13.263 -13.610   1.221  1.00 24.99           C
ATOM     86  C   ASP B 448     -12.359 -14.183   0.120  1.00 26.24           C
ATOM     87  O   ASP B 448     -11.238 -14.621   0.405  1.00 25.89           O
ATOM     88  CB  ASP B 448     -14.157 -14.751   1.748  1.00 34.85           C
ATOM     89  CG  ASP B 448     -14.941 -14.377   3.024  1.00 42.65           C
ATOM     90  OD1 ASP B 448     -14.456 -13.590   3.863  1.00 44.54           O
ATOM     91  OD2 ASP B 448     -16.053 -14.896   3.181  1.00 52.11           O1-
ATOM     92  N   VAL B 449     -12.855 -14.236  -1.122  1.00 23.89           N
ATOM     93  CA  VAL B 449     -12.053 -14.741  -2.240  1.00 28.97           C
ATOM     94  C   VAL B 449     -10.888 -13.792  -2.541  1.00 30.17           C
ATOM     95  O   VAL B 449      -9.784 -14.224  -2.828  1.00 26.99           O
ATOM     96  CB  VAL B 449     -12.933 -15.001  -3.516  1.00 27.36           C
ATOM     97  CG1 VAL B 449     -12.065 -15.392  -4.702  1.00 30.47           C
ATOM     98  CG2 VAL B 449     -13.948 -16.110  -3.225  1.00 31.39           C
ATOM     99  N   VAL B 450     -11.144 -12.490  -2.468  1.00 22.14           N
ATOM    100  CA  VAL B 450     -10.088 -11.502  -2.678  1.00 24.00           C
ATOM    101  C   VAL B 450      -9.099 -11.557  -1.497  1.00 28.14           C
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ATOM    102  O   VAL B 450      -7.895 -11.604  -1.703  1.00 22.14           O
ATOM    103  CB  VAL B 450     -10.671 -10.070  -2.838  1.00 24.56           C
ATOM    104  CG1 VAL B 450      -9.546  -9.048  -2.919  1.00 23.93           C
ATOM    105  CG2 VAL B 450     -11.550  -9.983  -4.086  1.00 23.61           C
ATOM    106  N   LYS B 451      -9.624 -11.611  -0.274  1.00 24.17           N
ATOM    107  CA  LYS B 451      -8.794 -11.700   0.912  1.00 26.44           C
ATOM    108  C   LYS B 451      -7.901 -12.950   0.827  1.00 29.24           C
ATOM    109  O   LYS B 451      -6.718 -12.894   1.169  1.00 29.81           O
ATOM    110  CB  LYS B 451      -9.659 -11.756   2.189  1.00 29.31           C
ATOM    111  CG  LYS B 451      -8.919 -11.350   3.458  1.00 33.98           C
ATOM    112  CD  LYS B 451      -9.524 -11.913   4.774  1.00 44.17           C
ATOM    113  CE  LYS B 451     -10.959 -11.524   5.032  1.00 43.86           C
ATOM    114  NZ  LYS B 451     -11.335 -11.767   6.484  1.00 35.88           N1+
ATOM    115  N   ALA B 452      -8.467 -14.076   0.375  1.00 26.61           N
ATOM    116  CA  ALA B 452      -7.711 -15.334   0.264  1.00 29.35           C
ATOM    117  C   ALA B 452      -6.569 -15.318  -0.765  1.00 33.20           C
ATOM    118  O   ALA B 452      -5.687 -16.161  -0.720  1.00 29.44           O
ATOM    119  CB  ALA B 452      -8.657 -16.473  -0.065  1.00 32.51           C
ATOM    120  N   HIS B 453      -6.582 -14.392  -1.706  1.00 27.83           N
ATOM    121  CA  HIS B 453      -5.543 -14.328  -2.725  1.00 28.12           C
ATOM    122  C   HIS B 453      -4.156 -14.018  -2.152  1.00 24.98           C
ATOM    123  O   HIS B 453      -4.007 -13.188  -1.261  1.00 27.78           O
ATOM    124  CB  HIS B 453      -5.924 -13.269  -3.768  1.00 28.02           C
ATOM    125  CG  HIS B 453      -5.148 -13.360  -5.046  1.00 25.43           C
ATOM    126  CD2 HIS B 453      -5.466 -13.899  -6.250  1.00 26.05           C
ATOM    127  ND1 HIS B 453      -3.885 -12.821  -5.188  1.00 25.33           N
ATOM    128  CE1 HIS B 453      -3.455 -13.039  -6.423  1.00 31.25           C
ATOM    129  NE2 HIS B 453      -4.403 -13.675  -7.092  1.00 27.35           N
ATOM    130  N   LYS B 454      -3.141 -14.706  -2.653  1.00 24.73           N
ATOM    131  CA  LYS B 454      -1.757 -14.532  -2.186  1.00 26.62           C
ATOM    132  C   LYS B 454      -1.259 -13.069  -2.258  1.00 25.84           C
ATOM    133  O   LYS B 454      -0.428 -12.665  -1.465  1.00 26.19           O
ATOM    134  CB  LYS B 454      -0.834 -15.478  -2.996  1.00 27.73           C
ATOM    135  CG  LYS B 454      -0.645 -15.068  -4.467  1.00 30.83           C
ATOM    136  CD  LYS B 454       0.282 -16.059  -5.190  1.00 38.87           C
ATOM    137  CE  LYS B 454       0.565 -15.644  -6.640  1.00  0.00           C
ATOM    138  NZ  LYS B 454       1.406 -14.422  -6.722  1.00  0.00           N1+
ATOM    139  N   ASP B 455      -1.757 -12.289  -3.206  1.00 24.11           N
ATOM    140  CA  ASP B 455      -1.348 -10.883  -3.303  1.00 25.33           C
ATOM    141  C   ASP B 455      -2.209  -9.913  -2.475  1.00 28.22           C
ATOM    142  O   ASP B 455      -2.082  -8.697  -2.643  1.00 25.03           O
ATOM    143  CB  ASP B 455      -1.327 -10.441  -4.770  1.00 21.53           C
ATOM    144  CG  ASP B 455      -0.188 -11.068  -5.556  1.00 23.58           C
ATOM    145  OD1 ASP B 455       0.824 -11.453  -4.949  1.00 25.27           O
ATOM    146  OD2 ASP B 455      -0.318 -11.175  -6.776  1.00 30.81           O1-
ATOM    147  N   SER B 456      -3.048 -10.416  -1.559  1.00 25.40           N
ATOM    148  CA  SER B 456      -3.936  -9.506  -0.808  1.00 22.65           C
ATOM    149  C   SER B 456      -3.212  -8.769   0.324  1.00 27.48           C
ATOM    150  O   SER B 456      -3.691  -7.743   0.780  1.00 23.32           O
ATOM    151  CB  SER B 456      -5.109 -10.247  -0.185  1.00 22.19           C
ATOM    152  OG  SER B 456      -4.637 -11.108   0.837  1.00 21.75           O
ATOM    153  N   TRP B 457      -2.072  -9.297   0.777  1.00 23.74           N
ATOM    154  CA  TRP B 457      -1.470  -8.860   2.045  1.00 23.09           C
ATOM    155  C   TRP B 457      -1.229  -7.333   2.181  1.00 19.92           C
ATOM    156  O   TRP B 457      -1.456  -6.817   3.242  1.00 23.66           O
ATOM    157  CB  TRP B 457      -0.218  -9.703   2.446  1.00 25.44           C
ATOM    158  CG  TRP B 457       0.955  -9.543   1.536  1.00 29.22           C
ATOM    159  CD1 TRP B 457       1.303 -10.363   0.499  1.00 30.22           C
ATOM    160  CD2 TRP B 457       1.960  -8.520   1.594  1.00 27.45           C
ATOM    161  CE2 TRP B 457       2.875  -8.775   0.552  1.00 33.88           C
ATOM    162  CE3 TRP B 457       2.173  -7.409   2.425  1.00 30.50           C
ATOM    163  NE1 TRP B 457       2.448  -9.897  -0.107  1.00 31.95           N
ATOM    164  CZ2 TRP B 457       3.972  -7.942   0.292  1.00 35.92           C
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ATOM    165  CZ3 TRP B 457       3.273  -6.588   2.171  1.00 32.28           C
ATOM    166  CH2 TRP B 457       4.155  -6.863   1.105  1.00 33.49           C
ATOM    167  N   PRO B 458      -0.844  -6.602   1.091  1.00 21.46           N
ATOM    168  CA  PRO B 458      -0.670  -5.155   1.273  1.00 22.29           C
ATOM    169  C   PRO B 458      -1.964  -4.364   1.469  1.00 22.13           C
ATOM    170  O   PRO B 458      -1.908  -3.181   1.806  1.00 22.00           O
ATOM    171  CB  PRO B 458      -0.001  -4.703  -0.039  1.00 24.12           C
ATOM    172  CG  PRO B 458       0.544  -6.009  -0.696  1.00 23.57           C
ATOM    173  CD  PRO B 458      -0.483  -7.019  -0.287  1.00 21.95           C
ATOM    174  N   PHE B 459      -3.101  -5.006   1.246  1.00 25.61           N
ATOM    175  CA  PHE B 459      -4.397  -4.345   1.094  1.00 23.65           C
ATOM    176  C   PHE B 459      -5.325  -4.769   2.226  1.00 23.44           C
ATOM    177  O   PHE B 459      -6.482  -4.393   2.245  1.00 20.65           O
ATOM    178  CB  PHE B 459      -5.026  -4.783  -0.241  1.00 24.70           C
ATOM    179  CG  PHE B 459      -4.149  -4.522  -1.417  1.00 23.89           C
ATOM    180  CD1 PHE B 459      -4.028  -3.240  -1.922  1.00 23.33           C
ATOM    181  CD2 PHE B 459      -3.360  -5.536  -1.973  1.00 21.83           C
ATOM    182  CE1 PHE B 459      -3.148  -2.952  -2.948  1.00 27.96           C
ATOM    183  CE2 PHE B 459      -2.492  -5.261  -3.038  1.00 23.60           C
ATOM    184  CZ  PHE B 459      -2.376  -3.983  -3.519  1.00 26.07           C
ATOM    185  N   LEU B 460      -4.819  -5.566   3.168  1.00 23.72           N
ATOM    186  CA  LEU B 460      -5.660  -6.150   4.225  1.00 23.50           C
ATOM    187  C   LEU B 460      -6.102  -5.135   5.260  1.00 26.89           C
ATOM    188  O   LEU B 460      -7.165  -5.283   5.866  1.00 25.98           O
ATOM    189  CB  LEU B 460      -4.937  -7.295   4.937  1.00 24.37           C
ATOM    190  CG  LEU B 460      -4.725  -8.561   4.102  1.00 23.37           C
ATOM    191  CD1 LEU B 460      -3.966  -9.682   4.838  1.00 25.91           C
ATOM    192  CD2 LEU B 460      -6.051  -9.083   3.570  1.00 27.11           C
ATOM    193  N   GLU B 461      -5.282  -4.115   5.471  1.00 25.18           N
ATOM    194  CA  GLU B 461      -5.551  -3.139   6.514  1.00 24.92           C
ATOM    195  C   GLU B 461      -5.360  -1.744   5.956  1.00 22.12           C
ATOM    196  O   GLU B 461      -4.668  -1.588   4.969  1.00 23.83           O
ATOM    197  CB  GLU B 461      -4.570  -3.351   7.657  1.00 26.18           C
ATOM    198  CG  GLU B 461      -4.934  -4.501   8.555  1.00 31.06           C
ATOM    199  CD  GLU B 461      -3.946  -4.684   9.704  1.00 30.23           C
ATOM    200  OE1 GLU B 461      -2.767  -4.986   9.442  1.00 34.71           O
ATOM    201  OE2 GLU B 461      -4.371  -4.543  10.850  1.00 36.32           O1-
ATOM    202  N   PRO B 462      -5.923  -0.724   6.629  1.00 21.01           N
ATOM    203  CA  PRO B 462      -5.637   0.640   6.242  1.00 22.25           C
ATOM    204  C   PRO B 462      -4.129   0.903   6.149  1.00 24.43           C
ATOM    205  O   PRO B 462      -3.329   0.399   6.985  1.00 23.97           O
ATOM    206  CB  PRO B 462      -6.259   1.472   7.364  1.00 26.14           C
ATOM    207  CG  PRO B 462      -7.270   0.584   8.001  1.00 28.29           C
ATOM    208  CD  PRO B 462      -6.800  -0.805   7.819  1.00 26.93           C
ATOM    209  N   VAL B 463      -3.747   1.695   5.155  1.00 24.51           N
ATOM    210  CA  VAL B 463      -2.354   1.977   4.905  1.00 26.26           C
ATOM    211  C   VAL B 463      -1.773   2.756   6.096  1.00 31.49           C
ATOM    212  O   VAL B 463      -2.372   3.727   6.573  1.00 28.31           O
ATOM    213  CB  VAL B 463      -2.169   2.771   3.604  1.00 31.84           C
ATOM    214  CG1 VAL B 463      -0.724   3.230   3.454  1.00 25.77           C
ATOM    215  CG2 VAL B 463      -2.646   1.936   2.406  1.00 24.00           C
ATOM    216  N   ASP B 464      -0.609   2.315   6.568  1.00 29.88           N
ATOM    217  CA  ASP B 464       0.123   2.970   7.665  1.00 32.13           C
ATOM    218  C   ASP B 464       1.087   3.944   7.008  1.00 33.38           C
ATOM    219  O   ASP B 464       1.979   3.512   6.255  1.00 31.14           O
ATOM    220  CB  ASP B 464       0.892   1.915   8.453  1.00 38.09           C
ATOM    221  CG  ASP B 464       1.616   2.476   9.676  1.00 36.64           C
ATOM    222  OD1 ASP B 464       1.928   3.689   9.767  1.00 34.96           O
ATOM    223  OD2 ASP B 464       1.889   1.662  10.564  1.00 40.48           O1-
ATOM    224  N   GLU B 465       0.897   5.240   7.270  1.00 30.58           N
ATOM    225  CA  GLU B 465       1.741   6.281   6.673  1.00 33.61           C
ATOM    226  C   GLU B 465       3.246   6.164   6.963  1.00 41.41           C
ATOM    227  O   GLU B 465       4.048   6.751   6.234  1.00 38.37           O
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ATOM    228  CB  GLU B 465       1.273   7.704   7.055  1.00 34.67           C
ATOM    229  CG  GLU B 465       0.675   8.448   5.894  1.00 42.56           C
ATOM    230  CD  GLU B 465       0.360   9.921   6.162  1.00 50.81           C
ATOM    231  OE1 GLU B 465      -0.389  10.519   5.348  1.00 44.26           O
ATOM    232  OE2 GLU B 465       0.847  10.483   7.163  1.00 46.54           O1-
ATOM    233  N   SER B 466       3.656   5.428   7.995  1.00 41.90           N
ATOM    234  CA  SER B 466       5.104   5.288   8.227  1.00 48.42           C
ATOM    235  C   SER B 466       5.771   4.261   7.286  1.00 55.44           C
ATOM    236  O   SER B 466       6.986   4.162   7.256  1.00 53.98           O
ATOM    237  CB  SER B 466       5.443   5.039   9.716  1.00 54.15           C
ATOM    238  OG  SER B 466       4.534   4.176  10.355  1.00 56.88           O
ATOM    239  N   TYR B 467       4.980   3.517   6.512  1.00 38.08           N
ATOM    240  CA  TYR B 467       5.490   2.631   5.463  1.00 41.92           C
ATOM    241  C   TYR B 467       4.958   3.083   4.080  1.00 36.62           C
ATOM    242  O   TYR B 467       5.078   2.353   3.094  1.00 37.70           O
ATOM    243  CB  TYR B 467       5.094   1.168   5.747  1.00 38.23           C
ATOM    244  CG  TYR B 467       5.503   0.631   7.110  1.00 56.36           C
ATOM    245  CD1 TYR B 467       6.714  -0.046   7.294  1.00 53.94           C
ATOM    246  CD2 TYR B 467       4.671   0.786   8.214  1.00 52.35           C
ATOM    247  CE1 TYR B 467       7.078  -0.535   8.544  1.00 53.63           C
ATOM    248  CE2 TYR B 467       5.026   0.312   9.452  1.00 52.82           C
ATOM    249  CZ  TYR B 467       6.226  -0.351   9.621  1.00 53.64           C
ATOM    250  OH  TYR B 467       6.557  -0.830  10.875  1.00 60.65           O
ATOM    251  N   ALA B 468       4.374   4.287   4.046  1.00 37.90           N
ATOM    252  CA  ALA B 468       3.681   4.856   2.876  1.00 39.01           C
ATOM    253  C   ALA B 468       3.644   6.364   3.039  1.00 35.48           C
ATOM    254  O   ALA B 468       2.570   6.970   3.252  1.00 32.78           O
ATOM    255  CB  ALA B 468       2.277   4.287   2.742  1.00 31.10           C
ATOM    256  N   PRO B 469       4.825   7.004   2.973  1.00 44.04           N
ATOM    257  CA  PRO B 469       4.935   8.439   3.212  1.00 37.48           C
ATOM    258  C   PRO B 469       3.933   9.278   2.453  1.00 36.24           C
ATOM    259  O   PRO B 469       3.710   9.054   1.254  1.00 35.42           O
ATOM    260  CB  PRO B 469       6.355   8.768   2.733  1.00 36.88           C
ATOM    261  CG  PRO B 469       7.115   7.533   2.943  1.00 40.54           C
ATOM    262  CD  PRO B 469       6.157   6.378   2.829  1.00 54.65           C
ATOM    263  N   ASN B 470       3.346  10.247   3.150  1.00 30.54           N
ATOM    264  CA  ASN B 470       2.379  11.173   2.554  1.00 33.10           C
ATOM    265  C   ASN B 470       1.047  10.571   2.024  1.00 27.75           C
ATOM    266  O   ASN B 470       0.299  11.249   1.308  1.00 24.89           O
ATOM    267  CB  ASN B 470       3.061  11.895   1.405  1.00 43.37           C
ATOM    268  CG  ASN B 470       2.590  13.296   1.250  1.00 47.35           C
ATOM    269  ND2 ASN B 470       2.293  13.688   0.013  1.00 46.84           N
ATOM    270  OD1 ASN B 470       2.522  14.041   2.221  1.00 54.68           O
ATOM    271  N   TYR B 471       0.777   9.314   2.335  1.00 29.04           N
ATOM    272  CA  TYR B 471      -0.362   8.598   1.741  1.00 30.02           C
ATOM    273  C   TYR B 471      -1.708   9.352   1.843  1.00 28.03           C
ATOM    274  O   TYR B 471      -2.441   9.473   0.854  1.00 24.97           O
ATOM    275  CB  TYR B 471      -0.522   7.203   2.381  1.00 28.12           C
ATOM    276  CG  TYR B 471      -1.505   6.344   1.627  1.00 23.91           C
ATOM    277  CD1 TYR B 471      -2.831   6.244   2.048  1.00 21.57           C
ATOM    278  CD2 TYR B 471      -1.109   5.649   0.449  1.00 24.47           C
ATOM    279  CE1 TYR B 471      -3.756   5.459   1.330  1.00 22.49           C
ATOM    280  CE2 TYR B 471      -1.998   4.865  -0.264  1.00 22.57           C
ATOM    281  CZ  TYR B 471      -3.337   4.781   0.178  1.00 23.59           C
ATOM    282  OH  TYR B 471      -4.234   4.037  -0.495  1.00 20.61           O
ATOM    283  N   TYR B 472      -2.031   9.859   3.019  1.00 25.92           N
ATOM    284  CA  TYR B 472      -3.366  10.444   3.237  1.00 26.03           C
ATOM    285  C   TYR B 472      -3.501  11.859   2.672  1.00 33.30           C
ATOM    286  O   TYR B 472      -4.608  12.375   2.516  1.00 30.84           O
ATOM    287  CB  TYR B 472      -3.782  10.342   4.691  1.00 27.48           C
ATOM    288  CG  TYR B 472      -4.002   8.915   5.081  1.00 22.28           C
ATOM    289  CD1 TYR B 472      -3.043   8.221   5.826  1.00 27.47           C
ATOM    290  CD2 TYR B 472      -5.131   8.228   4.666  1.00 23.18           C
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ATOM    291  CE1 TYR B 472      -3.206   6.884   6.150  1.00 25.14           C
ATOM    292  CE2 TYR B 472      -5.308   6.881   4.997  1.00 24.81           C
ATOM    293  CZ  TYR B 472      -4.340   6.225   5.745  1.00 24.30           C
ATOM    294  OH  TYR B 472      -4.514   4.928   6.062  1.00 24.43           O
ATOM    295  N   GLN B 473      -2.376  12.455   2.295  1.00 34.76           N
ATOM    296  CA  GLN B 473      -2.409  13.695   1.521  1.00 41.34           C
ATOM    297  C   GLN B 473      -2.694  13.430   0.050  1.00 28.18           C
ATOM    298  O   GLN B 473      -3.343  14.236  -0.607  1.00 37.77           O
ATOM    299  CB  GLN B 473      -1.100  14.470   1.677  1.00 57.10           C
ATOM    300  CG  GLN B 473      -1.113  15.852   1.028  1.00 71.05           C
ATOM    301  CD  GLN B 473       0.145  16.633   1.336  1.00 82.32           C
ATOM    302  NE2 GLN B 473       0.231  17.165   2.553  1.00 78.55           N
ATOM    303  OE1 GLN B 473       1.045  16.739   0.499  1.00 76.25           O
ATOM    304  N   ILE B 474      -2.225  12.307  -0.471  1.00 29.39           N
ATOM    305  CA  ILE B 474      -2.434  11.975  -1.879  1.00 28.05           C
ATOM    306  C   ILE B 474      -3.795  11.281  -2.121  1.00 31.31           C
ATOM    307  O   ILE B 474      -4.500  11.596  -3.090  1.00 24.16           O
ATOM    308  CB  ILE B 474      -1.294  11.073  -2.391  1.00 34.50           C
ATOM    309  CG1 ILE B 474       0.022  11.875  -2.418  1.00 35.49           C
ATOM    310  CG2 ILE B 474      -1.609  10.556  -3.801  1.00 26.94           C
ATOM    311  CD1 ILE B 474       1.264  11.041  -2.349  1.00 39.01           C
ATOM    312  N   ILE B 475      -4.155  10.361  -1.224  1.00 23.21           N
ATOM    313  CA  ILE B 475      -5.324   9.491  -1.401  1.00 22.39           C
ATOM    314  C   ILE B 475      -6.469   9.946  -0.468  1.00 20.46           C
ATOM    315  O   ILE B 475      -6.387   9.786   0.754  1.00 23.58           O
ATOM    316  CB  ILE B 475      -4.924   8.004  -1.160  1.00 18.95           C
ATOM    317  CG1 ILE B 475      -3.905   7.541  -2.204  1.00 22.04           C
ATOM    318  CG2 ILE B 475      -6.185   7.077  -1.144  1.00 22.10           C
ATOM    319  CD1 ILE B 475      -4.411   7.549  -3.684  1.00 20.47           C
ATOM    320  N   LYS B 476      -7.528  10.508  -1.073  1.00 23.75           N
ATOM    321  CA  LYS B 476      -8.622  11.150  -0.331  1.00 24.88           C
ATOM    322  C   LYS B 476      -9.750  10.205   0.083  1.00 22.05           C
ATOM    323  O   LYS B 476     -10.538  10.526   0.986  1.00 24.95           O
ATOM    324  CB  LYS B 476      -9.187  12.318  -1.153  1.00 30.48           C
ATOM    325  CG  LYS B 476      -8.147  13.430  -1.468  1.00 40.76           C
ATOM    326  CD  LYS B 476      -7.411  13.800  -0.196  1.00 43.90           C
ATOM    327  CE  LYS B 476      -6.555  15.023  -0.336  1.00 49.25           C
ATOM    328  NZ  LYS B 476      -5.944  15.242   0.997  1.00 49.82           N1+
ATOM    329  N   ALA B 477      -9.834   9.051  -0.577  1.00 21.77           N
ATOM    330  CA  ALA B 477     -10.811   8.007  -0.255  1.00 20.17           C
ATOM    331  C   ALA B 477     -10.070   6.665  -0.032  1.00 18.44           C
ATOM    332  O   ALA B 477     -10.135   5.752  -0.842  1.00 21.52           O
ATOM    333  CB  ALA B 477     -11.908   7.886  -1.350  1.00 20.70           C
ATOM    334  N   PRO B 478      -9.372   6.547   1.098  1.00 20.97           N
ATOM    335  CA  PRO B 478      -8.646   5.320   1.334  1.00 21.94           C
ATOM    336  C   PRO B 478      -9.621   4.165   1.496  1.00 23.13           C
ATOM    337  O   PRO B 478     -10.754   4.358   1.979  1.00 20.34           O
ATOM    338  CB  PRO B 478      -7.866   5.584   2.632  1.00 22.44           C
ATOM    339  CG  PRO B 478      -8.481   6.854   3.213  1.00 23.79           C
ATOM    340  CD  PRO B 478      -9.083   7.591   2.092  1.00 17.91           C
ATOM    341  N   MET B 479      -9.163   2.976   1.100  1.00 19.63           N
ATOM    342  CA  MET B 479      -9.950   1.781   1.232  1.00 20.08           C
ATOM    343  C   MET B 479      -9.054   0.565   1.377  1.00 19.31           C
ATOM    344  O   MET B 479      -7.956   0.537   0.847  1.00 20.71           O
ATOM    345  CB  MET B 479     -10.882   1.616   0.001  1.00 20.18           C
ATOM    346  CG  MET B 479     -12.011   0.557   0.171  1.00 21.13           C
ATOM    347  SD  MET B 479     -12.941   0.620   1.722  1.00 24.16           S
ATOM    348  CE  MET B 479     -13.633   2.334   1.634  1.00 21.03           C
ATOM    349  N   ASP B 480      -9.533  -0.433   2.108  1.00 18.97           N
ATOM    350  CA  ASP B 480      -8.784  -1.652   2.255  1.00 18.26           C
ATOM    351  C   ASP B 480      -9.775  -2.739   2.595  1.00 17.65           C
ATOM    352  O   ASP B 480     -10.966  -2.467   2.870  1.00 16.93           O
ATOM    353  CB  ASP B 480      -7.773  -1.503   3.384  1.00 20.69           C
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ATOM    354  CG  ASP B 480      -8.459  -1.240   4.690  1.00 23.79           C
ATOM    355  OD1 ASP B 480      -8.865  -0.068   4.986  1.00 21.90           O
ATOM    356  OD2 ASP B 480      -8.682  -2.255   5.362  1.00 21.59           O1-
ATOM    357  N   ILE B 481      -9.276  -3.975   2.594  1.00 14.92           N
ATOM    358  CA  ILE B 481     -10.172  -5.146   2.821  1.00 17.12           C
ATOM    359  C   ILE B 481     -10.837  -5.184   4.182  1.00 19.83           C
ATOM    360  O   ILE B 481     -12.035  -5.524   4.288  1.00 19.23           O
ATOM    361  CB  ILE B 481      -9.469  -6.486   2.466  1.00 18.17           C
ATOM    362  CG1 ILE B 481      -9.100  -6.513   0.991  1.00 20.23           C
ATOM    363  CG2 ILE B 481     -10.359  -7.692   2.879  1.00 21.75           C
ATOM    364  CD1 ILE B 481      -7.933  -7.474   0.617  1.00 18.14           C
ATOM    365  N   SER B 482     -10.083  -4.808   5.222  1.00 19.18           N
ATOM    366  CA  SER B 482     -10.594  -4.782   6.591  1.00 23.68           C
ATOM    367  C   SER B 482     -11.784  -3.803   6.702  1.00 20.70           C
ATOM    368  O   SER B 482     -12.850  -4.130   7.263  1.00 21.26           O
ATOM    369  CB  SER B 482      -9.475  -4.395   7.558  1.00 22.67           C
ATOM    370  OG  SER B 482     -10.013  -4.095   8.831  1.00 40.64           O
ATOM    371  N   SER B 483     -11.606  -2.622   6.118  1.00 19.36           N
ATOM    372  CA  SER B 483     -12.652  -1.613   6.093  1.00 20.52           C
ATOM    373  C   SER B 483     -13.894  -2.117   5.341  1.00 19.87           C
ATOM    374  O   SER B 483     -15.021  -1.903   5.794  1.00 19.75           O
ATOM    375  CB  SER B 483     -12.106  -0.275   5.554  1.00 21.70           C
ATOM    376  OG  SER B 483     -11.080   0.239   6.444  1.00 20.80           O
ATOM    377  N   MET B 484     -13.712  -2.828   4.223  1.00 20.61           N
ATOM    378  CA  MET B 484     -14.857  -3.303   3.451  1.00 22.20           C
ATOM    379  C   MET B 484     -15.603  -4.355   4.277  1.00 23.88           C
ATOM    380  O   MET B 484     -16.854  -4.382   4.323  1.00 22.73           O
ATOM    381  CB  MET B 484     -14.437  -3.824   2.066  1.00 21.70           C
ATOM    382  CG  MET B 484     -14.056  -2.707   1.092  1.00 22.95           C
ATOM    383  SD  MET B 484     -13.666  -3.284  -0.583  1.00 22.83           S
ATOM    384  CE  MET B 484     -12.020  -3.909  -0.305  1.00 17.77           C
ATOM    385  N   GLU B 485     -14.849  -5.153   5.015  1.00 21.56           N
ATOM    386  CA  GLU B 485     -15.453  -6.187   5.842  1.00 25.03           C
ATOM    387  C   GLU B 485     -16.289  -5.604   6.999  1.00 24.05           C
ATOM    388  O   GLU B 485     -17.411  -6.056   7.264  1.00 24.00           O
ATOM    389  CB  GLU B 485     -14.364  -7.145   6.347  1.00 25.77           C
ATOM    390  CG  GLU B 485     -14.955  -8.365   6.968  1.00 30.57           C
ATOM    391  CD  GLU B 485     -13.994  -9.553   7.033  1.00 34.77           C
ATOM    392  OE1 GLU B 485     -12.797  -9.445   6.650  1.00 32.37           O
ATOM    393  OE2 GLU B 485     -14.482 -10.607   7.506  1.00 34.48           O1-
ATOM    394  N   LYS B 486     -15.745  -4.587   7.659  1.00 26.00           N
ATOM    395  CA  LYS B 486     -16.457  -3.854   8.683  1.00 25.29           C
ATOM    396  C   LYS B 486     -17.704  -3.160   8.129  1.00 23.02           C
ATOM    397  O   LYS B 486     -18.694  -3.051   8.821  1.00 22.58           O
ATOM    398  CB  LYS B 486     -15.575  -2.798   9.374  1.00 29.32           C
ATOM    399  CG  LYS B 486     -14.437  -3.284  10.309  1.00 33.42           C
ATOM    400  CD  LYS B 486     -13.454  -2.128  10.406  1.00 39.36           C
ATOM    401  CE  LYS B 486     -12.578  -2.083  11.627  1.00 54.51           C
ATOM    402  NZ  LYS B 486     -12.024  -0.676  11.698  1.00 38.28           N1+
ATOM    403  N   LYS B 487     -17.663  -2.679   6.900  1.00 21.60           N
ATOM    404  CA  LYS B 487     -18.807  -1.966   6.328  1.00 24.00           C
ATOM    405  C   LYS B 487     -19.883  -2.986   5.970  1.00 24.31           C
ATOM    406  O   LYS B 487     -21.070  -2.785   6.256  1.00 25.41           O
ATOM    407  CB  LYS B 487     -18.391  -1.141   5.112  1.00 22.98           C
ATOM    408  CG  LYS B 487     -17.581   0.080   5.458  1.00 21.34           C
ATOM    409  CD  LYS B 487     -17.112   0.886   4.233  1.00 20.12           C
ATOM    410  CE  LYS B 487     -18.252   1.607   3.497  1.00 20.30           C
ATOM    411  NZ  LYS B 487     -17.670   2.492   2.430  1.00 17.88           N1+
ATOM    412  N   LEU B 488     -19.459  -4.120   5.416  1.00 23.08           N
ATOM    413  CA  LEU B 488     -20.391  -5.233   5.248  1.00 29.13           C
ATOM    414  C   LEU B 488     -21.084  -5.644   6.535  1.00 28.20           C
ATOM    415  O   LEU B 488     -22.300  -5.714   6.562  1.00 26.47           O
ATOM    416  CB  LEU B 488     -19.699  -6.468   4.665  1.00 28.78           C
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ATOM    417  CG  LEU B 488     -19.580  -6.482   3.159  1.00 34.58           C
ATOM    418  CD1 LEU B 488     -18.656  -7.636   2.841  1.00 28.49           C
ATOM    419  CD2 LEU B 488     -20.956  -6.582   2.448  1.00 33.37           C
ATOM    420  N   ASN B 489     -20.298  -5.932   7.582  1.00 27.32           N
ATOM    421  CA  ASN B 489     -20.846  -6.361   8.857  1.00 28.16           C
ATOM    422  C   ASN B 489     -21.684  -5.255   9.511  1.00 34.39           C
ATOM    423  O   ASN B 489     -22.641  -5.549  10.203  1.00 33.26           O
ATOM    424  CB  ASN B 489     -19.740  -6.795   9.818  1.00 30.48           C
ATOM    425  CG  ASN B 489     -19.133  -8.105   9.424  1.00 35.08           C
ATOM    426  ND2 ASN B 489     -17.817  -8.162   9.353  1.00 36.51           N
ATOM    427  OD1 ASN B 489     -19.853  -9.066   9.196  1.00 41.25           O
ATOM    428  N   GLY B 490     -21.319  -3.992   9.280  1.00 31.29           N
ATOM    429  CA  GLY B 490     -21.987  -2.867   9.896  1.00 29.24           C
ATOM    430  C   GLY B 490     -23.219  -2.398   9.145  1.00 30.69           C
ATOM    431  O   GLY B 490     -23.841  -1.420   9.555  1.00 27.42           O
ATOM    432  N   GLY B 491     -23.596  -3.085   8.065  1.00 27.00           N
ATOM    433  CA  GLY B 491     -24.725  -2.655   7.239  1.00 29.29           C
ATOM    434  C   GLY B 491     -24.559  -1.262   6.616  1.00 28.06           C
ATOM    435  O   GLY B 491     -25.531  -0.528   6.420  1.00 25.41           O
ATOM    436  N   LEU B 492     -23.332  -0.914   6.269  1.00 25.58           N
ATOM    437  CA  LEU B 492     -22.994   0.404   5.717  1.00 25.03           C
ATOM    438  C   LEU B 492     -22.956   0.454   4.194  1.00 21.88           C
ATOM    439  O   LEU B 492     -22.556   1.468   3.616  1.00 26.89           O
ATOM    440  CB  LEU B 492     -21.655   0.865   6.276  1.00 24.97           C
ATOM    441  CG  LEU B 492     -21.699   1.362   7.720  1.00 25.84           C
ATOM    442  CD1 LEU B 492     -20.322   1.344   8.297  1.00 22.29           C
ATOM    443  CD2 LEU B 492     -22.336   2.787   7.849  1.00 22.74           C
ATOM    444  N   TYR B 493     -23.335  -0.632   3.545  1.00 21.54           N
ATOM    445  CA  TYR B 493     -23.645  -0.609   2.107  1.00 24.54           C
ATOM    446  C   TYR B 493     -25.145  -0.663   1.872  1.00 23.91           C
ATOM    447  O   TYR B 493     -25.827  -1.563   2.380  1.00 27.16           O
ATOM    448  CB  TYR B 493     -22.994  -1.783   1.363  1.00 21.73           C
ATOM    449  CG  TYR B 493     -21.498  -1.726   1.374  1.00 21.91           C
ATOM    450  CD1 TYR B 493     -20.809  -0.688   0.730  1.00 19.48           C
ATOM    451  CD2 TYR B 493     -20.754  -2.674   2.044  1.00 21.29           C
ATOM    452  CE1 TYR B 493     -19.429  -0.614   0.752  1.00 22.39           C
ATOM    453  CE2 TYR B 493     -19.325  -2.631   2.048  1.00 22.22           C
ATOM    454  CZ  TYR B 493     -18.673  -1.599   1.401  1.00 21.69           C
ATOM    455  OH  TYR B 493     -17.294  -1.494   1.418  1.00 22.06           O
ATOM    456  N   CYS B 494     -25.656   0.284   1.088  1.00 24.27           N
ATOM    457  CA  CYS B 494     -27.059   0.305   0.698  1.00 28.60           C
ATOM    458  C   CYS B 494     -27.310  -0.595  -0.496  1.00 28.51           C
ATOM    459  O   CYS B 494     -28.401  -1.118  -0.627  1.00 30.87           O
ATOM    460  CB  CYS B 494     -27.535   1.738   0.374  1.00 26.96           C
ATOM    461  SG  CYS B 494     -27.343   2.853   1.789  1.00 28.24           S
ATOM    462  N   THR B 495     -26.320  -0.769  -1.364  1.00 24.42           N
ATOM    463  CA  THR B 495     -26.469  -1.628  -2.524  1.00 23.73           C
ATOM    464  C   THR B 495     -25.142  -2.319  -2.851  1.00 25.27           C
ATOM    465  O   THR B 495     -24.065  -1.913  -2.380  1.00 23.62           O
ATOM    466  CB  THR B 495     -26.870  -0.850  -3.810  1.00 25.65           C
ATOM    467  CG2 THR B 495     -28.275  -0.146  -3.666  1.00 26.96           C
ATOM    468  OG1 THR B 495     -25.820   0.072  -4.149  1.00 24.23           O
ATOM    469  N   LYS B 496     -25.259  -3.327  -3.709  1.00 26.91           N
ATOM    470  CA  LYS B 496     -24.108  -4.103  -4.226  1.00 31.14           C
ATOM    471  C   LYS B 496     -23.090  -3.189  -4.886  1.00 23.38           C
ATOM    472  O   LYS B 496     -21.912  -3.280  -4.634  1.00 25.71           O
ATOM    473  CB  LYS B 496     -24.625  -5.112  -5.258  1.00 34.39           C
ATOM    474  CG  LYS B 496     -23.703  -6.222  -5.655  1.00 52.19           C
ATOM    475  CD  LYS B 496     -24.473  -7.277  -6.507  1.00 54.10           C
ATOM    476  CE  LYS B 496     -23.589  -7.900  -7.598  1.00 65.42           C
ATOM    477  NZ  LYS B 496     -24.015  -9.274  -8.031  1.00 53.52           N1+
ATOM    478  N   GLU B 497     -23.554  -2.306  -5.749  1.00 24.21           N
ATOM    479  CA  GLU B 497     -22.684  -1.399  -6.500  1.00 26.92           C
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ATOM    480  C   GLU B 497     -21.782  -0.532  -5.594  1.00 20.91           C
ATOM    481  O   GLU B 497     -20.667  -0.187  -5.967  1.00 21.60           O
ATOM    482  CB  GLU B 497     -23.598  -0.521  -7.397  1.00 29.67           C
ATOM    483  CG  GLU B 497     -22.917   0.456  -8.339  1.00 36.55           C
ATOM    484  CD  GLU B 497     -23.914   1.464  -8.971  1.00 52.45           C
ATOM    485  OE1 GLU B 497     -25.105   1.500  -8.565  1.00 49.62           O
ATOM    486  OE2 GLU B 497     -23.512   2.227  -9.878  1.00 53.93           O1-
ATOM    487  N   GLU B 498     -22.261  -0.182  -4.400  1.00 19.94           N
ATOM    488  CA  GLU B 498     -21.524   0.656  -3.472  1.00 20.52           C
ATOM    489  C   GLU B 498     -20.315  -0.105  -2.949  1.00 18.10           C
ATOM    490  O   GLU B 498     -19.231   0.450  -2.811  1.00 19.99           O
ATOM    491  CB  GLU B 498     -22.426   1.079  -2.319  1.00 27.19           C
ATOM    492  CG  GLU B 498     -22.097   2.407  -1.676  1.00 30.12           C
ATOM    493  CD  GLU B 498     -22.998   2.702  -0.476  1.00 30.63           C
ATOM    494  OE1 GLU B 498     -24.161   2.181  -0.451  1.00 25.76           O
ATOM    495  OE2 GLU B 498     -22.510   3.397   0.455  1.00 27.41           O1-
ATOM    496  N   PHE B 499     -20.493  -1.392  -2.718  1.00 19.15           N
ATOM    497  CA  PHE B 499     -19.360  -2.275  -2.373  1.00 20.13           C
ATOM    498  C   PHE B 499     -18.349  -2.438  -3.513  1.00 20.46           C
ATOM    499  O   PHE B 499     -17.104  -2.345  -3.312  1.00 18.71           O
ATOM    500  CB  PHE B 499     -19.906  -3.634  -1.928  1.00 25.56           C
ATOM    501  CG  PHE B 499     -18.867  -4.733  -1.870  1.00 21.06           C
ATOM    502  CD1 PHE B 499     -18.027  -4.837  -0.793  1.00 24.29           C
ATOM    503  CD2 PHE B 499     -18.754  -5.656  -2.896  1.00 21.57           C
ATOM    504  CE1 PHE B 499     -17.082  -5.851  -0.722  1.00 23.98           C
ATOM    505  CE2 PHE B 499     -17.812  -6.697  -2.834  1.00 23.92           C
ATOM    506  CZ  PHE B 499     -16.972  -6.785  -1.733  1.00 24.55           C
ATOM    507  N   VAL B 500     -18.870  -2.700  -4.716  1.00 18.05           N
ATOM    508  CA  VAL B 500     -18.028  -2.806  -5.900  1.00 21.30           C
ATOM    509  C   VAL B 500     -17.190  -1.527  -6.087  1.00 17.89           C
ATOM    510  O   VAL B 500     -15.998  -1.590  -6.424  1.00 18.39           O
ATOM    511  CB  VAL B 500     -18.895  -3.132  -7.137  1.00 18.81           C
ATOM    512  CG1 VAL B 500     -18.129  -2.914  -8.495  1.00 20.80           C
ATOM    513  CG2 VAL B 500     -19.533  -4.533  -6.981  1.00 19.95           C
ATOM    514  N   ASN B 501     -17.791  -0.358  -5.844  1.00 18.29           N
ATOM    515  CA  ASN B 501     -17.055   0.895  -5.932  1.00 19.18           C
ATOM    516  C   ASN B 501     -15.940   1.001  -4.949  1.00 17.71           C
ATOM    517  O   ASN B 501     -14.887   1.580  -5.246  1.00 18.52           O
ATOM    518  CB  ASN B 501     -17.995   2.107  -5.778  1.00 24.05           C
ATOM    519  CG  ASN B 501     -18.863   2.310  -6.985  1.00 33.74           C
ATOM    520  ND2 ASN B 501     -19.950   3.086  -6.825  1.00 30.59           N
ATOM    521  OD1 ASN B 501     -18.593   1.752  -8.053  1.00 35.48           O
ATOM    522  N   ASP B 502     -16.147   0.478  -3.746  1.00 18.66           N
ATOM    523  CA  ASP B 502     -15.075   0.453  -2.767  1.00 18.38           C
ATOM    524  C   ASP B 502     -13.938  -0.419  -3.255  1.00 18.45           C
ATOM    525  O   ASP B 502     -12.800   0.003  -3.197  1.00 18.82           O
ATOM    526  CB  ASP B 502     -15.554  -0.003  -1.414  1.00 20.16           C
ATOM    527  CG  ASP B 502     -16.194   1.147  -0.604  1.00 21.15           C
ATOM    528  OD1 ASP B 502     -16.285   2.269  -1.145  1.00 20.93           O
ATOM    529  OD2 ASP B 502     -16.542   0.906   0.567  1.00 24.37           O1-
ATOM    530  N   MET B 503     -14.234  -1.609  -3.764  1.00 19.08           N
ATOM    531  CA  MET B 503     -13.150  -2.449  -4.339  1.00 19.53           C
ATOM    532  C   MET B 503     -12.369  -1.747  -5.433  1.00 18.18           C
ATOM    533  O   MET B 503     -11.152  -1.757  -5.430  1.00 19.79           O
ATOM    534  CB  MET B 503     -13.703  -3.723  -4.951  1.00 28.96           C
ATOM    535  CG  MET B 503     -13.778  -4.799  -4.011  1.00 36.98           C
ATOM    536  SD  MET B 503     -12.210  -5.685  -3.702  1.00 24.71           S
ATOM    537  CE  MET B 503     -13.116  -6.719  -2.635  1.00 24.37           C
ATOM    538  N   LYS B 504     -13.082  -1.135  -6.370  1.00 19.81           N
ATOM    539  CA  LYS B 504     -12.488  -0.396  -7.466  1.00 20.71           C
ATOM    540  C   LYS B 504     -11.625   0.758  -6.965  1.00 19.55           C
ATOM    541  O   LYS B 504     -10.516   0.967  -7.478  1.00 19.25           O
ATOM    542  CB  LYS B 504     -13.559   0.149  -8.436  1.00 25.10           C
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ATOM    543  CG  LYS B 504     -14.217  -0.907  -9.292  1.00 27.59           C
ATOM    544  CD  LYS B 504     -15.307  -0.286 -10.196  1.00 37.23           C
ATOM    545  CE  LYS B 504     -16.077  -1.320 -11.012  1.00 44.06           C
ATOM    546  NZ  LYS B 504     -17.394  -0.748 -11.505  1.00 47.73           N1+
ATOM    547  N   THR B 505     -12.121   1.475  -5.967  1.00 18.03           N
ATOM    548  CA  THR B 505     -11.357   2.536  -5.296  1.00 19.72           C
ATOM    549  C   THR B 505     -10.050   2.043  -4.687  1.00 19.13           C
ATOM    550  O   THR B 505      -9.012   2.701  -4.815  1.00 18.84           O
ATOM    551  CB  THR B 505     -12.196   3.289  -4.215  1.00 21.94           C
ATOM    552  CG2 THR B 505     -11.320   4.365  -3.500  1.00 21.05           C
ATOM    553  OG1 THR B 505     -13.287   3.954  -4.854  1.00 22.10           O
ATOM    554  N   MET B 506     -10.104   0.884  -4.040  1.00 18.22           N
ATOM    555  CA  MET B 506      -8.891   0.318  -3.464  1.00 19.28           C
ATOM    556  C   MET B 506      -7.806   0.124  -4.550  1.00 16.00           C
ATOM    557  O   MET B 506      -6.650   0.509  -4.348  1.00 16.75           O
ATOM    558  CB  MET B 506      -9.204  -0.982  -2.725  1.00 19.28           C
ATOM    559  CG  MET B 506      -7.967  -1.609  -2.075  1.00 21.39           C
ATOM    560  SD  MET B 506      -8.401  -3.045  -1.116  1.00 20.62           S
ATOM    561  CE  MET B 506      -8.538  -4.248  -2.414  1.00 19.41           C
ATOM    562  N   PHE B 507      -8.163  -0.479  -5.684  1.00 17.73           N
ATOM    563  CA  PHE B 507      -7.228  -0.707  -6.791  1.00 16.22           C
ATOM    564  C   PHE B 507      -6.737   0.582  -7.405  1.00 19.79           C
ATOM    565  O   PHE B 507      -5.554   0.727  -7.678  1.00 18.67           O
ATOM    566  CB  PHE B 507      -7.878  -1.560  -7.918  1.00 17.76           C
ATOM    567  CG  PHE B 507      -8.463  -2.857  -7.430  1.00 18.22           C
ATOM    568  CD1 PHE B 507      -7.767  -3.654  -6.562  1.00 21.31           C
ATOM    569  CD2 PHE B 507      -9.702  -3.293  -7.890  1.00 21.72           C
ATOM    570  CE1 PHE B 507      -8.303  -4.880  -6.124  1.00 19.98           C
ATOM    571  CE2 PHE B 507     -10.236  -4.504  -7.439  1.00 20.55           C
ATOM    572  CZ  PHE B 507      -9.552  -5.268  -6.543  1.00 19.68           C
ATOM    573  N   ARG B 508      -7.655   1.518  -7.656  1.00 21.91           N
ATOM    574  CA  ARG B 508      -7.305   2.811  -8.242  1.00 21.48           C
ATOM    575  C   ARG B 508      -6.342   3.581  -7.336  1.00 21.25           C
ATOM    576  O   ARG B 508      -5.342   4.147  -7.822  1.00 20.39           O
ATOM    577  CB  ARG B 508      -8.593   3.614  -8.505  1.00 22.15           C
ATOM    578  CG  ARG B 508      -8.461   4.824  -9.362  1.00 36.98           C
ATOM    579  CD  ARG B 508      -9.862   5.436  -9.657  1.00 37.09           C
ATOM    580  NE  ARG B 508     -10.510   5.832  -8.406  1.00 55.94           N
ATOM    581  CZ  ARG B 508     -11.664   5.350  -7.930  1.00 51.31           C
ATOM    582  NH1 ARG B 508     -12.099   5.796  -6.751  1.00 37.97           N
ATOM    583  NH2 ARG B 508     -12.393   4.454  -8.616  1.00 39.32           N1+
ATOM    584  N   ASN B 509      -6.623   3.604  -6.025  1.00 20.68           N
ATOM    585  CA  ASN B 509      -5.706   4.219  -5.066  1.00 20.18           C
ATOM    586  C   ASN B 509      -4.296   3.640  -5.181  1.00 22.82           C
ATOM    587  O   ASN B 509      -3.303   4.347  -5.044  1.00 21.66           O
ATOM    588  CB  ASN B 509      -6.136   3.997  -3.601  1.00 18.16           C
ATOM    589  CG  ASN B 509      -7.388   4.750  -3.213  1.00 20.28           C
ATOM    590  ND2 ASN B 509      -8.008   4.312  -2.123  1.00 19.58           N
ATOM    591  OD1 ASN B 509      -7.839   5.667  -3.909  1.00 20.88           O
ATOM    592  N   CYS B 510      -4.207   2.331  -5.332  1.00 20.00           N
ATOM    593  CA  CYS B 510      -2.880   1.682  -5.381  1.00 17.96           C
ATOM    594  C   CYS B 510      -2.061   2.168  -6.559  1.00 19.12           C
ATOM    595  O   CYS B 510      -0.900   2.566  -6.405  1.00 20.04           O
ATOM    596  CB  CYS B 510      -3.030   0.180  -5.416  1.00 18.46           C
ATOM    597  SG  CYS B 510      -1.424  -0.640  -5.472  1.00 22.05           S
ATOM    598  N   ARG B 511      -2.673   2.197  -7.731  1.00 22.35           N
ATOM    599  CA  ARG B 511      -2.012   2.666  -8.919  1.00 23.03           C
ATOM    600  C   ARG B 511      -1.670   4.157  -8.806  1.00 23.36           C
ATOM    601  O   ARG B 511      -0.623   4.579  -9.278  1.00 25.50           O
ATOM    602  CB  ARG B 511      -2.924   2.430 -10.113  1.00 26.11           C
ATOM    603  CG  ARG B 511      -2.346   2.906 -11.422  1.00 32.14           C
ATOM    604  CD  ARG B 511      -3.153   2.362 -12.621  1.00 37.22           C
ATOM    605  NE  ARG B 511      -2.388   1.344 -13.370  1.00 40.09           N
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ATOM    606  CZ  ARG B 511      -2.580   0.018 -13.317  1.00 38.93           C
ATOM    607  NH1 ARG B 511      -1.810  -0.781 -14.051  1.00 37.19           N
ATOM    608  NH2 ARG B 511      -3.525  -0.528 -12.543  1.00 33.42           N1+
ATOM    609  N   LYS B 512      -2.552   4.939  -8.175  1.00 20.40           N
ATOM    610  CA  LYS B 512      -2.356   6.387  -8.079  1.00 28.20           C
ATOM    611  C   LYS B 512      -1.188   6.668  -7.141  1.00 27.78           C
ATOM    612  O   LYS B 512      -0.322   7.493  -7.452  1.00 30.47           O
ATOM    613  CB  LYS B 512      -3.632   7.083  -7.604  1.00 30.83           C
ATOM    614  CG  LYS B 512      -3.485   8.436  -6.921  1.00 39.11           C
ATOM    615  CD  LYS B 512      -3.236   9.560  -7.904  1.00 60.33           C
ATOM    616  CE  LYS B 512      -3.782  10.884  -7.382  1.00 63.25           C
ATOM    617  NZ  LYS B 512      -4.656  11.514  -8.403  1.00 74.76           N1+
ATOM    618  N   TYR B 513      -1.149   5.971  -6.011  1.00 22.13           N
ATOM    619  CA  TYR B 513      -0.116   6.222  -5.025  1.00 22.40           C
ATOM    620  C   TYR B 513       1.219   5.621  -5.450  1.00 26.76           C
ATOM    621  O   TYR B 513       2.222   6.319  -5.458  1.00 23.12           O
ATOM    622  CB  TYR B 513      -0.539   5.766  -3.611  1.00 22.93           C
ATOM    623  CG  TYR B 513       0.537   6.032  -2.588  1.00 24.38           C
ATOM    624  CD1 TYR B 513       0.832   7.330  -2.194  1.00 23.88           C
ATOM    625  CD2 TYR B 513       1.317   5.001  -2.077  1.00 25.09           C
ATOM    626  CE1 TYR B 513       1.835   7.598  -1.292  1.00 28.19           C
ATOM    627  CE2 TYR B 513       2.340   5.258  -1.172  1.00 30.92           C
ATOM    628  CZ  TYR B 513       2.578   6.574  -0.776  1.00 31.57           C
ATOM    629  OH  TYR B 513       3.598   6.894   0.107  1.00 29.70           O
ATOM    630  N   ASN B 514       1.237   4.347  -5.833  1.00 21.81           N
ATOM    631  CA  ASN B 514       2.489   3.639  -6.090  1.00 23.58           C
ATOM    632  C   ASN B 514       3.046   3.754  -7.529  1.00 25.17           C
ATOM    633  O   ASN B 514       4.235   3.544  -7.754  1.00 23.34           O
ATOM    634  CB  ASN B 514       2.290   2.180  -5.756  1.00 21.74           C
ATOM    635  CG  ASN B 514       1.964   1.954  -4.314  1.00 24.71           C
ATOM    636 ND2  ASN B 514       3.035   2.166  -3.393  1.00 21.71           O
ATOM    637 OD1  ASN B 514       0.829   1.569  -3.956  1.00 24.46           N
ATOM    638  N   GLY B 515       2.213   4.129  -8.476  1.00 24.17           N
ATOM    639  CA  GLY B 515       2.656   4.234  -9.866  1.00 24.25           C
ATOM    640  C   GLY B 515       2.309   3.047 -10.735  1.00 28.07           C
ATOM    641  O   GLY B 515       2.139   1.903 -10.258  1.00 20.96           O
ATOM    642  N   GLU B 516       2.248   3.318 -12.031  1.00 29.60           N
ATOM    643  CA  GLU B 516       1.848   2.327 -13.022  1.00 34.87           C
ATOM    644  C   GLU B 516       2.612   1.008 -12.929  1.00 26.17           C
ATOM    645  O   GLU B 516       2.025  -0.072 -13.102  1.00 30.02           O
ATOM    646  CB  GLU B 516       2.047   2.935 -14.431  1.00 40.26           C
ATOM    647  CG  GLU B 516       1.678   2.047 -15.603  1.00 55.25           C
ATOM    648  CD  GLU B 516       0.264   1.511 -15.505  1.00 67.88           C
ATOM    649  OE1 GLU B 516      -0.632   2.255 -15.032  1.00 65.44           O
ATOM    650  OE2 GLU B 516       0.054   0.338 -15.891  1.00 49.59           O1-
ATOM    651  N   SER B 517       3.912   1.083 -12.710  1.00 27.35           N
ATOM    652  CA  SER B 517       4.807  -0.076 -12.852  1.00 26.92           C
ATOM    653  C   SER B 517       5.273  -0.610 -11.493  1.00 24.76           C
ATOM    654  O   SER B 517       6.151  -1.463 -11.422  1.00 28.33           O
ATOM    655  CB ASER B 517       5.976   0.293 -13.772  0.50 31.19           C
ATOM    656  OG ASER B 517       5.487   0.611 -15.074  0.50 28.90           O
ATOM    657  N   SER B 518       4.677  -0.096 -10.420  1.00 22.62           N
ATOM    658  CA  SER B 518       4.999  -0.532  -9.077  1.00 22.32           C
ATOM    659  C   SER B 518       4.708  -2.018  -8.947  1.00 22.38           C
ATOM    660  O   SER B 518       3.730  -2.528  -9.488  1.00 19.33           O
ATOM    661  CB  SER B 518       4.147   0.215  -8.071  1.00 19.25           C
ATOM    662  OG  SER B 518       4.350  -0.263  -6.759  1.00 21.56           O
ATOM    663  N   GLU B 519       5.554  -2.699  -8.191  1.00 23.61           N
ATOM    664  CA  GLU B 519       5.286  -4.065  -7.776  1.00 24.81           C
ATOM    665  C   GLU B 519       3.942  -4.163  -7.028  1.00 22.08           C
ATOM    666  O   GLU B 519       3.235  -5.160  -7.123  1.00 17.92           O
ATOM    667  CB  GLU B 519       6.436  -4.555  -6.891  1.00 25.12           C
ATOM    668  CG  GLU B 519       7.765  -4.670  -7.680  1.00 25.18           C
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ATOM    669  CD  GLU B 519       7.606  -5.540  -8.872  1.00 29.44           C
ATOM    670  OE1 GLU B 519       7.311  -6.726  -8.642  1.00 36.19           O
ATOM    671  OE2 GLU B 519       7.709  -5.068 -10.026  1.00 28.15           O1-
ATOM    672  N   TYR B 520       3.585  -3.117  -6.313  1.00 19.75           N
ATOM    673  CA  TYR B 520       2.306  -3.085  -5.621  1.00 18.02           C
ATOM    674  C   TYR B 520       1.157  -2.991  -6.595  1.00 17.46           C
ATOM    675  O   TYR B 520       0.115  -3.558  -6.332  1.00 19.03           O
ATOM    676  CB  TYR B 520       2.254  -1.936  -4.600  1.00 18.48           C
ATOM    677  CG  TYR B 520       3.244  -2.148  -3.502  1.00 22.48           C
ATOM    678  CD1 TYR B 520       3.011  -3.102  -2.503  1.00 24.65           C
ATOM    679  CD2 TYR B 520       4.434  -1.420  -3.456  1.00 27.12           C
ATOM    680  CE1 TYR B 520       3.936  -3.318  -1.475  1.00 25.36           C
ATOM    681  CE2 TYR B 520       5.382  -1.631  -2.433  1.00 27.36           C
ATOM    682  CZ  TYR B 520       5.129  -2.574  -1.445  1.00 33.29           C
ATOM    683  OH  TYR B 520       6.093  -2.794  -0.473  1.00 27.49           O
ATOM    684  N   THR B 521       1.339  -2.282  -7.708  1.00 17.78           N
ATOM    685  CA  THR B 521       0.292  -2.202  -8.726  1.00 17.27           C
ATOM    686  C   THR B 521       0.127  -3.521  -9.446  1.00 19.27           C
ATOM    687  O   THR B 521      -0.991  -3.900  -9.774  1.00 21.59           O
ATOM    688  CB  THR B 521       0.526  -0.996  -9.685  1.00 18.92           C
ATOM    689  CG2 THR B 521      -0.610  -0.854 -10.716  1.00 18.74           C
ATOM    690  OG1 THR B 521       0.630   0.189  -8.897  1.00 22.35           O
ATOM    691  N   LYS B 522       1.221  -4.241  -9.688  1.00 20.06           N
ATOM    692  CA  LYS B 522       1.130  -5.574 -10.256  1.00 23.04           C
ATOM    693  C   LYS B 522       0.306  -6.492  -9.334  1.00 21.90           C
ATOM    694  O   LYS B 522      -0.498  -7.291  -9.794  1.00 18.93           O
ATOM    695  CB ALYS B 522       2.528  -6.158 -10.483  0.50 24.47           C
ATOM    696  CG ALYS B 522       3.322  -5.445 -11.588  0.50 33.71           C
ATOM    697  CD ALYS B 522       4.769  -5.950 -11.661  0.50 38.67           C
ATOM    698  CE ALYS B 522       5.482  -5.448 -12.916  0.50 44.03           C
ATOM    699  NZ ALYS B 522       5.791  -3.995 -12.866  0.50 47.50           N1+
ATOM    700  N   MET B 523       0.528  -6.396  -8.028  1.00 20.29           N
ATOM    701  CA  MET B 523      -0.262  -7.157  -7.083  1.00 18.00           C
ATOM    702  C   MET B 523      -1.733  -6.744  -7.156  1.00 17.76           C
ATOM    703  O   MET B 523      -2.633  -7.590  -7.115  1.00 18.11           O
ATOM    704  CB  MET B 523       0.280  -6.980  -5.673  1.00 18.53           C
ATOM    705  CG  MET B 523       1.735  -7.533  -5.544  1.00 24.23           C
ATOM    706  SD  MET B 523       2.525  -7.111  -3.973  1.00 25.40           S
ATOM    707  CE  MET B 523       1.715  -8.332  -3.031  1.00 21.03           C
ATOM    708  N   SER B 524      -1.968  -5.444  -7.204  1.00 19.31           N
ATOM    709  CA  SER B 524      -3.326  -4.919  -7.270  1.00 19.77           C
ATOM    710  C   SER B 524      -4.025  -5.456  -8.520  1.00 19.38           C
ATOM    711  O   SER B 524      -5.207  -5.815  -8.486  1.00 19.78           O
ATOM    712  CB  SER B 524      -3.271  -3.379  -7.295  1.00 20.92           C
ATOM    713  OG  SER B 524      -4.565  -2.842  -7.428  1.00 21.29           O
ATOM    714  N   ASP B 525      -3.291  -5.512  -9.635  1.00 16.42           N
ATOM    715  CA  ASP B 525      -3.871  -6.003 -10.892  1.00 18.34           C
ATOM    716  C   ASP B 525      -4.255  -7.489 -10.807  1.00 18.54           C
ATOM    717  O   ASP B 525      -5.289  -7.878 -11.331  1.00 20.32           O
ATOM    718  CB  ASP B 525      -2.941  -5.799 -12.064  1.00 18.84           C
ATOM    719  CG  ASP B 525      -2.832  -4.341 -12.524  1.00 26.52           C
ATOM    720  OD1 ASP B 525      -3.643  -3.457 -12.160  1.00 21.83           O
ATOM    721  OD2 ASP B 525      -1.890  -4.082 -13.281  1.00 26.22           O1-
ATOM    722  N   ASN B 526      -3.437  -8.309 -10.149  1.00 21.39           N
ATOM    723  CA  ASN B 526      -3.813  -9.692  -9.866  1.00 24.71           C
ATOM    724  C   ASN B 526      -5.043  -9.798  -8.978  1.00 20.69           C
ATOM    725  O   ASN B 526      -5.912 -10.644  -9.237  1.00 21.47           O
ATOM    726  CB  ASN B 526      -2.674 -10.463  -9.202  1.00 26.72           C
ATOM    727  CG  ASN B 526      -1.716 -11.007 -10.178  1.00 32.31           C
ATOM    728  ND2 ASN B 526      -0.443 -10.956  -9.829  1.00 35.31           N
ATOM    729  OD1 ASN B 526      -2.093 -11.464 -11.266  1.00 32.17           O
ATOM    730  N   LEU B 527      -5.123  -8.965  -7.934  1.00 20.30           N
ATOM    731  CA  LEU B 527      -6.303  -8.969  -7.057  1.00 22.51           C
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ATOM    732  C   LEU B 527      -7.555  -8.519  -7.798  1.00 21.86           C
ATOM    733  O   LEU B 527      -8.658  -9.036  -7.565  1.00 21.32           O
ATOM    734  CB  LEU B 527      -6.157  -8.050  -5.832  1.00 24.90           C
ATOM    735  CG  LEU B 527      -5.497  -8.547  -4.568  1.00 32.86           C
ATOM    736  CD1 LEU B 527      -5.719  -7.471  -3.452  1.00 28.23           C
ATOM    737  CD2 LEU B 527      -6.062  -9.917  -4.209  1.00 28.39           C
ATOM    738  N   GLU B 528      -7.377  -7.537  -8.664  1.00 21.02           N
ATOM    739  CA  GLU B 528      -8.463  -7.032  -9.456  1.00 20.49           C
ATOM    740  C   GLU B 528      -9.011  -8.119 -10.400  1.00 20.20           C
ATOM    741  O   GLU B 528     -10.217  -8.274 -10.536  1.00 19.76           O
ATOM    742  CB  GLU B 528      -8.040  -5.773 -10.215  1.00 22.31           C
ATOM    743  CG  GLU B 528      -9.171  -5.141 -11.000  1.00 24.03           C
ATOM    744  CD  GLU B 528      -8.898  -3.722 -11.531  1.00 27.16           C
ATOM    745  OE1 GLU B 528      -7.839  -3.120 -11.315  1.00 30.22           O
ATOM    746  OE2 GLU B 528      -9.795  -3.190 -12.188  1.00 38.18           O1-
ATOM    747  N   ARG B 529      -8.142  -8.849 -11.094  1.00 19.79           N
ATOM    748  CA  ARG B 529      -8.580 -10.025 -11.829  1.00 19.41           C
ATOM    749  C   ARG B 529      -9.333 -11.049 -10.946  1.00 19.69           C
ATOM    750  O   ARG B 529     -10.412 -11.556 -11.317  1.00 19.94           O
ATOM    751  CB  ARG B 529      -7.391 -10.671 -12.535  1.00 21.63           C
ATOM    752  CG  ARG B 529      -7.032  -9.997 -13.812  1.00 23.34           C
ATOM    753  CD  ARG B 529      -5.879 -10.704 -14.548  1.00 24.50           C
ATOM    754  NE  ARG B 529      -4.606 -10.582 -13.846  1.00 27.51           N
ATOM    755  CZ  ARG B 529      -3.740  -9.581 -14.027  1.00 25.38           C
ATOM    756  NH1 ARG B 529      -2.616  -9.576 -13.355  1.00 29.50           N
ATOM    757  NH2 ARG B 529      -3.982  -8.597 -14.890  1.00 28.38           N1+
ATOM    758  N   CYS B 530      -8.792 -11.341  -9.770  1.00 22.92           N
ATOM    759  CA  CYS B 530      -9.434 -12.251  -8.829  1.00 22.81           C
ATOM    760  C   CYS B 530     -10.866 -11.790  -8.498  1.00 26.45           C
ATOM    761  O   CYS B 530     -11.797 -12.589  -8.479  1.00 20.91           O
ATOM    762  CB  CYS B 530      -8.579 -12.382  -7.571  1.00 25.32           C
ATOM    763  SG  CYS B 530      -9.318 -13.310  -6.227  1.00 24.50           S
ATOM    764  N   PHE B 531     -11.011 -10.491  -8.272  1.00 22.01           N
ATOM    765  CA  PHE B 531     -12.292  -9.836  -7.992  1.00 21.18           C
ATOM    766  C   PHE B 531     -13.286  -9.952  -9.133  1.00 20.91           C
ATOM    767  O   PHE B 531     -14.412 -10.397  -8.915  1.00 21.73           O
ATOM    768  CB  PHE B 531     -12.038  -8.348  -7.699  1.00 22.39           C
ATOM    769  CG  PHE B 531     -13.283  -7.518  -7.604  1.00 21.09           C
ATOM    770  CD1 PHE B 531     -14.200  -7.753  -6.581  1.00 26.66           C
ATOM    771  CD2 PHE B 531     -13.521  -6.501  -8.500  1.00 23.82           C
ATOM    772  CE1 PHE B 531     -15.365  -6.950  -6.476  1.00 26.00           C
ATOM    773  CE2 PHE B 531     -14.693  -5.709  -8.411  1.00 25.88           C
ATOM    774  CZ  PHE B 531     -15.591  -5.938  -7.395  1.00 23.60           C
ATOM    775  N   HIS B 532     -12.844  -9.603 -10.335  1.00 24.83           N
ATOM    776  CA  HIS B 532     -13.695  -9.671 -11.512  1.00 25.18           C
ATOM    777  C   HIS B 532     -14.228 -11.080 -11.768  1.00 25.78           C
ATOM    778  O   HIS B 532     -15.368 -11.246 -12.179  1.00 29.41           O
ATOM    779  CB  HIS B 532     -12.984  -9.136 -12.745  1.00 28.90           C
ATOM    780  CG  HIS B 532     -12.831  -7.649 -12.739  1.00 31.12           C
ATOM    781  ND1 HIS B 532     -13.594  -6.678 -12.180  1.00 31.67           N
ATOM    782  CD2 HIS B 532     -11.766  -7.007 -13.334  1.00 37.29           C
ATOM    783  NE2 HIS B 532     -11.889  -5.702 -13.157  1.00 39.25           N
ATOM    784  CE1 HIS B 532     -12.985  -5.476 -12.450  1.00 31.85           C
ATOM    785  N   ARG B 533     -13.380 -12.075 -11.539  1.00 23.93           N
ATOM    786  CA  ARG B 533     -13.743 -13.453 -11.691  1.00 25.83           C
ATOM    787  C   ARG B 533     -14.742 -13.828 -10.620  1.00 25.72           C
ATOM    788  O   ARG B 533     -15.766 -14.428 -10.926  1.00 24.71           O
ATOM    789  CB  ARG B 533     -12.515 -14.377 -11.618  1.00 24.82           C
ATOM    790  CG  ARG B 533     -12.862 -15.847 -11.560  1.00 26.83           C
ATOM    791  CD  ARG B 533     -13.711 -16.260 -12.748  1.00 29.43           C
ATOM    792  NE  ARG B 533     -13.988 -17.699 -12.830  1.00 28.32           N
ATOM    793  CZ  ARG B 533     -14.761 -18.233 -13.769  1.00 30.32           C
ATOM    794  NH1 ARG B 533     -15.344 -17.454 -14.675  1.00 34.79           N
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ATOM    795  NH2 ARG B 533     -14.968 -19.533 -13.813  1.00 30.23           N1+
ATOM    796  N   ALA B 534     -14.457 -13.465  -9.370  1.00 24.06           N
ATOM    797  CA  ALA B 534     -15.390 -13.683  -8.260  1.00 24.13           C
ATOM    798  C   ALA B 534     -16.785 -13.085  -8.536  1.00 23.71           C
ATOM    799  O   ALA B 534     -17.814 -13.684  -8.222  1.00 27.45           O
ATOM    800  CB  ALA B 534     -14.802 -13.092  -6.960  1.00 22.26           C
ATOM    801  N   MET B 535     -16.814 -11.920  -9.151  1.00 24.34           N
ATOM    802  CA  MET B 535     -18.070 -11.276  -9.487  1.00 25.98           C
ATOM    803  C   MET B 535     -18.849 -11.976 -10.614  1.00 30.40           C
ATOM    804  O   MET B 535     -20.034 -11.669 -10.814  1.00 30.04           O
ATOM    805  CB  MET B 535     -17.839  -9.795  -9.838  1.00 24.69           C
ATOM    806  CG  MET B 535     -17.372  -8.951  -8.661  1.00 23.09           C
ATOM    807  SD  MET B 535     -18.608  -8.685  -7.385  1.00 29.88           S
ATOM    808  CE  MET B 535     -19.866  -7.837  -8.364  1.00 24.71           C
ATOM    809  N   MET B 536     -18.216 -12.890 -11.361  1.00 29.21           N
ATOM    810  CA  MET B 536     -18.936 -13.670 -12.417  1.00 36.23           C
ATOM    811  C   MET B 536     -19.704 -14.891 -11.855  1.00 38.97           C
ATOM    812  O   MET B 536     -20.809 -15.224 -12.309  1.00 51.73           O
ATOM    813  CB  MET B 536     -17.948 -14.233 -13.452  1.00 32.52           C
ATOM    814  CG  MET B 536     -17.031 -13.238 -14.112  1.00 30.14           C
ATOM    815  SD  MET B 536     -15.863 -14.064 -15.229  1.00 30.08           S
ATOM    816  CE  MET B 536     -17.008 -14.876 -16.348  1.00 35.82           C
ATOM    817  N   LYS B 537     -19.071 -15.566 -10.890  1.00 48.72           N
ATOM    818  CA  LYS B 537     -19.286 -16.996 -10.598  1.00 70.81           C
ATOM    819  C   LYS B 537     -19.636 -17.202  -9.129  1.00 62.78           C
ATOM    820  OXT LYS B 537     -18.836 -17.813  -8.378  1.00 62.78           O1-
ATOM    821  O   LYS B 537     -20.695 -16.775  -8.673  1.00 77.30           O
ATOM    822  CB  LYS B 537     -18.030 -17.773 -11.034  1.00 51.31           C
ATOM    823  CG  LYS B 537     -18.062 -19.285 -10.740  1.00  0.00           C
ATOM    824  CD  LYS B 537     -19.237 -20.048 -11.377  1.00  0.00           C
ATOM    825  CE  LYS B 537     -19.334 -19.886 -12.901  1.00  0.00           C
ATOM    826  NZ  LYS B 537     -18.162 -20.460 -13.607  1.00  0.00           N1+
TER     827      LYS B 537
HETATM  828  N2  LIG     0       0.357  -0.345   0.287  1.00  0.00           N
HETATM  829  N3  LIG     0       3.529   1.432  -0.449  1.00  0.00           N
HETATM  830  C13 LIG     0       2.208  -1.154   1.590  1.00  0.00           C
HETATM  831  C14 LIG     0       0.911  -1.212   1.231  1.00  0.00           C
HETATM  832  C15 LIG     0      -1.039  -0.537  -0.080  1.00  0.00           C
HETATM  833  C16 LIG     0       1.112   0.688  -0.316  1.00  0.00           C
HETATM  834  C17 LIG     0       2.512   0.663   0.051  1.00  0.00           C
HETATM  835  C18 LIG     0       3.067  -0.209   0.966  1.00  0.00           C
HETATM  836  C19 LIG     0       4.452   0.035   1.030  1.00  0.00           C
HETATM  837  C20 LIG     0       4.710   1.065   0.147  1.00  0.00           C
HETATM  838  O22 LIG     0       0.637   1.521  -1.083  1.00  0.00           O
HETATM  839  C   LIG     0       2.647  -2.113   2.636  1.00  0.00           C
HETATM  840  O   LIG     0       2.414  -3.313   2.532  1.00  0.00           O
HETATM  841  N   LIG     0       3.263  -1.506   3.713  1.00  0.00           N
HETATM  842  N   LIG     0       4.152  -4.552   6.558  1.00  0.00           N1+
HETATM  843  C   LIG     0       4.585  -5.370   7.744  1.00  0.00           C
HETATM  844  C   LIG     0       5.327  -3.885   5.885  1.00  0.00           C
HETATM  845  C   LIG     0       4.857  -3.187   4.617  1.00  0.00           C
HETATM  846  C   LIG     0       3.719  -2.207   4.908  1.00  0.00           C
HETATM  847  C   LIG     0       2.570  -2.876   5.669  1.00  0.00           C
HETATM  848  C   LIG     0       3.071  -3.563   6.930  1.00  0.00           C
TER     849      LIG     0
HETATM  850  N2  LIG     0       0.169  -0.250   0.414  1.00  0.00           N
HETATM  851  N3  LIG     0       3.586   1.006  -0.268  1.00  0.00           N
HETATM  852  C13 LIG     0       1.781  -1.015   2.035  1.00  0.00           C
HETATM  853  C14 LIG     0       0.524  -0.987   1.544  1.00  0.00           C
HETATM  854  C15 LIG     0      -1.192  -0.362  -0.094  1.00  0.00           C
HETATM  855  C16 LIG     0       1.095   0.577  -0.257  1.00  0.00           C
HETATM  856  C17 LIG     0       2.445   0.445   0.241  1.00  0.00           C
HETATM  857  C18 LIG     0       2.807  -0.320   1.332  1.00  0.00           C
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HETATM  858  C19 LIG     0       4.201  -0.221   1.496  1.00  0.00           C
HETATM  859  C20 LIG     0       4.660   0.605   0.489  1.00  0.00           C
HETATM  860  O22 LIG     0       0.790   1.329  -1.178  1.00  0.00           O
HETATM  861  C   LIG     0       2.061  -1.819   3.266  1.00  0.00           C
HETATM  862  O   LIG     0       3.063  -2.520   3.366  1.00  0.00           O
HETATM  863  N   LIG     0       1.105  -1.655   4.256  1.00  0.00           N
HETATM  864  N   LIG     0       0.316  -2.333   8.335  1.00  0.00           N1+
HETATM  865  C   LIG     0       0.159  -2.791   9.760  1.00  0.00           C
HETATM  866  C   LIG     0      -0.328  -3.298   7.370  1.00  0.00           C
HETATM  867  C   LIG     0      -0.290  -2.704   5.971  1.00  0.00           C
HETATM  868  C   LIG     0       1.137  -2.347   5.540  1.00  0.00           C
HETATM  869  C   LIG     0       1.830  -1.467   6.583  1.00  0.00           C
HETATM  870  C   LIG     0       1.756  -2.058   7.983  1.00  0.00           C
TER     871      LIG     0
HETATM  872  N2  LIG     0       0.610  -0.485   0.429  1.00  0.00           N
HETATM  873  N3  LIG     0       3.642   1.384  -0.571  1.00  0.00           N
HETATM  874  C13 LIG     0       2.559  -1.150   1.687  1.00  0.00           C
HETATM  875  C14 LIG     0       1.243  -1.264   1.400  1.00  0.00           C
HETATM  876  C15 LIG     0      -0.803  -0.719   0.172  1.00  0.00           C
HETATM  877  C16 LIG     0       1.296   0.506  -0.303  1.00  0.00           C
HETATM  878  C17 LIG     0       2.706   0.571   0.007  1.00  0.00           C
HETATM  879  C18 LIG     0       3.344  -0.201   0.961  1.00  0.00           C
HETATM  880  C19 LIG     0       4.697   0.197   0.992  1.00  0.00           C
HETATM  881  C20 LIG     0       4.857   1.170   0.026  1.00  0.00           C
HETATM  882  O22 LIG     0       0.756   1.249  -1.118  1.00  0.00           O
HETATM  883  C   LIG     0       3.057  -2.041   2.782  1.00  0.00           C
HETATM  884  O   LIG     0       2.317  -2.389   3.702  1.00  0.00           O
HETATM  885  N   LIG     0       4.370  -2.458   2.667  1.00  0.00           N
HETATM  886  N   LIG     0       7.195  -4.054   5.432  1.00  0.00           N1+
HETATM  887  C   LIG     0       7.931  -4.870   6.459  1.00  0.00           C
HETATM  888  C   LIG     0       5.926  -3.462   5.998  1.00  0.00           C
HETATM  889  C   LIG     0       5.306  -2.538   4.960  1.00  0.00           C
HETATM  890  C   LIG     0       5.003  -3.305   3.671  1.00  0.00           C
HETATM  891  C   LIG     0       6.286  -3.940   3.128  1.00  0.00           C
HETATM  892  C   LIG     0       6.946  -4.839   4.166  1.00  0.00           C
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