Supplementary Information

Computational investigation of BMS-984923 against Alzheimer's Amyloid-beta (Aβ) structures : Insights into their molecular interactions and inhibition of aggregation

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Table S1a: Docking table for system 2. Cluster rank is the hierarchical ordering of conformational clusters (based on RMSD 2 Å) of generated ligand binding poses, where clusters are ranked according to the lowest binding energy within each cluster, with the top-ranked cluster representing the most energetically favorable binding mode. Docking scores obtained from the AutoDock GA runs. The best ranked energy implies the best ranked conformation with the lowest binding energy and is highlighted as red in colour. MBE indicate the mean binding energy of the cluster. CF refers to the frequency of occurrence of a particular pose or conformation among the GA runs. All energies are in kcal mol^{-1}.

Cluster Rank	Best ranked energy	MBE	CF
1	-5.50	-5.09	10
2	-5.48	-4.84	8
3	-5.39	-4.61	10
4	-5.13	-4.67	7
5	-5.12	-4.67	10

Table S1b: Docking table for system 4

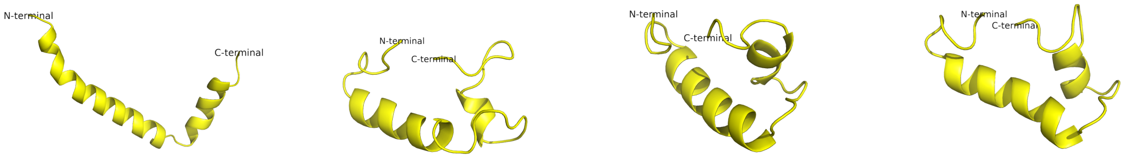
Cluster Rank	Best ranked energy	MBE	CF
1	-6.86	-5.90	9
2	-6.06	-5.87	4
3	-5.95	-5.58	31
4	-5.80	-5.06	6
5	-5.71	-5.32	6

Table S1c: Docking table for system 6

Cluster Rank	Best ranked energy	MBE	CF
1	-6.58	-5.80	13
2	-6.38	-5.87	13
3	-6.33	-5.44	6
4	-6.10	-5.34	9
5	-6.00	-5.40	10

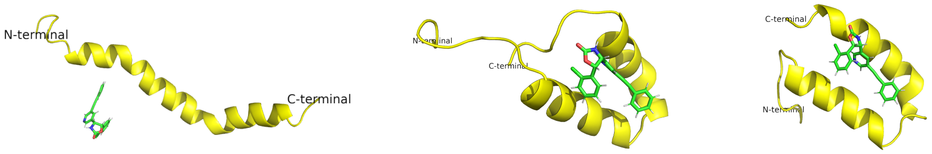
Table S2: Docking table for the extracted structures from the system 1(monomer) simulation

Time	Best ranked energy	MBE	CF
0ns	-5.92	-5.24	24
50ns	-6.86	-5.90	9
100ns	-5.84	-4.87	18
150ns	-6.58	-5.80	13
200ns	-6.29	-5.21	9
250ns	-5.64	-4.97	9
300ns	-6.07	-5.29	12
350ns	-6.33	-6.01	15
400ns	-6.00	-5.63	11
450ns	-6.32	-5.38	21
500ns	-5.76	-5.06	6

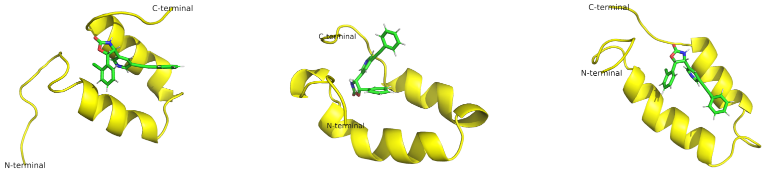


(a) 0ns (b) 100ns (c) 200ns (d) 300ns

(e) 400ns (f) 500ns

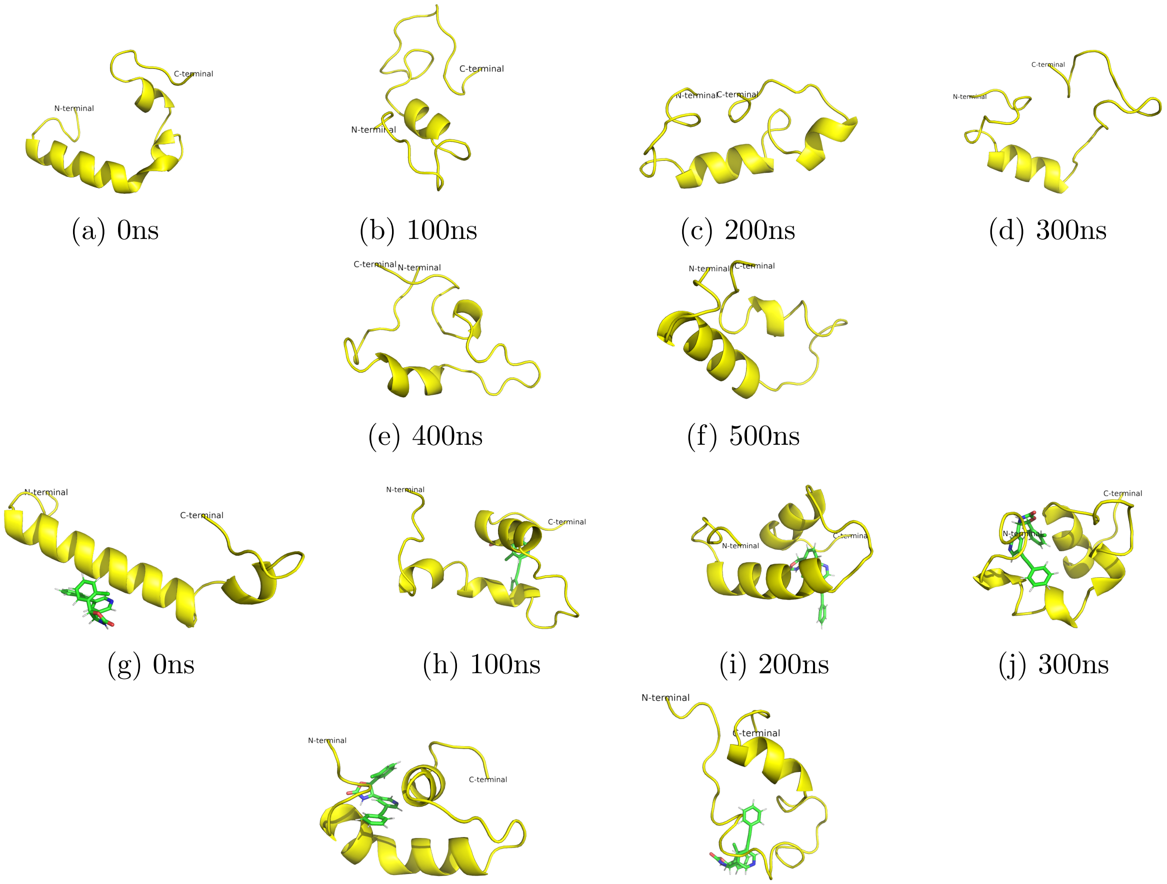


(g) 0ns (h) 100ns (i) 200ns



(j) 300ns (k) 400ns (l) 500ns

Figure S1: Snapshots generated at different points of time in system 1 and 2: monomer (a-f) and complex (g-l). Images are generated with the help of PyMol visualization software.



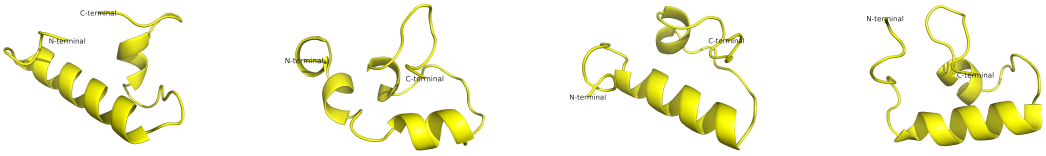
(a) 0ns (b) 100ns (c) 200ns (d) 300ns

(e) 400ns (f) 500ns

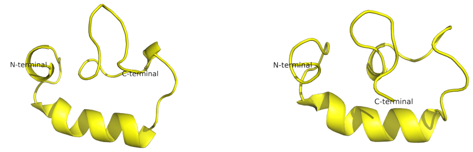
(g) 0ns (h) 100ns (i) 200ns (j) 300ns

(k) 400ns (l) 500ns

Figure S2: Snapshots generated at different points of time in system 3 and 4: monomer (a-f) and complex (g-l). Images are generated with the help of PyMol visualization software.

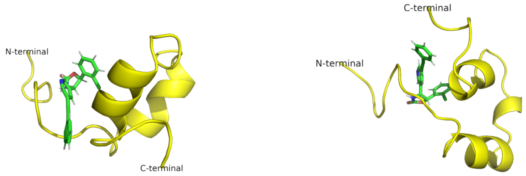


(a) 0ns (b) 100ns (c) 200ns (d) 300ns



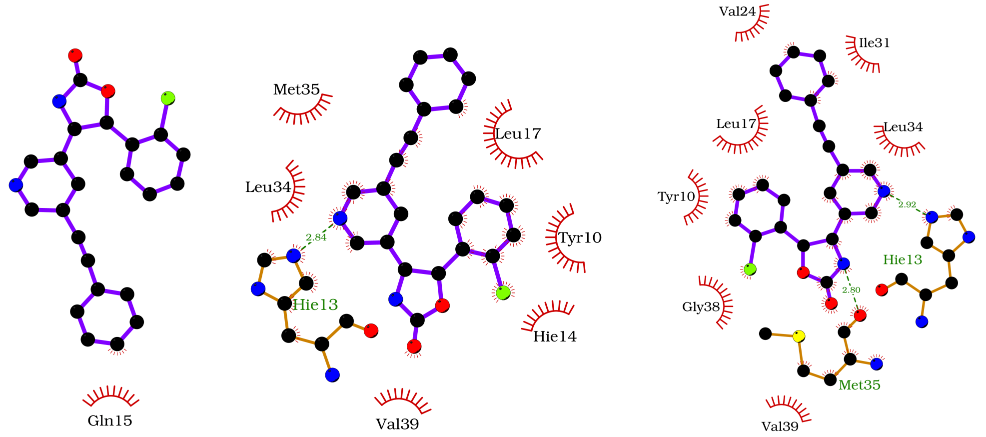
(e) 400ns (f) 500ns

(g) 0ns (h) 100ns (i) 200ns (j) 300ns

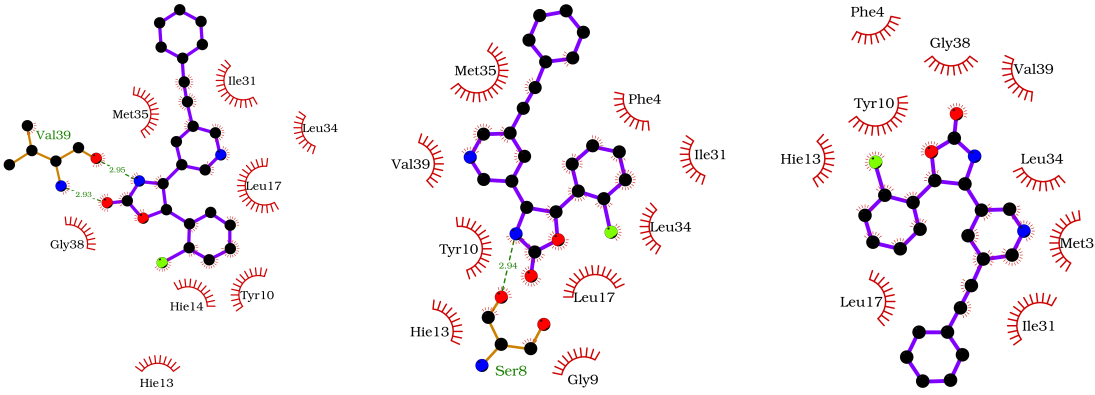


(k) 400ns (l) 500ns

Figure S3: Snapshots generated at different points of time in system 5 and 6: monomer (a-f) and complex (g-l). Images are generated with the help of PyMol visualization software.

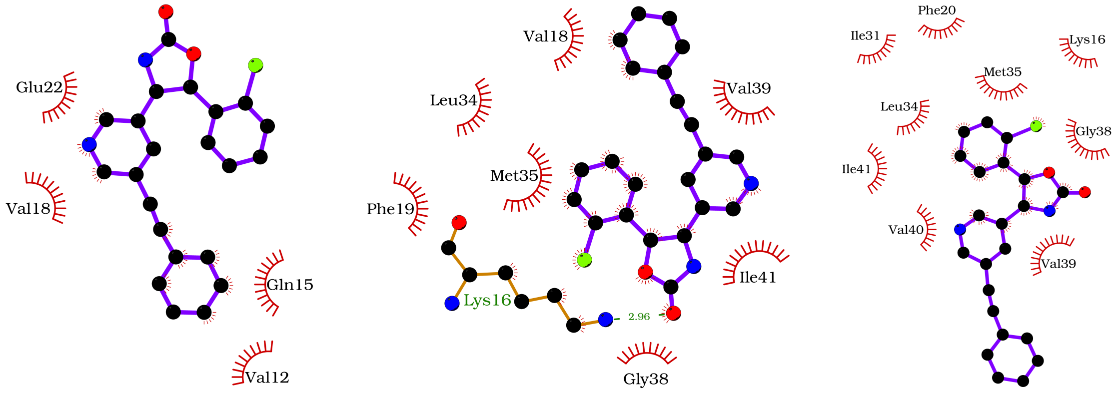


(a) 0ns (b) 100ns (c) 200ns

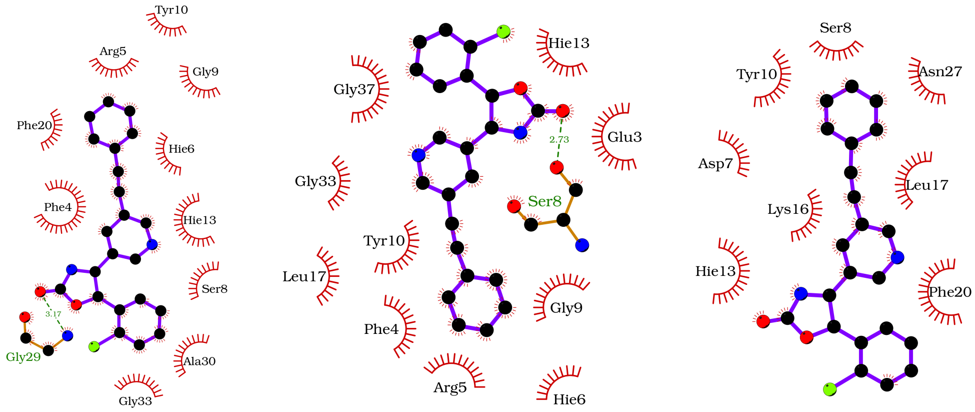


(d) 300ns (e) 400ns (f) 500ns

Figure S4: 2D interaction plot in system 2.Images are generated with the help of Ligplot+ visualization software.

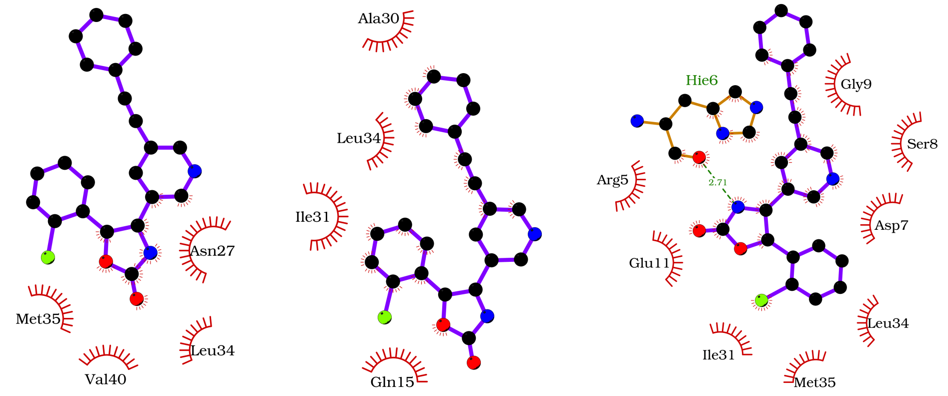


(a) 0ns (b) 100ns (c) 200ns

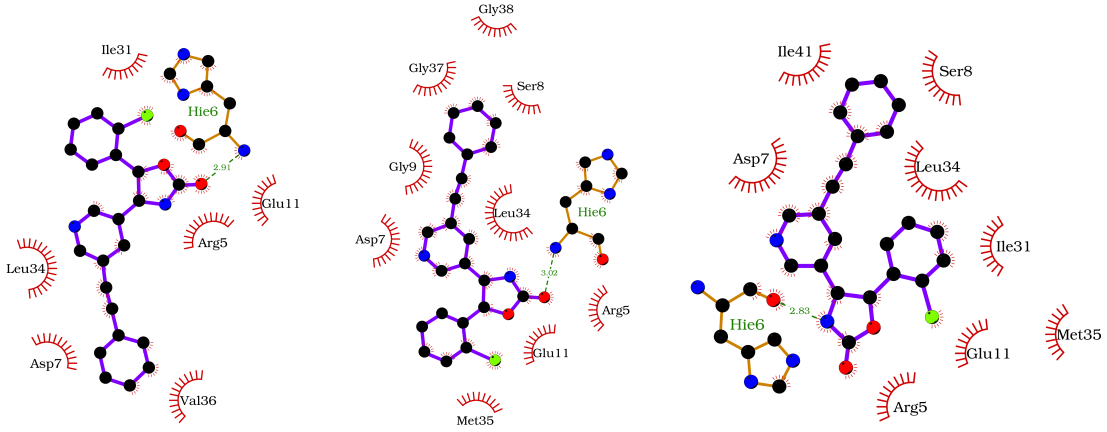


(d) 300ns (e) 400ns (f) 500ns

Figure S5: 2D interaction plot in system 4: complex. Images are generated with the help of Ligplot+ visualization software.



(a) 0ns (b) 100ns (c) 200ns

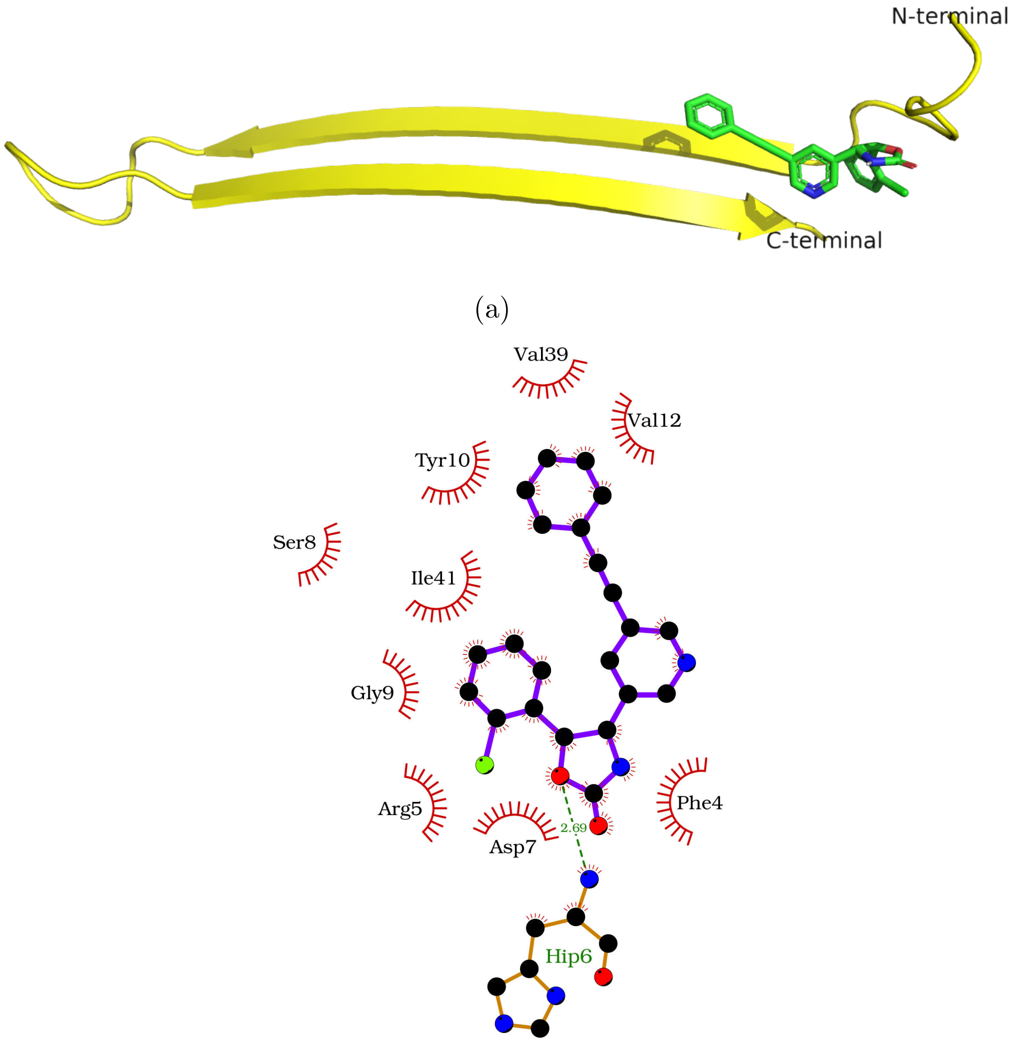


(d) 300ns (e) 400ns (f) 500ns

Figure S6: 2D interaction plot in system 6: complex. Images are generated with the help of Ligplot+ visualization software.

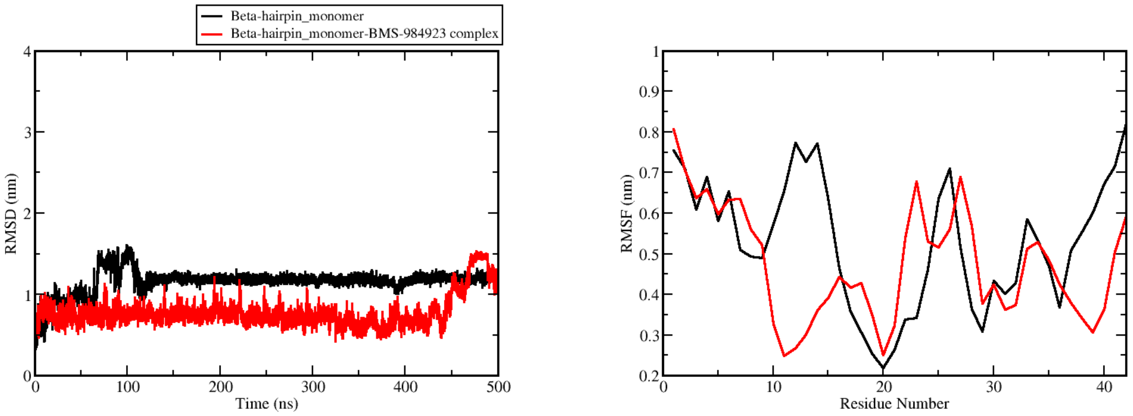
Table S3: Docking table for β-hairpin-BMS-984923 complex

Cluster Rank	Best ranked energy	MBE	CF
1	-6.99	-5.86	7
2	-6.38	-6.06	4
3	-6.27	-5.79	14
4	-6.26	-5.79	8
5	-6.08	-5.38	8



(b)

Figure S7: Structures of (a) docked complex of the β-hairpin structure with BMS-984923 and (b) 2D interaction image of the docked complex.



(a) RMSD

(b) RMSF

Figure S8: (a) RMSD and (b) RMSF profiles of the β-hairpin (black) and β-hairpin-BMS-984923 complex (red) from the 500ns MD simulations.

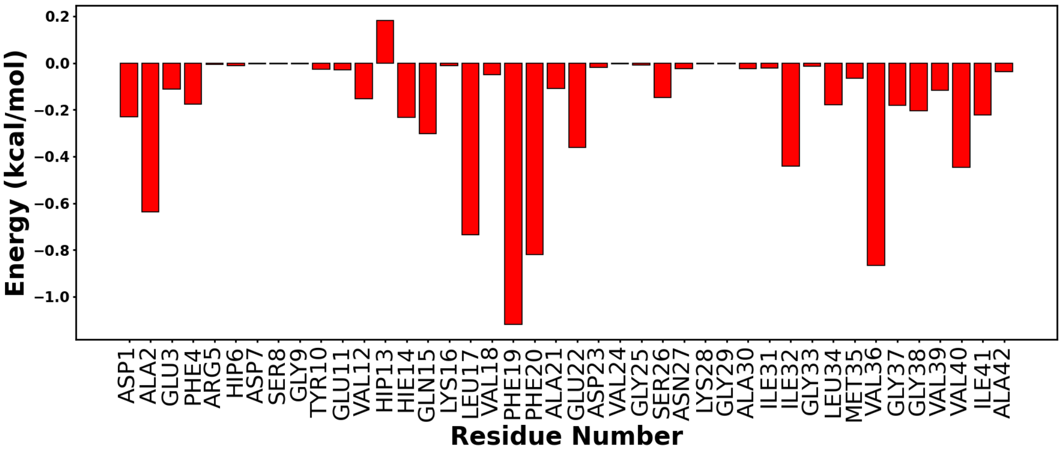


Figure S9: Per-residue binding free energy contribution to MM-PBSA in the β-hairpin-BMS-984923 complex.

Table S4: Binding free energy (MM-PBSA) components of the β-hairpin-BMS-984923 complex.All energies are in kcal mol^{-1}.

Energy term	Value (kcal mol^{-1})
ΔE_{vdW}	-25.0 ± 5.0
ΔE_{Ele}	-11.0 ± 6.6
$\Delta E_{\mathrm{Polar}}$	19.0 ± 6.0
$\Delta E_{\mathrm{Nonpolar}}$	-3.0 ± 0.4
$\Delta G_{\mathrm{Binding}}$	-20.0 ± 4.0