# Supplementary material

## Development of novel HER2 inhibitors against gastric cancer derived from flavonoid source of *Syzygium alternifolium* through molecular dynamics and pharmacophore based screening

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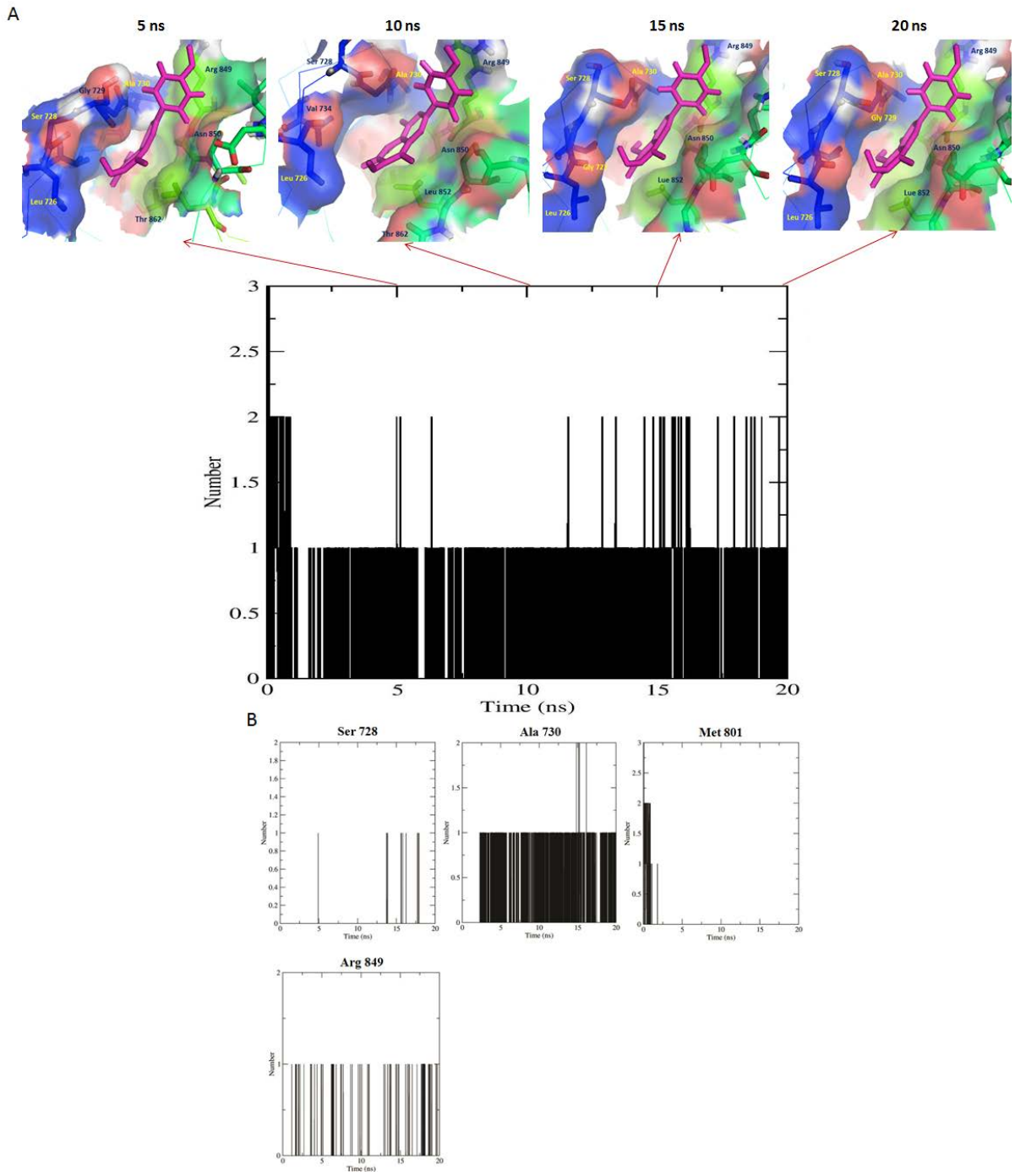


**Figure S1A.** The snapshots of docking pose of compound **1** and total H-bond intensity at various time scale intervals in 20 ns complex MD simulations with HER2, **B.**Hydrogen bonds diagram between compound **1** and active site residues viz., Ser728, Ala730, Met801 and Arg849 of HER2, Black squares indicate the presence of H-bond and white ones correspond to the absence of H-bond throughout the time scale of 20 ns MD simulations.

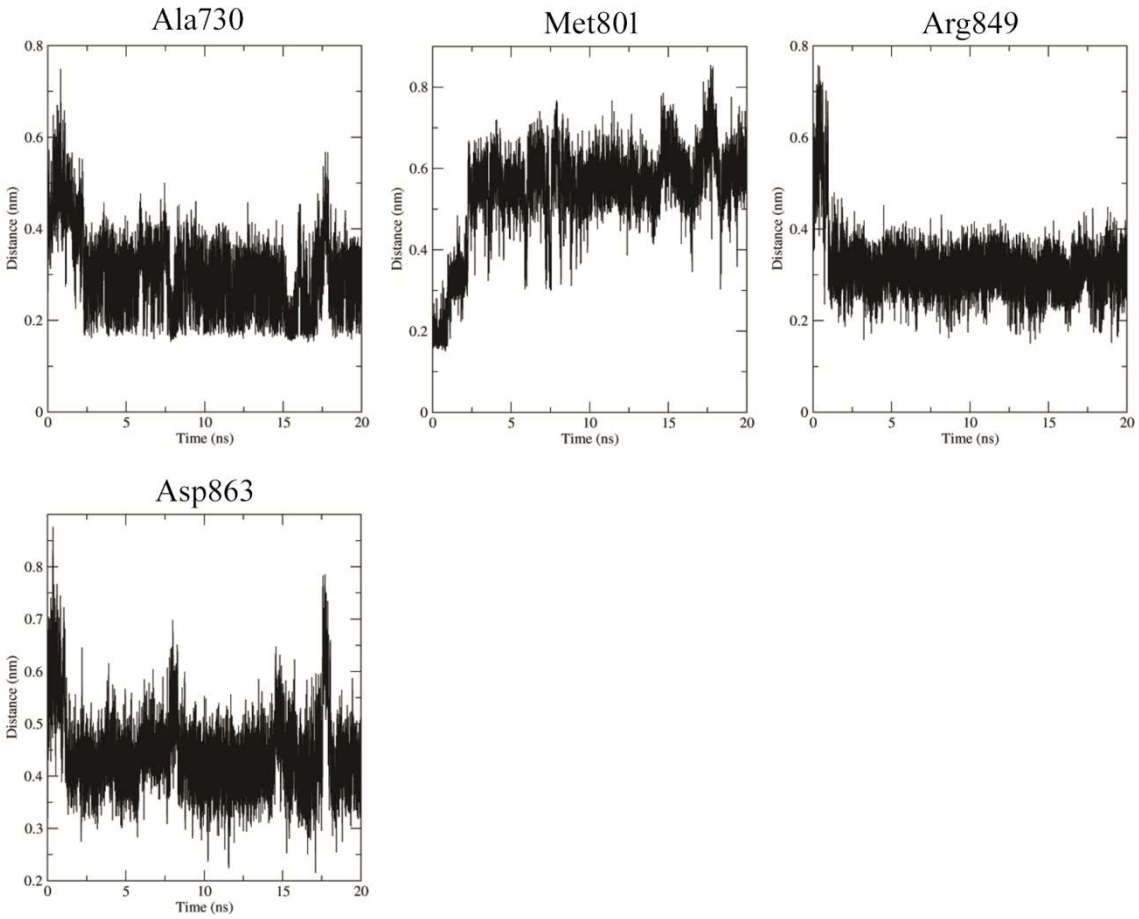


**Figure S2** Distance between hydrogen bonding residues viz., Ala 730, Met 801, Arg 849, and Asp 863 with compound **1** in a complex protein of HER2b, comparatively depicted throughout 20 ns simulation period.

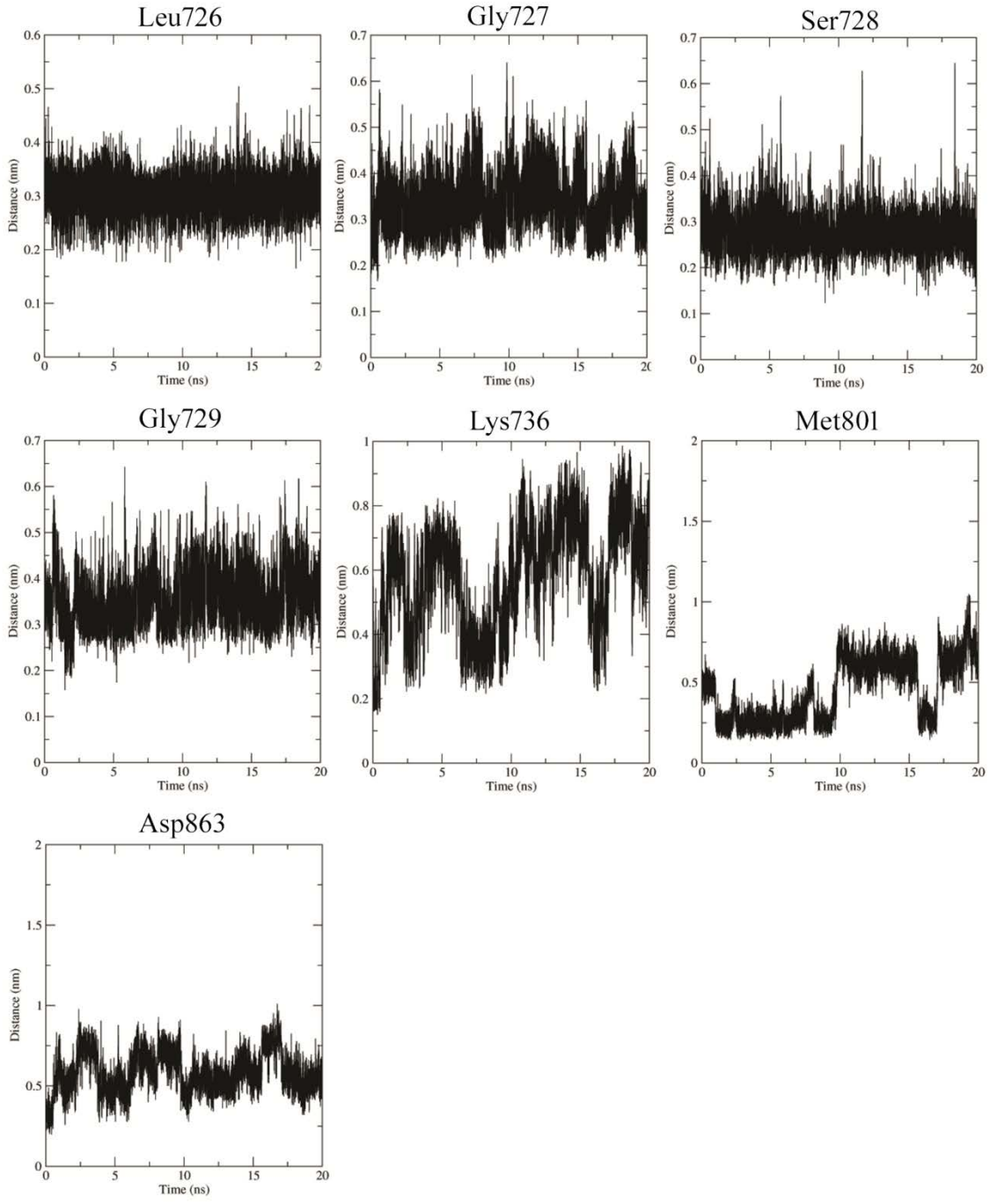


**Figure. S3**Distance between hydrogen bonding residues viz. Leu 726,Gly 727, Ser 728, Gly 729,Lys 736, Met 801, and Asp 863 with compound **2** in a complex protein of HER2c, comparatively depicted throughout 20 ns simulation period.

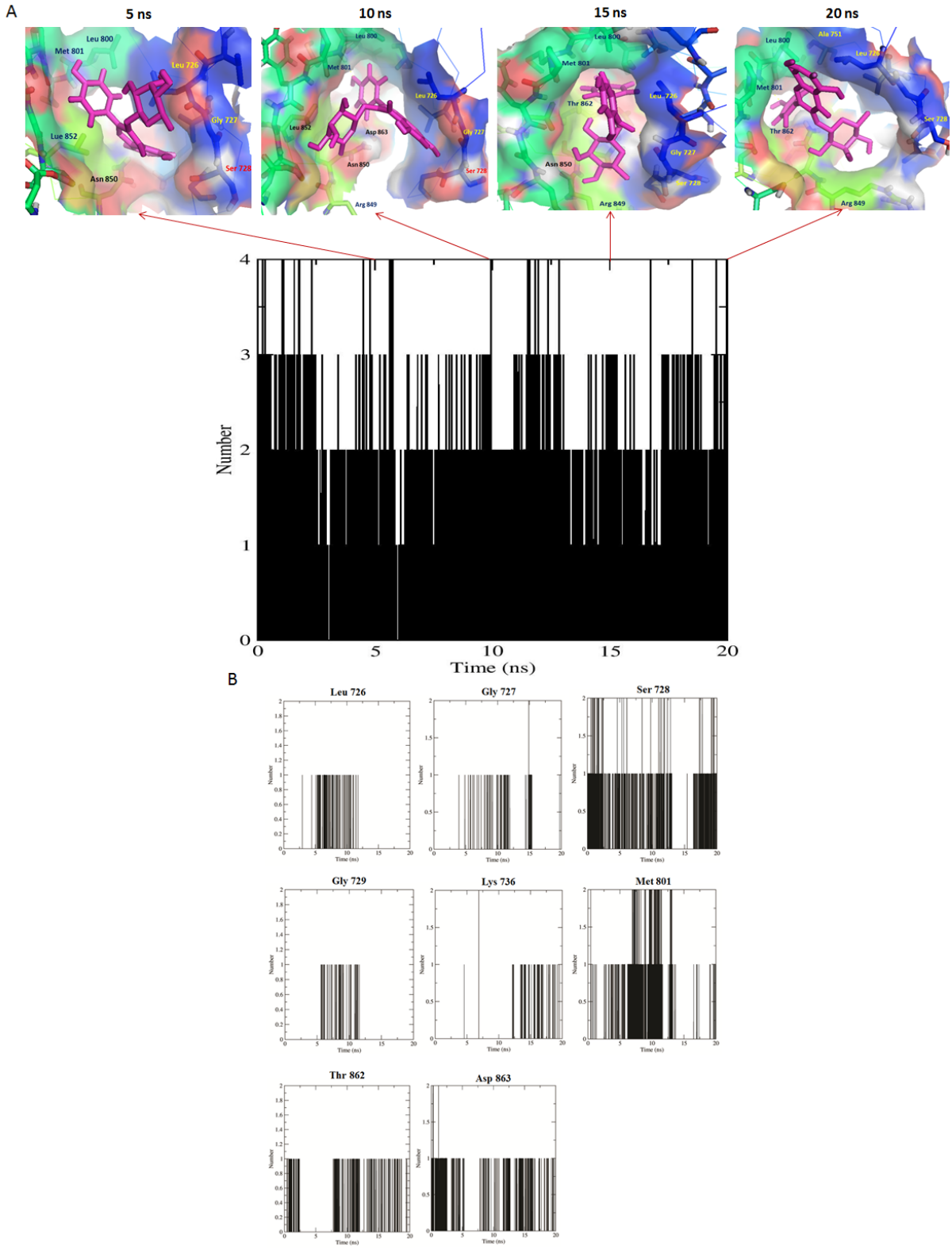


**Figure S4 A**The snapshots of docking pose of compound **3** and total H-bond intensity at various time scale intervals in 20 ns complex MD simulations with HER2**, B.**Hydrogen bonds diagram between compound **3** and active site residues viz., Leu726, Gly726, Ser728, Gly729, Lys736, Met801, Thr862 and Asp863 of HER2, Black squares indicate the presence of H-bond and white ones correspond tothe absence of H-bond throughout the time scale of 20 ns MD simulations.

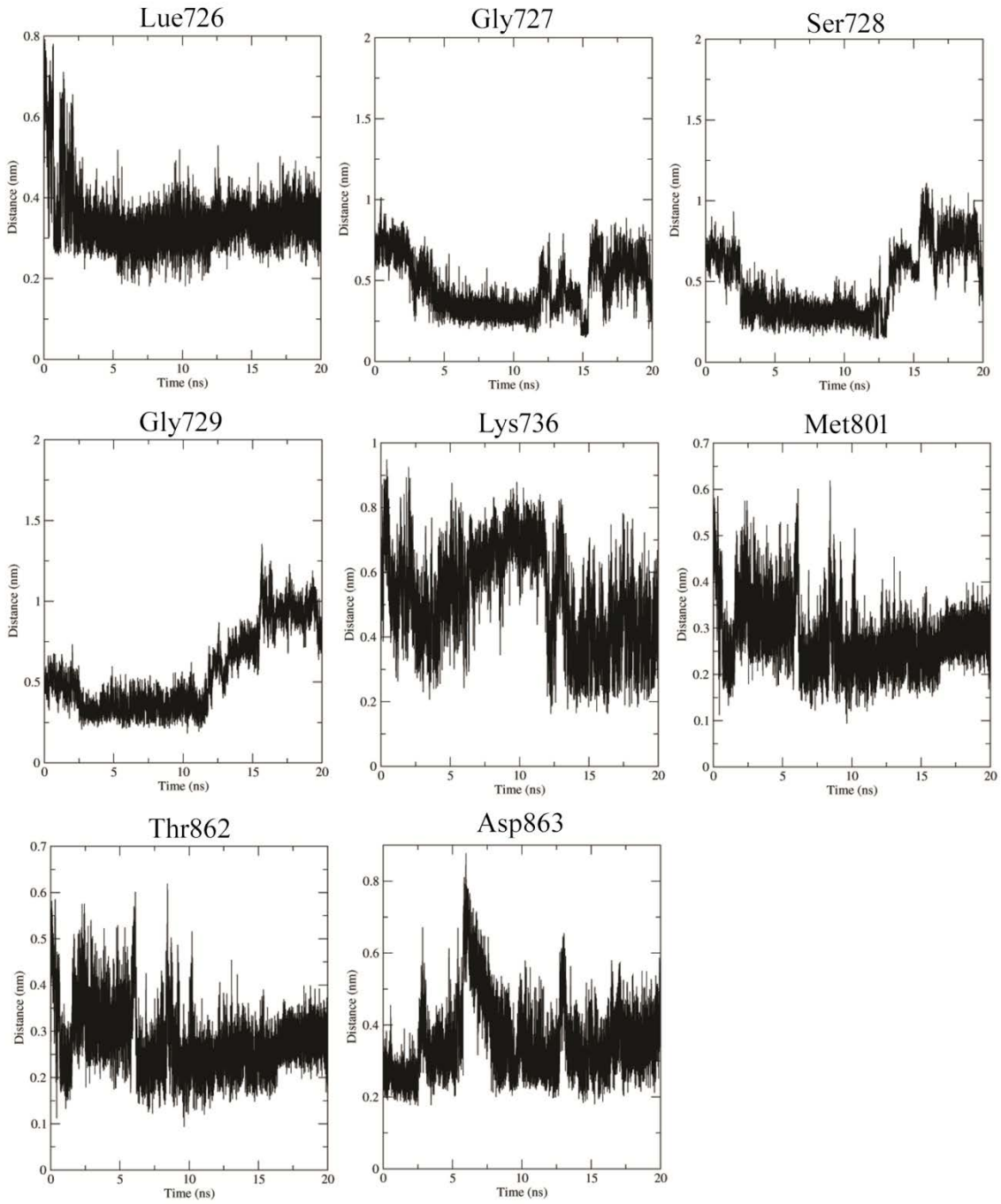


**Figure S5** Distance between hydrogen bonding residues viz. Leu 726, Gly 727, Ser 728, Gly 729, Lys 736, Met 801, Thr 862 and Asp 863 with compound **3** in a complex protein of HER2d, comparatively depicted throughout 20 ns simulation period.

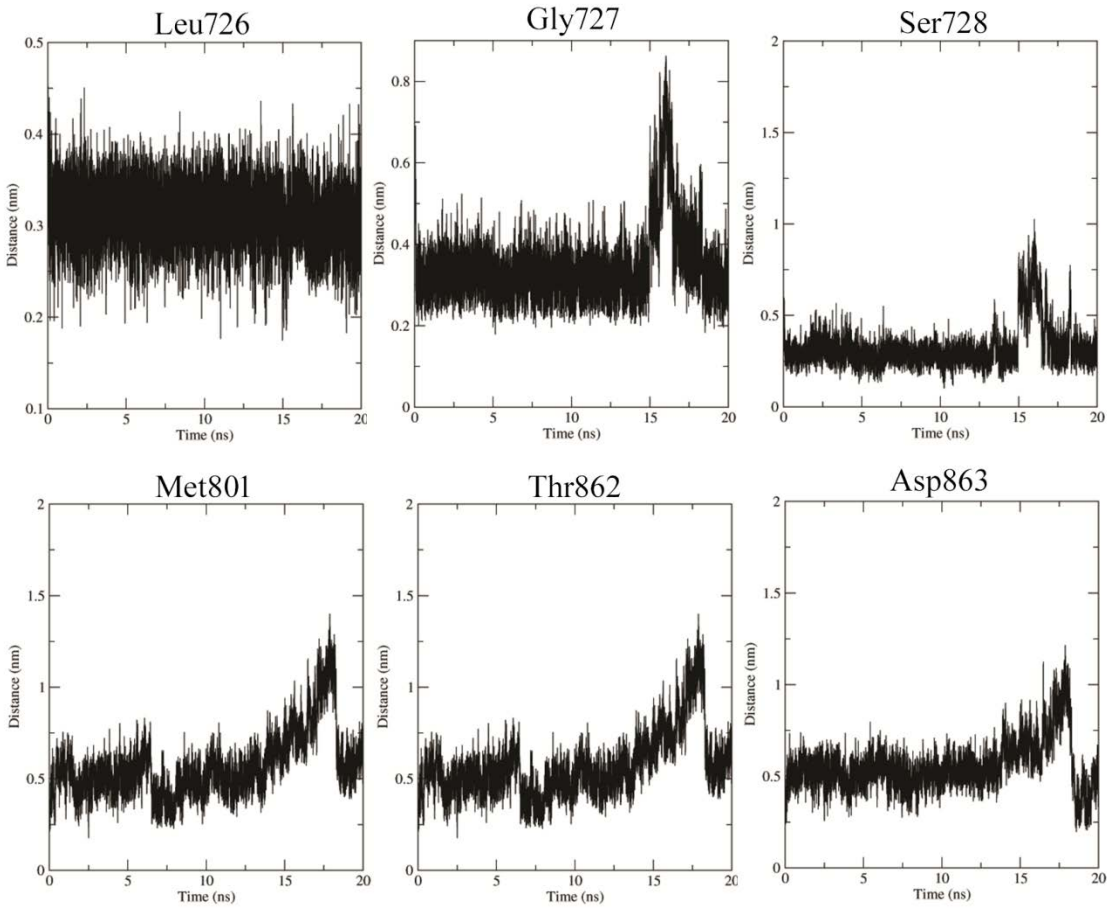


**Figure S6** Distance between hydrogen bonding residues viz. Leu 726, Gly 727, Ser 728, Met 801, Thr 862 and Asp 863 with ZINC67903192 in a complex protein of HER2e, comparatively depicted throughout 20 ns simulation period.

**Table S1**

The list of pharmacophore hits for HER2-Compound **2** complex and its physico-chemical properties.

| S.No | mol | rmsd | mseq | b_rotN | Weight | a_acc | a_don | SlogP |
|---|---|---|---|---|---|---|---|---|
| 1 | ZINC67903192 | 0.536928 | 1 | 6 | 594.522 | 14 | 9 | -1.5844 |
| 2 | ZINC67903197 | 0.582157 | 2 | 6 | 594.522 | 14 | 9 | -1.5844 |
| 3 | ZINC59763389 | 0.796897 | 3 | 5 | 564.496 | 13 | 8 | -0.9453 |
| 4 | ZINC59763395 | 0.783681 | 4 | 5 | 564.496 | 13 | 8 | -0.9453 |
| 5 | ZINC85816423 | 0.601657 | 5 | 9 | 772.662 | 20 | 13 | -4.0546 |
| 6 | ZINC85816425 | 0.601468 | 6 | 9 | 772.662 | 20 | 13 | -4.0546 |
| 7 | ZINC85816428 | 0.736348 | 7 | 9 | 772.662 | 20 | 13 | -4.0546 |
| 8 | ZINC85816432 | 0.736335 | 8 | 9 | 772.662 | 20 | 13 | -4.0546 |
| 9 | ZINC85507936 | 0.629833 | 9 | 7 | 626.52 | 16 | 11 | -2.9064 |
| 10 | ZINC85816022 | 0.582267 | 10 | 7 | 626.52 | 16 | 11 | -2.9064 |
| 11 | ZINC85816467 | 0.791578 | 11 | 10 | 788.661 | 21 | 14 | -5.0822 |
| 12 | ZINC85816470 | 0.650954 | 12 | 10 | 788.661 | 21 | 14 | -5.0822 |
| 13 | ZINC85815711 | 0.651054 | 13 | 6 | 596.494 | 15 | 10 | -2.2673 |
| 14 | ZINC85815706 | 0.582267 | 14 | 6 | 596.494 | 15 | 10 | -2.2673 |
| 15 | ZINC85816026 | 0.650954 | 15 | 7 | 626.52 | 16 | 11 | -2.9064 |
| 16 | ZINC85816347 | 0.751353 | 16 | 8 | 756.663 | 19 | 12 | -3.027 |
| 17 | ZINC85816374 | 0.823635 | 17 | 9 | 772.662 | 20 | 13 | -4.0546 |
| 18 | ZINC85816382 | 0.823287 | 18 | 9 | 772.662 | 20 | 13 | -4.0546 |
| 19 | ZINC85816460 | 0.581897 | 19 | 10 | 788.661 | 21 | 14 | -5.0822 |
| 20 | ZINC85816463 | 0.647945 | 20 | 10 | 788.661 | 21 | 14 | -5.0822 |
| 21 | ZINC59764808 | 0.797006 | 21 | 5 | 580.495 | 14 | 9 | -1.2397 |
| 22 | ZINC59764812 | 0.783414 | 22 | 5 | 580.495 | 14 | 9 | -1.2397 |
| 23 | ZINC85531791 | 0.526649 | 23 | 6 | 610.521 | 15 | 10 | -1.8788 |

| S.No | mol | rmsd | mseq | b_rotN | Weight | a_acc | a_don | SlogP |
|---|---|---|---|---|---|---|---|---|
| 24 | ZINC59766057 | 0.745063 | 24 | 5 | 596.494 | 15 | 10 | -1.5341 |
| 25 | ZINC59766065 | 0.742473 | 25 | 5 | 596.494 | 15 | 10 | -1.5341 |
| 26 | ZINC85948558 | 0.774123 | 26 | 7 | 610.521 | 15 | 9 | -1.9643 |
| 27 | ZINC85948547 | 0.774294 | 27 | 7 | 610.521 | 15 | 9 | -1.9643 |
| 28 | ZINC86048481 | 0.644746 | 28 | 8 | 656.546 | 17 | 11 | -2.8978 |
| 29 | ZINC86048475 | 0.644507 | 29 | 8 | 656.546 | 17 | 11 | -2.8978 |
| 30 | ZINC85931428 | 0.773715 | 30 | 9 | 670.573 | 17 | 10 | -2.5948 |
| 31 | ZINC85931420 | 0.77392 | 31 | 9 | 670.573 | 17 | 10 | -2.5948 |
| 32 | ZINC59764341 | 0.62403 | 32 | 10 | 607.497 | 12 | 8 | -1.8986 |
| 33 | ZINC59764345 | 0.62403 | 33 | 10 | 607.497 | 12 | 8 | -1.8986 |
| 34 | ZINC59585850 | 0.712897 | 34 | 4 | 464.379 | 11 | 8 | -0.7306 |

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