Supporting Information

Discovery of small molecule inhibitors of *Leishmania Braziliensis* Hsp90 chaperone

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LbHsp90N      MTETFAFQAEINQLMSLIINTFYSNKEIFLRELISNASDACDKIRYQSLTDPSVLGEETH (60)
LmHsp90N      MTETFAFQAEINQLMSLIINTFYSNKEIFLRELISNASDACDKIRYQSLTDPSVLGESPR (60)
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LbHsp90N      LRVRVVPDKANKTLTVEDNGIGMTKADLVNNLGTIARSGTKAFMEALEAGGDMSMIGQFG (120)
LmHsp90N      LCIRVVPDKENKTLTVEDNGIGMTKADLVNNLGTIARSGTKAFMEALEAGGDMSMIGQFG (120)
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LbHsp90N      VGFYSAYLVADRVTVVSKNNSDEAYVWESSAGGTFTITSVPESDMKRGTRITLHLKEDQQ (180)
LmHsp90N      VGFYSAYLVADRVTVTSKNNSDESYVWESSAGGTFTITSTPESDMKRGTRITLHLKEDQM (180)
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LbHsp90N      EYLEERRVKELIKKHSEFIGYDIELMVEKTAEKEVTDEDEE(221)
LmHsp90N      EYLEPRRLKELIKKHSEFIGYDIELMVEKTTEKEVTDEDEE(221)
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Figure S1. Sequence alignment between LbHsp90N and LmHsp90N. Residues involved in ATP binding are indicated by a red dot above the residue.

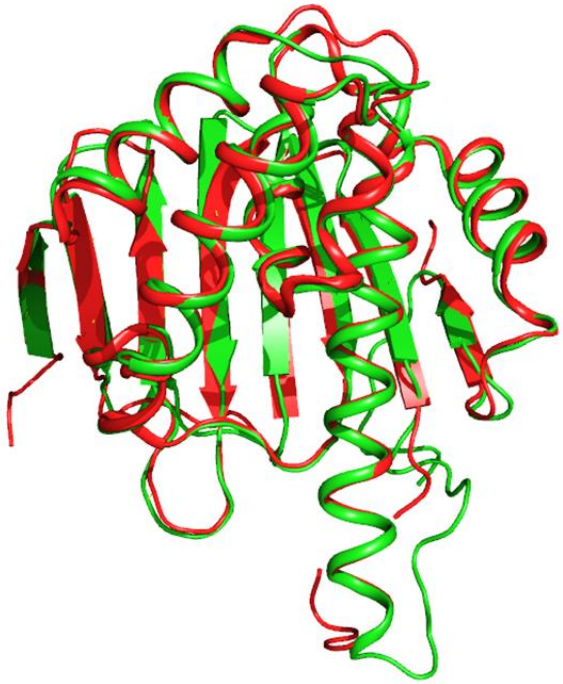

Figure S2. Structural superposition between the template, LmHsp90N (PDB ID 3U67 (21)) and the model obtained through the homology modeling displayed as red and green cartoon, respectively.

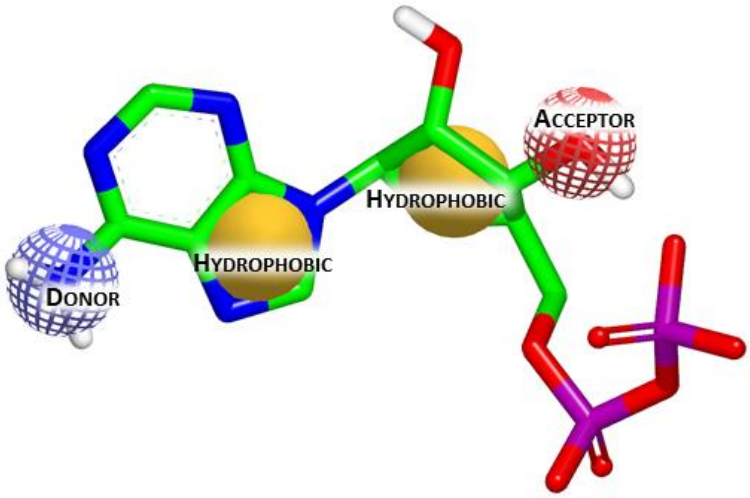

Figure S3. The main features of the ADP query are highlighted as spheres. Query features are coloured as follows: hydrophobic = yellow; acceptor = red; donor = blue.

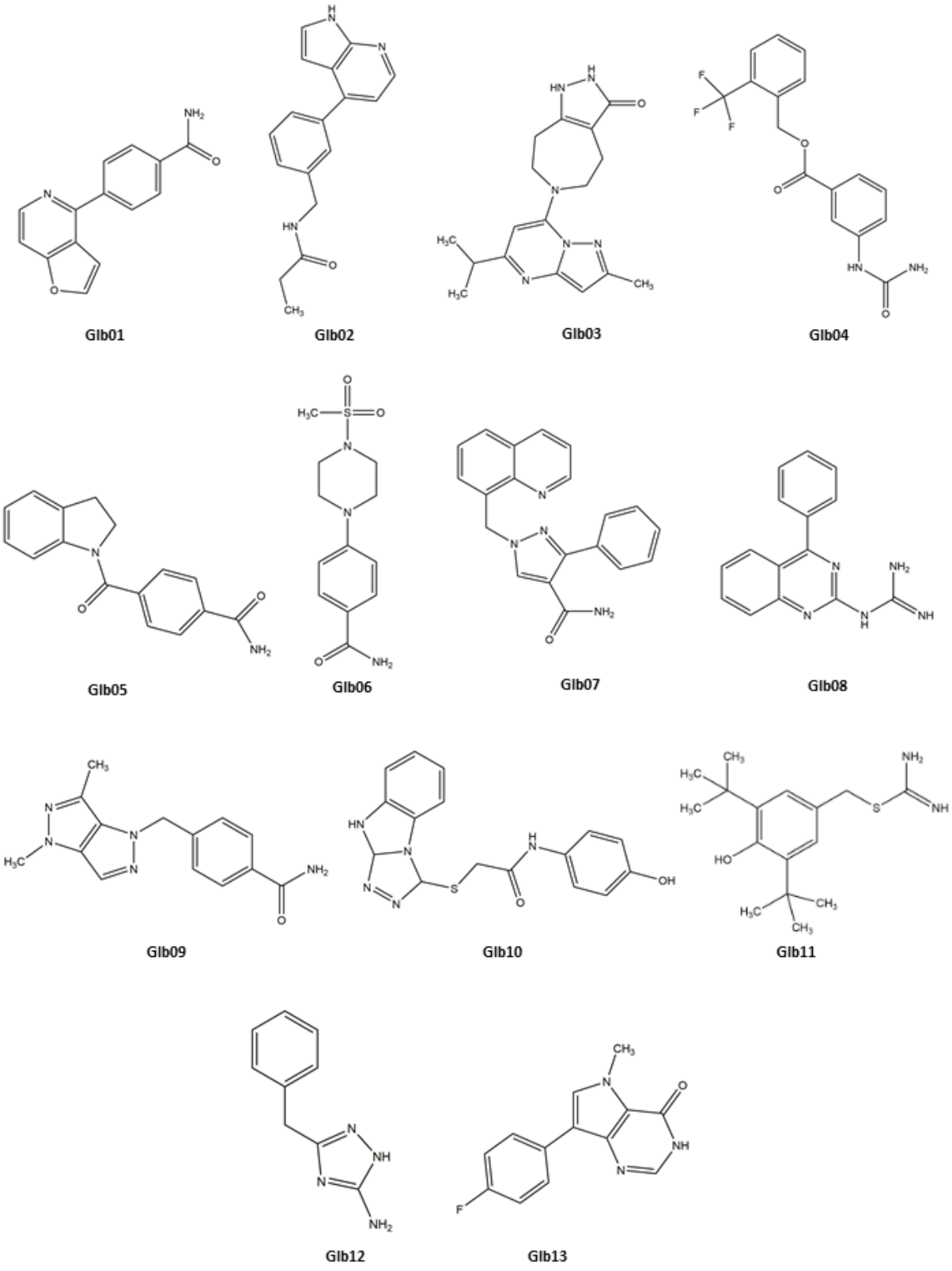

Figure S4. Chemical structure of compounds identified in the first round of virtual screening against LbHsp90N.

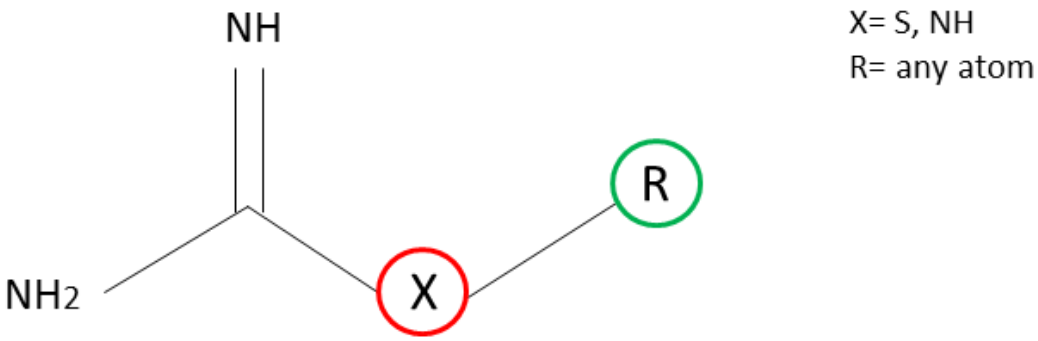

Figure S5. 2D representation of Glb08 and Glb11 substructure. X can be either a sulphur or an amino group whereas R can be any chemical group.

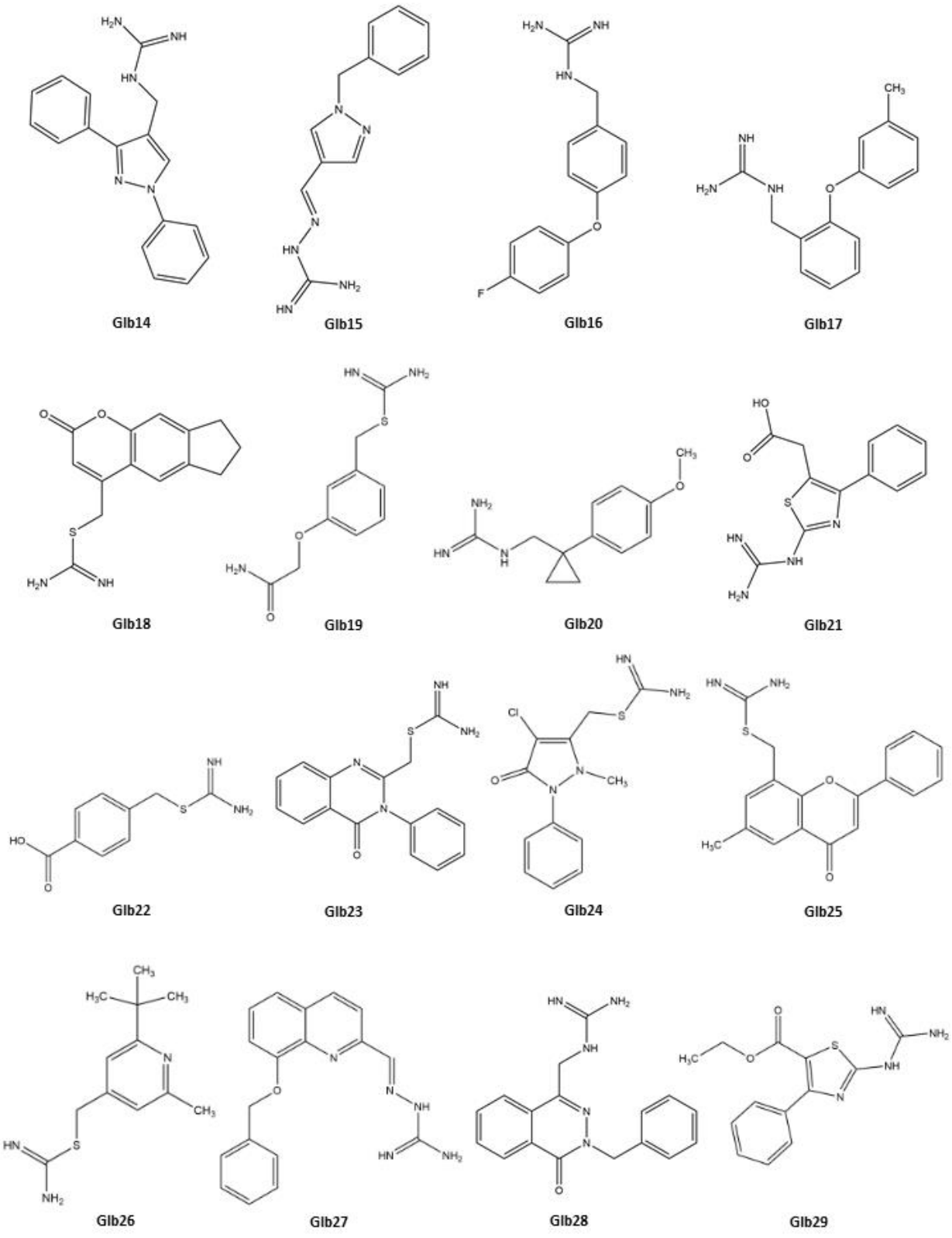

Figure S6. Chemical structure of compounds identified in the second round of virtual screening against LbHsp90N.

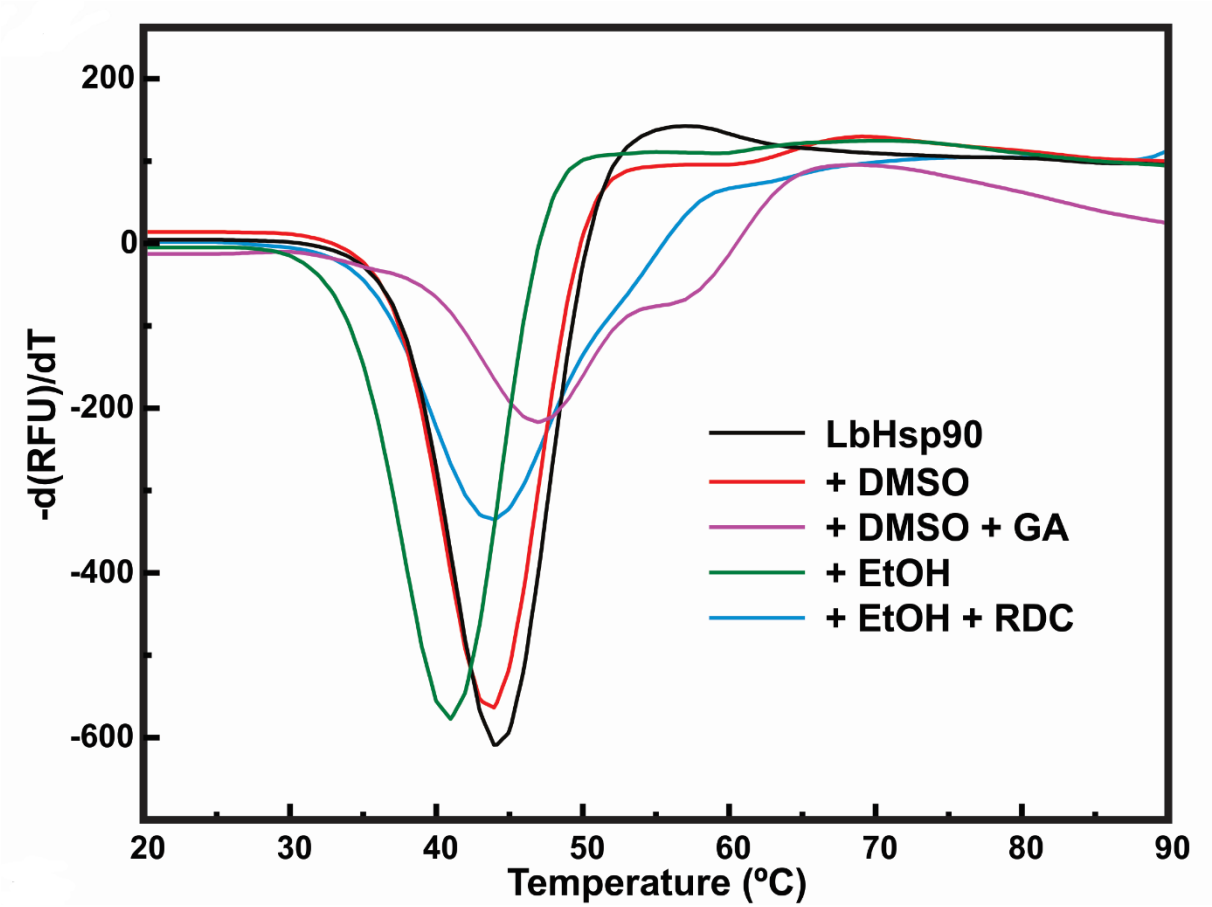

Figure S7. DSF experiments for LbHsp90 and LbHsp90N recombinant proteins. Representative DSF experiments for LbHsp90 in the absence and presence of GA or RDC. DMSO and ethanol were used as vehicles for those compounds. The curves represent the first derivative of the raw data of a representative set of DSF experiments for LbHsp90 with known ligands of Hsp90 N-terminal domains, such as GA and RDC. The plot represents the first derivative of the raw data showing a transition centered at around 45 ºC, which is correlated to its N-terminal domain as previously reported by differential scanning calorimetry. GA and RDC induced a shift of the curves to higher temperatures when compared to the LbHsp90 in the presence of DMSO and ethanol, which were used as vehicles for GA and RDC respectively. The melting temperature (Tm) for each condition were determined as the peak of the first derivative and each value is an average of three curves.