Supplementary information 2 Application of structure-based drug design to generate selective PDE 9A (A, B) and PDE10A inhibitors.

Stacking against the conserved phenylalanine and hydrogen bonding with the invariant glutamine are two characteristics of most PDE inhibitors, as shown in the examples of the binding of 6-amino-pyrazolopyrimidinone-derived PDE9\textsuperscript{1,2} (A, B) and pyrazoloquinoline-derived PDE10\textsuperscript{3,4,5} (C, D) inhibitors in the active site pockets. Dotted lines represent hydrogen bonds. (A,C) Ribbon diagram of the inhibitor (yellow sticks).Dotted lines represent hydrogen bonds. (B,D) Surface model of the inhibitor binding.


