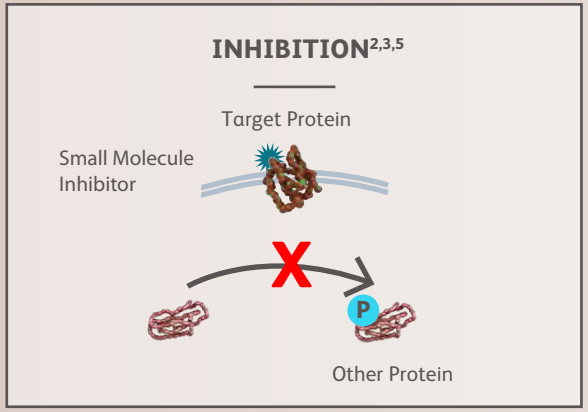
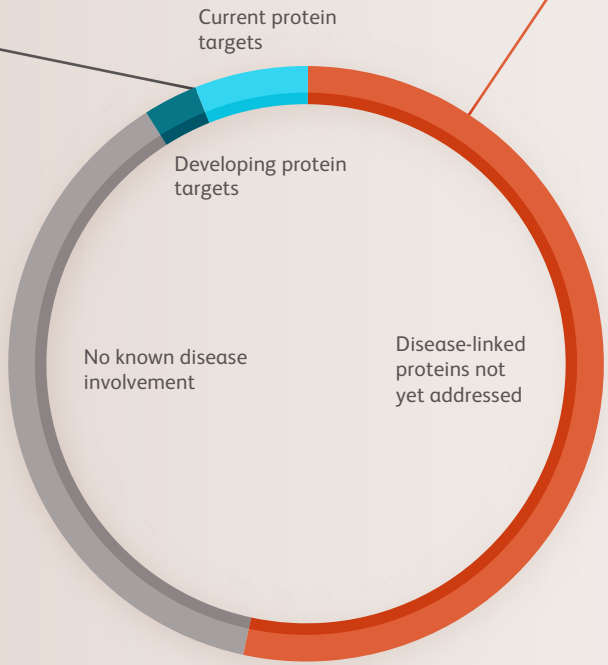
There is untapped potential for targeting in the human proteome[1-4]

Traditional pharmacology inhibits a single protein domain while others remain functional.[2,3,5]



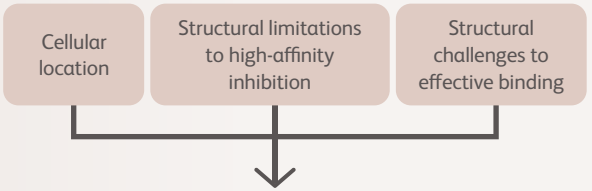
Note: components are not to scale

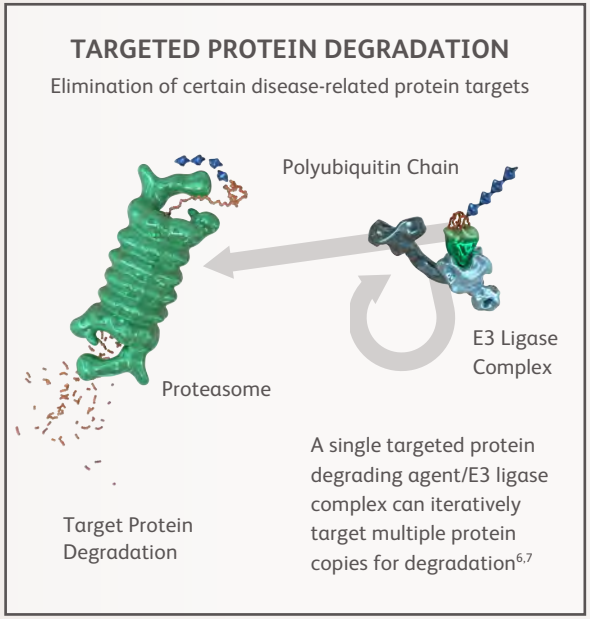
This approach may only be viable for 10% of all proteins.[2]



Traditionally "undruggable" targets[1-3,5]

Reasons for chemical intractability:





Note: components are not to scale

Proteasomal protein degradation can be harnessed to provide a unique way to potentially address traditionally "undruggable" protein targets that contribute to disease progression[6,8-10]

1. Oprea TI, et al. *Nat Rev Drug Discov*. 2018;17(5):317-332. 2. Hopkins AL, Groom CR. *Nat Rev Drug Discov*. 2002;1(9):727-730. 3. Che Y, et al. *Bioorg Med Chem Lett*. 2018;28(15):2585-2592. 4. Chamberlain PP, Hamann LG. *Nat Chem Biol*. 2019;15(10):937-944. 5. An S, Fu L. *EBioMedicine*. 2018;36;553-562. 6. Chamberlain PP, Cathers BE. *Drug Disc Today: Tech*. 2019;31:29-34. 7. Bondeson DP et al. *Nat Chem Biol*. 2015;11:611-617. 8. Kronke J et al. *Science*. 2014;343:301-305. 9. Gandhi AK et al. *Br J Haematol*. 2014;164:811-821. 10. Matyskiela ME et al. *Nature*. 2016;535:252-257.

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