Lithium is the drug of choice for bipolar disorder. However it has many unwanted and intolerable side effects, and not all patients respond to lithium therapy. There is no other drug that is specifically used for the treatment of bipolar disorder. There is a crucial need for a better ‘mood stabiliser’ and ‘anti-suicidal’ drug.

In our search for lithium mimetics, we screened a library of compounds, with a known safety profile, against the enzyme inositol monophosphatase. This enzyme is inhibited at therapeutic concentrations of lithium, and is the putative target of lithium in the treatment of bipolar disorder.

We found an inhibitor with an IC$_{50}$ of 2 $\mu$M in vitro (n= 5) with this approach. To further validate our inhibitor as a possible mood-stabiliser, we tested it in animal models. To test whether or not the drug crosses the blood brain barrier, we performed an ex vivo assay. We injected mice with the drug, dissected and homogenised the brains and used the homogenate to test for enzyme inhibition in a Michaelis-Menton curve. We found lower enzymatic activity in the homogenate of the animals treated with the drug. This suggests that the drug crosses the blood brain barrier. We then progressed to behavioural testing in animals.

We have tested our drug in the amphetamine induced hyperactivity model. We injected the mice with amphetamine followed by the drug/vehicle. The mice treated with 5 mg/kg of the drug are significantly less hyperactive than the ones treated with vehicle (p <0.05, n= 7). Lithium also attenuates amphetamine induced hyperactivity.

We have found a compound that mimics aspects of lithium like behaviour and is known to be safe in humans. Although further behavioural work will be carried out, this compound can be used in Phase II clinical trials in bipolar patients since it has a known favourable safety profile.