Treating Duchenne muscular dystrophy

December 2 2013

(Medical Xpress)—Reviving a gene which is 'turned down' after birth could be the key to treating Duchenne muscular dystrophy (DMD), an incurable muscle-wasting condition that affects one in every 3,500 boys.

Boys with DMD have difficulty walking between the ages of one and three and are likely to be in a wheelchair by age 12. Sadly, they rarely live past their twenties or thirties.

For the past 17 years, Professor Dame Kay Davies and Professor Steve

Davies at Oxford University have been working on treatments for the condition, which is caused by a lack of the muscle protein, dystrophin.

In recent months they have found a number of new groups of molecules which can increase the levels of utrophin, a protein related to dystrophin. Greater levels of utrophin can make up for the lack of dystrophin to restore muscle function. They have worked with Isis Innovation, Oxford's technology transfer arm, to strike a deal with Summit, a drug development company with a focus on DMD.

"Duchenne muscular dystrophy is a devastating muscle wasting disease for which there is no known cure," said Professor Kay Davies. "These boys all still have the utrophin gene – and that's what we're taking advantage of. In adult muscle, utrophin is present in very low amounts, and we aim to increase the amount to levels which will help protect the muscle in these boys.

"If this approach, called utrophin modulation, really works as we hope, we could treat these boys very early on, increase their quality of life and length of life. They would walk for longer.

"This is a disease that really needs effective treatment – it takes many families by surprise because of the high new mutation rate which occurs in dystrophin protein such that boys with no family history of the disease can be affected."

The Oxford team have been working with Summit, an Oxford spin-out company, to develop their first drug for Duchenne Muscular Dystrophy, SMT C1100. In 2012, SMT C1100 successfully completed a Phase 1 trial which showed the drug could safely circulate through the bloodstreams of healthy volunteers. It is now about to enter clinical trials in people with DMD.

Professor Kay Davies said: "In our ideal world the first molecule we developed with Summit plc, SMT C1100, will have a beneficial effect in these patients. But although SMT C1100 looks promising, we asked ourselves - can we find other drugs that might do even better?"

The new deal will see a research collaboration formed between the University of Oxford and Summit to further the development of the new set of molecules.

Professor Steve Davies said: "We want to ensure that this utrophin modulation therapeutic approach has the best chance of success in the shortest time for treating Duchenne Muscular Dystrophy. We are delighted to join forces with Summit plc in developing, alongside first in class SMT C1100, these back-up and potentially best in class candidates."

Tom Hockaday, Managing Director of Isis Innovation, said: "Isis is delighted to support Professors Kay Davies and Steve Davies in this vital work. Having a number of potential drug candidates in development greatly increases the chances of reaching the ultimate goal, which is to successfully treat this incurable disease."

Glyn Edwards, Chief Executive Officer at Summit, said: "The alliance provides access to differentiated classes of utrophin modulators, potentially with new mechanisms, to complement our clinical candidate SMT C1100 while also establishing a strong drug pipeline for the future. Importantly, the alliance cements our long-term relationship with two scientific leaders at the University of Oxford."

Provided by Oxford University