BIOBUSINESS BRIEFS

DEAL WATCH

Biogen and Amicus to pursue genetically validated Parkinson's disease target

Biogen Idec has teamed up with Amicus Therapeutics to develop a new approach to Parkinson's disease based on targeting the lysosomal enzyme β-glucocerebrosidase (GBA; also known as β-glucosidase). Preclinical studies have shown that increasing the activity of GBA in the brain might prevent the aggregation of α-synuclein, which is a feature of a group of neurodegenerative disorders that includes Parkinson's disease and dementia with Lewy bodies (*Proc. Natl. Acad. Sci. USA* **110**, 3537–3542; 2013).

Genetic mutations in *GBA1* that significantly reduce the enzyme's activity cause Gaucher's disease — the most common lysosomal storage disease. They are also the most widespread genetic risk factor for Parkinson's disease.

> "increasing the activity of GBA in the brain might prevent the aggregation of α-synuclein"

Indeed, "genetic analysis has indicated that sporadic Parkinson's disease patients are five times more likely to carry a *GBA1* mutation compared to unaffected controls", explains Dimitri Krainc, Chairman of the Department of Neurology and Director of the Center for Rare Neurological Diseases, Northwestern University Feinberg School of Medicine, Chicago, USA, and co-founder of Lysosomal Therapeutics. The genetic and clinical 'validation' of the target could represent an important advantage over previous strategies pursued for Parkinson's disease, he says. Furthermore, a recent study (*Cell* **146**, 37–52; 2011) also suggested that aggregates of α-synuclein can themselves inhibit the lysosomal activity of wild-type GBA, causing a positive, self-propagating pathogenic feedback loop. Thus, therapies that activate GBA could lead to neuroprotection and/or disease reversal in cases in which *GBA1* is not mutated.

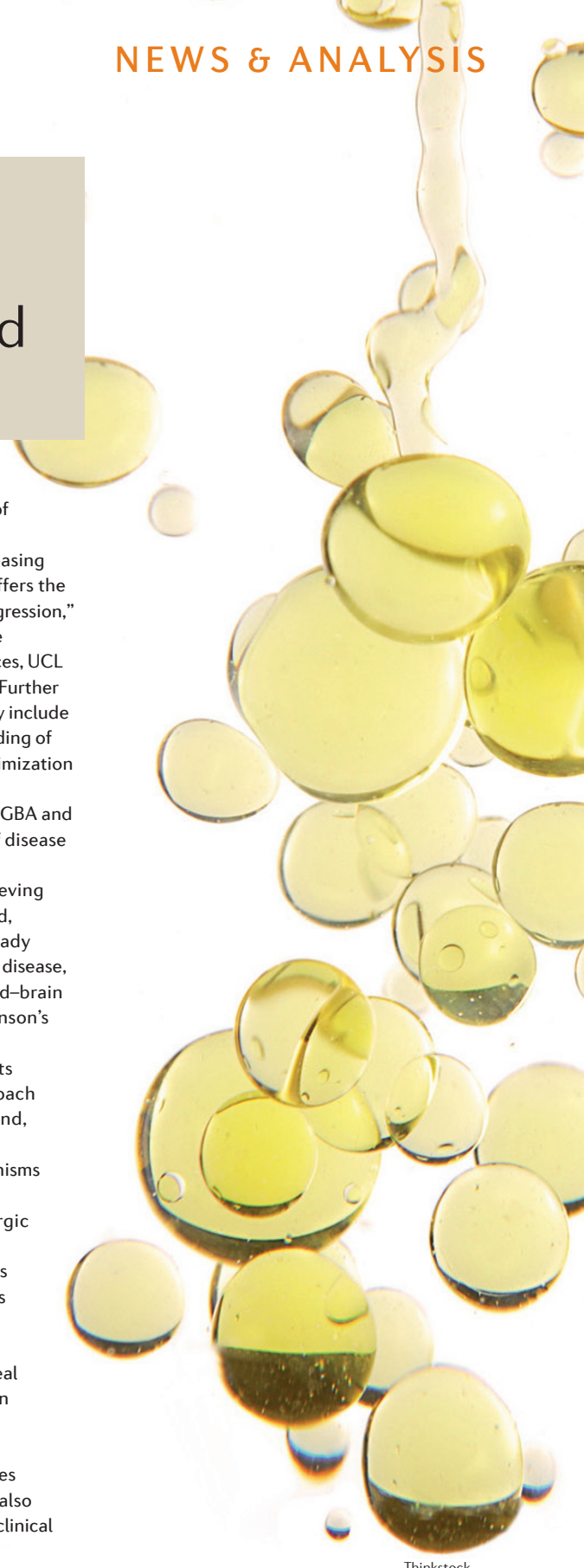
Current treatments for Parkinson's disease alleviate some of the symptoms but do not affect the progression of the disease. "If increasing GBA does lower α-synuclein, this offers the opportunity potentially to slow progression," says Anthony Schapira, Head of the Department of Clinical Neurosciences, UCL Institute of Neurology, London, UK. Further advantages of pursuing this strategy include the existing mechanistic understanding of GBA, which could help with the optimization of candidate molecules for patient treatment, and the potential use of GBA and its lipid substrates as biomarkers of disease progression, adds Krainc.

The main challenge will be achieving sufficient brain penetration. Indeed, recombinant forms of GBA are already used for the treatment of Gaucher's disease, but their inability to cross the blood–brain barrier precludes their use in Parkinson's disease.

Nevertheless, as Schapira points out: "This is an entirely novel approach to Parkinson's disease treatment and, if successful, has the potential to address relevant underlying mechanisms of disease that are common to dopaminergic and non-dopaminergic neurodegeneration." In addition, it may be possible to screen patients for deficient GBA activity and thus personalize treatment with GBA activators.

The full financial terms of the deal have not been disclosed, but Biogen Idec will be responsible for funding all discovery, development and commercialization activities. Besides Amicus, Lysosomal Therapeutics is also working in the area, conducting preclinical studies on small molecules that act as GBA-activating chaperones for the treatment of Parkinson's disease, Gaucher's disease and other lysosomal storage diseases.

Monica Hoyos Flight



Thinkstock