AKB - 5169

Hypoxia-inducible factors (HIFs) are ancient transcription factors that are stabilized when the availability of oxygen is limited (that is, during hypoxia), and drive a transcriptional programme that promotes hypoxia adaptation1. HIFs were initially discovered ~20 years ago by Gregg Semenza and colleagues; studies of erythropoietin (EPO) gene regulation showed that HIFs are transcriptional regulators of hypoxia- or anaemia-associated increases in EPO release and concomitant increases in erythropoiesis2,3. Subsequent studies then implicated HIFs in the regulation of the glycolytic pathway4,5.

Such findings have steered the field of hypoxia research into a completely new direction, with an exciting focus on understanding the molecular mechanisms that alter cellular responses to conditions of limited oxygen availability. Moreover, mounting evidence indicates that HIFs have important roles in a wide range of diseases, including conditions characterized by ischaemia and inflammation6–12. Consequently, pharmacological approaches to enhance or inhibit the stabilization of HIFs are considered promising11,12. Indeed, various ongoing clinical studies are examining orally bioavailable small-molecule activators of HIFs for the treatment of renal anaemia. Similarly, studies have identified digoxin and other cardiac glycosides as HIF inhibitors13. Given the important functional role of HIFs in ischaemic and inflammatory diseases, and the interdependent relationship between inflammation and hypoxia or ischaemia, strategies aimed at modulating hypoxia-signalling pathways for the treatment of ischaemic and inflammatory diseases are gaining considerable attention.

Janssen Agreement includes a license to develop and commercialize AKB-5169, a preclinical compound in development as an oral treatment for IBD. There is one issued patent and two pending patent applications covering the AKB-5169 composition of matter, pharmaceutical compositions, and methods of treating anemia by administration of AKB-5169, respectively, in the United States, and additional patents issued or pending in many other major Jurisdictions worldwide, including Europe, Japan, China, Brazil, Russia and India. The expected expiration dates for these patents are between 2029 and 2038 plus any extensions or adjustments of term available under national law.