Modulator of WIP1 levels to treat Wolfram syndrome (BIO15148)
Product factsheet

- **Product**: WIP1 gene therapy / inhibitor of WIP1 degradation

- **Potential applications**: Wolfram syndrome (WS) is an autosomal recessive neurodegenerative disorder characterized by diabetes insipidus/mellitus, optic atrophy and deafness.

- Loss of function of WFS1 is responsible for WS

- Gene therapy aiming at WFS1 normal expression is impossible due to the size of the WFS1 gene

- **Mechanism**: unexpected key role of WFS1 and WIP1 in ER-mitochondria crosstalk which reconciles the ER expression of WFS1 with the mitochondrial phenotype
  - WFS1 forms a complex with WIP1 (official name undisclosed), to promote ER-mitochondrial Ca2+ transfer in response to stimuli that generate inositol-1,4,5-triphosphate.
  - WFS1 associates with WIP1 to prevent its degradation by the proteasome.
  - WIP1 regulates VDAC expression and mitochondrial respiratory chain.

- **Phase of development**: POC in vitro and in vivo
  - WS patients fibroblasts show diminution of WIP1 protein expression
  - WS patients fibroblasts treatment with proteasome restores levels of WIP1 to a level comparable to normal patients
  - Expression of WIP1 in WS patients fibroblasts can overcome WFS1 deficiency and restore mitochondrial respiration

- **Patents**: PCT/EP2017/056940, TARGETING THE NEURONAL CALCIUM SENSOR 1 FOR TREATING WOLFRAM SYNDROME

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Proof of concept

Restoration of WIP1 expression in cells of WS patients can overcome WFS1 deficiency and mitochondrial respiratory defects.
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