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In Memoriam

Professor Philippe Crine: a hero for children with hypophosphatasia

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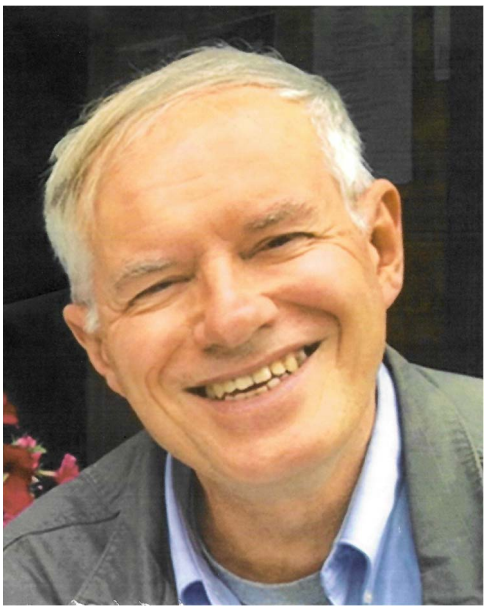

Philippe Crine 1946 - 2023.

Philippe Crine, the father of asfotase alfa treatment for hypophosphatasia (HPP), died on June 13, 2023 at the age of 76. Medical research has lost a great biochemist, a pioneer, and a visionary who conceptualized and developed a miracle therapy for HPP,[1,2] the genetic disorder from mutations in the ALPL gene encoding tissue-nonspecific alkaline phosphatase.[2] HPP features poorly mineralized bones that fracture and deform, often with lifelong handicap and sometimes death in infancy.

Philippe Crine was born in Belgium and emigrated to Canada in 1968 for graduate studies at the Université de Montréal under Pr. Walter Verly. After his PhD (1974), he moved to Brandeis University to study DNA repair. In 1975, his curiosity was attracted by the discovery of enkephalin/endorphin neuropeptides and he joined Pr. Michel Chrétien at the Institut de recherches cliniques de Montréal to study endorphins. He was the first to show how β-endorphin is made enzymatically from ProOpioMelanoCortin. From there, molecular enzymology and protein chemistry became the focus of Philippe's research. In 1978, he joined the Department of Biochemistry at the Université de Montréal as professor, later as Chair of the department (1989-1997), and then vice-dean of research at the Faculty of Medicine (1999-2002).

Professor Crine worked with professors Guy Boileau (Department of Biochemistry) and Denis Gravel (Department of Chemistry) to create BioMep, a start-up aiming at enzyme replacement therapies. In 1998, their first localization of endopeptidase Pex in bone and teeth[3] centered them on bone diseases. Under his leadership, the company evolved as Enobia and produced for HPP a soluble hydroxyapatite-targeted recombinant tissue-nonspecific ALP. To move ALP to preclinical and then clinical trials, Philippe collaborated with 2 bone disease specialists, Michael P. Whyte, MD from Washington University (MO, USA) and Cheryl Rockman-Greenberg, MD from the University of Manitoba (MA, Canada).

Professors Whyte and Rockman-Greenberg documented rescue and significant improvement for newborns, infants, and children severely affected by HPP given what would be called asfotase alfa.[1,2,4-8]

Professor Rockman-Greenberg knew that HPP was most prevalent among the Mennonite population in Canada where it caused life-threatening HPP in 1/2500 live births vs 1/100 000 in the general population. After a phase 1 study there concerning the safety and pharmacology of asfotase alfa (called ENB- 0040), phase 2 clinical trials started at the Winnipeg site[2,5,7] and internationally. In October 2008, baby Amy from Northern Ireland was enrolled and airlifted to

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Winnipeg. «I was at the airport to meet the family. Baby Amy stayed with us for 6 months before returning home. She is now a thriving 16-year-old young lady».

This is in short how Philippe Crine with colleagues devised a revolutionary therapy, asfotase alfa. Vivid recollections of Philippe's life and work were provided by Annie Mear, his widow,[9] and Deborah Fowler, Founder and President of the American Soft Bones Foundation.[10] Scientists and clinicians alike remember Philippe as an inspiring teacher who shared his quest for excellence, his desire to discover, and his instinct for innovation. In a video, see a newborn on a respirator fighting to survive who with treatment breathed freely and thrived. https://youtu.be/gcM_do5dino. Thank you Professor Crine.

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