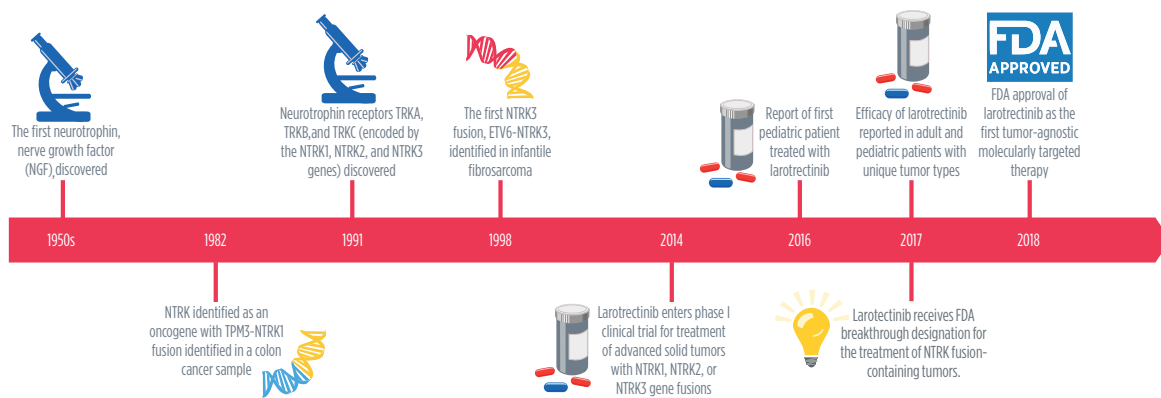


FIGURE 12

RESEARCH MILESTONES ON THE ROAD TO DEVELOPING LAROTRECTINIB



Larotrectinib (Vitrakvi) is the first molecularly targeted therapeutic to be approved by the FDA for use in a tissue-agnostic way. Since its November 2018 approval, larotrectinib has been benefiting children and adults who have solid tumors that test positive for the NTRK gene-fusion biomarker. Decades of basic, translational, and clinical research paved the way for the landmark approval of larotrectinib, starting with the seminal identification of the first neurotrophin, nerve growth factor, in the 1950s. Other basic research milestones on the way

to the FDA approval are the identification of the neurotrophin receptor proteins, TRKA, TRKB, and TRKC, and the genes that encode these proteins, NTRK1, NTRK2, and NTRK3, and the discovery that NTRK fusion genes and proteins fuel the growth of a wide array of cancer types that occur in adults and children. Together, this body of research led to the development of larotrectinib, which targets TRKA, TRKB, and TRKC, and its testing in basket clinical trials involving patients who have cancers driven by an NTRK gene fusion.