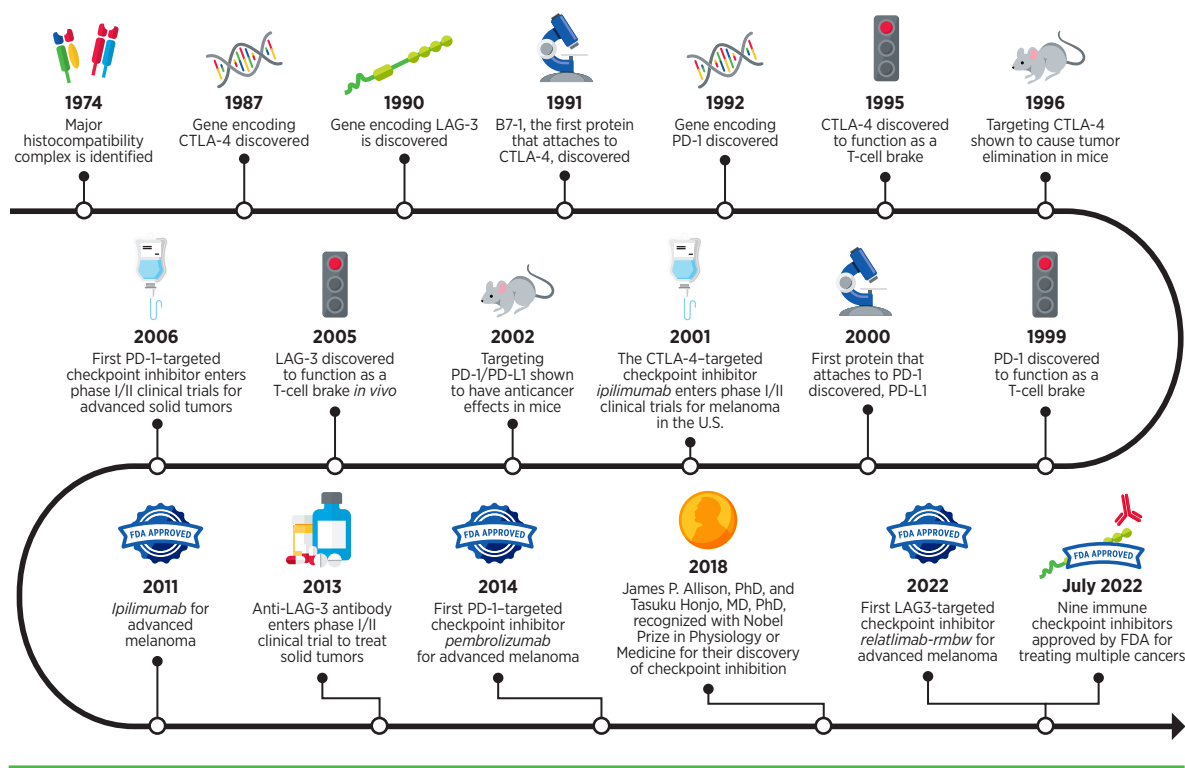


FIGURE 11

Decades of Breakthroughs Along the Way to Developing Immune Checkpoint Inhibitors



Immune checkpoint inhibitors (ICIs) are cancer immunotherapeutics that work by releasing “brakes” called immune checkpoint (IC) proteins on the surface of cancer-fighting immune cells called T cells. Decades of rapid advances in basic and clinical research led to the approval of the first ICI, *ipilimumab* (Yervoy), by the U.S. Food and Drug Administration (FDA) in March 2011. *Ipilimumab* targets an IC protein on T cells called CTLA-4. Several other ICIs target a second immune checkpoint protein called PD-1. The first of these immunotherapeutics approved by FDA was *pembrolizumab* (Keytruda) in September 2014, and

dostarlimab-gxly—the newest member of this class of immunotherapeutics—was approved in April 2021. In March 2022, FDA approved a new ICI targeting a different IC protein, LAG-3. Other basic research milestones along the way to the FDA approvals include the identification of the brake function of CTLA-4, PD-1, and LAG-3, identification of the proteins that attach to and trigger the brake function of CTLA-4, PD-1, and LAG-3, and the demonstration that immunotherapeutics targeting these brakes can protect them from being triggered.