This led to the formulation of the "antiangiogenesis" therapeutic concept for treatment of tumors (Folkman 1971). The subsequent purification of VEGF-A and its cloning in 1989 (Leung et al. 1989) facilitated the discovery of bevacizumab, the first anti-VEGF-A antibody (Presta et al. 1997). Another example is the discovery of imatinib for the treatment of chronic myelogenous leukemia (CML) (Capdeville et al. 2002). A chromosomal abnormality, the "Philadelphia chromosome," was discovered in 1960 in white blood cells of patients with CML. In 1973 the Philadelphia chromosome was shown to be a translocation between chromosomes 9 and 22. A series of subsequent discoveries resulted 1985 in the insight that the chromosomal translocation leads to the expression of the BCR-Abl fusion protein and the hypothesis that its tyrosine kinase activity drives malignant transformation (Shtivelman et al. 1985). Imatinib was subsequently developed as an inhibitor of the BCR-Abl kinase. The pace in the advancement of such fundamental science for the discovery of drug targets has dramatically increased with the sequencing of the human genome and the establishment of next-generation sequencing technologies. Many recently approved drugs, in particular in the oncology field, are targeting proteins that have been identified through human genetic information. This includes the discovery of ibrutinib, an inhibitor of Bruton's tyrosine kinase for the treatment of B-cell lymphomas (Honigberg et al. 2010); vemurafenib, an inhibitor of the activating mutant $BRAF^{V600E}$ protein for melanoma (Sala et al. 2008); and the Janus kinase 1 and 2 inhibitor ruxolitinib for myeloproliferative neoplasms (Quintás-Cardama et al. 2010).

Pharmaceutical or small molecular weight tool compounds have similarly helped to study complex biological systems and allowed the identification and characterization of novel drug targets. One of many examples is the discovery and validation of phosphodiesterase four isoenzymes for the treatment of lung diseases using nonspecific and isoenzyme-specific inhibitors (Torphy and Undem 1991). This ultimately led to the discovery of roflumilast for the treatment of chronic obstructive pulmonary disease. Over the past decades, these pharmacological tools were more and more complemented with biological tools, in particular antibodies, to study the functional roles of secreted proteins and receptors in vitro and in vivo. Many of these biological tools were directly developed as therapeutics once the target characterization and validation studies proofed promising. A showcase is cytotoxic T-lymphocyte-associated protein-4 (CTLA-4), a member of the immunoglobulin superfamily, which is expressed on the surface of T cells and transmits an inhibitory signal to these cells. The relevant scientific findings that define this target were made using specific monoclonal antibodies which block the binding to its ligands CD80 and CD86 on antigen-presenting cells thus leading to T-cell activation (Linsley et al. 1992) as well as with a CTLA4-IgG Fc fusion protein which binds to CD80 and CD86 and prevents T-cell activation (Linsley et al. 1991). The former has been developed as therapeutic for cancer immunotherapy (ipilimumab) and the latter for the treatment of rheumatoid arthritis (abatacept). Other important biological tools today are based on interference RNA (RNA_i) (Mohr et al. 2014) and CRISPR (clustered regularly interspaced short palindromic repeats) (Doudna and Charpentier 2014) technologies which allow specific gene expression silencing or even enable surgical genome editing, respectively.