Identifying effective therapies for the treatment of progressive forms of multiple sclerosis (MS) is a highly relevant priority and one of the greatest challenges for the global MS community. Better understanding of the mechanisms involved in progression of the disease, novel trial designs, drug repurposing strategies, and new models of collaboration may assist in identifying effective therapies. In this review, we discuss various therapies under study in phase II or III trials, including antioxidants (idebenone); tyrosine kinase inhibitors (masitinib); sphingosine receptor modulators (siponimod); monoclonal antibodies (anti-leucine-rich repeat and immunoglobulin-like domain containing neurite outgrowth inhibitor receptor-interacting protein-1, natalizumab, ocrelizumab, intrathecal rituximab); hematopoietic stem cell therapy; statins and other possible neuroprotective agents (amiloride, riluzole, fluoxetine, oxcarbazepine); lithium; phosphodiesterase inhibitors (ibudilast); hormone-based therapies (adrenocorticotropic hormone and erythropoietin); T-cell receptor peptide vaccine (NeuroVax); autologous T-cell immunotherapy (Tcelna); MIS416 (a microparticulate immune response modifier); dopamine antagonists (domperidone); and nutritional supplements, including lipoic acid, biotin, and sunphenon epigallocatechin-3-gallate (green tea extract). Given ongoing and planned clinical trial initiatives, and the largest ever focus of the global research
community on progressive MS, future prospects for developing targeted therapeutics aimed at reducing disability in progressive forms of MS appear promising.