Brexit and Trump are radically changing the economic landscape over the coming years, generating more uncertainty in the world economy and, among others, making it more difficult for Italy to go back to healthy economic growth. To this end, the main challenges lie in redressing public finances and boosting innovation across enterprises. Given the current mix of relatively high level of taxation and public debt, low productivity, EMU policy constraints and long standing economic stagnation, there is no alternative to restructuring public expenditure, lowering taxation and expenses, and raising competitiveness by heightening private and public investment, research activities linked to innovation, and productivity. This task cannot be carried out but by evaluating to scale down all expenditure commitments in the budget, including pensions and other social entitlements, as both no longer appear to be sustainable in the context of prolonged recession since 2008 and dim prospects. The feasibility of such a radical approach to a poorly treated economic malaise is contingent on structural reforms, also affecting basic laws. Spurring R&I across most firms is a stepping stone towards economic renewal, as current conditions show a widening gap with respect to partner countries in several fields that are crucial for productivity and growth. Innovation policy in this decade has failed to address the many impediments for most firms, i.e. the SMEs, to become more innovative and competitive, thereby lowering growth potential. Major failures in innovation are in creating a system involving all stakeholders from new-knowledge sources to financiers, drawing a strategy to this end and implementing support measures with continuity and adequate resources. Only lately this approach has been adopted by launching Industry 4.0 program, but still some improvements should be introduced to make it effective.