Mobile group II introns are bacterial mobile genetic elements that are thought to be evolutionary ancestors of spliceosomal introns, LINE elements, retroviruses, and telomerase in higher organisms. They consist of an autocatalytic intron RNA (a “ribozyme”) and intron-encoded reverse transcriptase, which function together to promote intron mobility to new DNA sites. During their evolution as mobile genetic elements, mobile group II introns acquired novel activities that we have adapted for biotechnological applications, first as gene targeting vectors (“targetrons”) and more recently as a source of thermostable group II intron reverse transcriptases (TGIRTs). TGIRTs have novel activities that open new approaches for next-generation RNA sequencing (RNA-seq), analysis of non-coding RNAs, and RNA-based diagnostics. In recent work, TGIRT-seq of extracellular RNAs in one-ml of human plasma identified RNAs representing a substantial proportion of the human transcriptome, including miRNAs and other ncRNAs that cannot be analyzed readily by conventional reverse transcriptases.