(113 protocols) of all gene transfer clinical trials worldwide have used some kind of lipid/DNA complexes [3, 4]. For instance, an adjuvant cationic liposome–DNA complex (CLDC) platform (JVRX-100, formulated with noncoding plasmid DNA [48, 49]) has been developed by Juvaris Biotherapeutics Inc., a Pleasanton, CA-based company, and is gaining momentum in cancer gene therapy [50]. Currently, a clinical study is recruiting for a phase I trial for patients with relapse or refractory leukemia [51].

While much attention in the field of gene therapy has been mainly focused on the development of more promising gene-based therapeutics in terms of highly efficient delivery vectors with reduced toxicity and increased stability *in vivo* [22, 23, 52, 53], surprisingly little attention has been paid to their physicochemical stability on a pharmaceutically relevant time scale (i.e., 18–24 months). Clearly, stable formulations must be developed as nucleic acid-based therapeutics moves from clinical trials to market approval. Indeed, a prominent challenge of preparing naked DNA and a suspension of lipid/DNA complexes as aqueous formulations is that they generally face physical and chemical instabilities during processing and storage [54–60]. It is acknowledged that prolonged storage of DNA and lipoplexes in aqueous formulations is difficult to achieve considering the high sensitivity of both DNA [61–64] and lipids [65–67] to hydrolytic and oxidative degradation. Furthermore, aqueous suspensions of nonviral vectors are known to aggregate over time [46, 68]. For instance, the high tendency of lipid/DNA complexes to aggregate in aqueous suspensions has prompted the use of these liposomal formulations within a short period of time after preparation [69, 70], and aggregation is further exacerbated in the highly concentrated suspensions prepared for clinical studies [71]. Additional stresses such as agitation and freeze-thawing can also contribute to lipid/DNA complex aggregation [72]. Accordingly, long-term storage of vector systems in suspensions presents crucial difficulties [55, 69, 72]. By analogy, it is well accepted that chemical degradation of DNA is enhanced in aqueous formulations (e.g., depurination [73], deamination [74], depyrimidination [75], and hydrolytic cleavage [76]), and researches in an attempt to inhibit acid-catalyzed degradation mechanisms during prolonged storage have formulated DNA at alkaline conditions (pH 8.5, [61]). However, oxidative damage (i.e., free-radical oxidation-induced chemical degradation) becomes a serious problem not only for DNA formulations (i.e., loss of supercoil (SC) content and base modification [61–63, 77, 78]) but also for those preparations containing a lipid component that is known to degrade rapidly under these conditions (i.e., lipid peroxidation, [65, 66, 79]). Alternatively, frozen formulations have been developed in order to prevent the aforementioned problems (reviewed by Anchordoquy et al., [80]). While recovery of biological activity and DNA integrity has been demonstrated for frozen formulations [60, 71, 72, 81], the maintenance of stable liquid and/or frozen nonviral formulations require formulation and cold storage conditions that limit their large-scale production, storage, as well as their distribution to some regions of the world [55, 69, 82]. Therefore, the development of dehydrated formulations represents an effective approach for stabilization of large standardized batches of DNA or lipid/DNA complexes that would be resistant to shipping stresses and offer the potential for prolonged storage at room temperature [55, 83, 84]. In fact, there has been