others have failed to demonstrate the presence of BVDV p7 in particles.[328] Other economically important animal viruses, such as the avian CoV infectious bronchitis virus, are also likely to encode viroporins, yet these are not yet characterised. However, although showing potential as drug targets, understanding of animal viroporins lags behind those of mammalian viruses with the exception of M2, making it unlikely that these will be exploited in the near future.

9.6 Conclusion and Future Perspectives: How Can Viroporin Inhibitors Fit into Modern Clinical Drug Discovery Scenarios?

The spectre of amantadine and rimantadine in the treatment of influenza represents a double-edged sword when proposing viroporins as targets for modern-day drug development. Although providing a precedent that such a strategy can be deployed in a clinical setting, their relatively poor potency combined with resistance issues (likely linked to application as monotherapies) has led to a perception that viroporin-targeted programmes will not generate effective antivirals. Moreover, this has been compounded by inappropriate application of both adamantanes and imino sugars during HCV trials. However, this flies in the face of successful drugs developed targeting cellular ion channels, which have been critical for cardiac medicine, *etc*. Few other scenarios exist where application of an extremely limited chemical toolbox to poorly characterised proteins encoded by diverse and highly variable viruses has led to such dismissive attitudes. Clearly, characterisation of membrane channels is technically challenging and investigators must start somewhere, yet preliminary, often disappointing, results of studies using prototype viroporin inhibitors should be interpreted with appropriate caveats when assessing their viability as targets.

The commonly employed tools of inhibitor discovery are often not forthcoming in the case of viroporins, namely robust protein production and screening assays, atomic structures and defined SARs based on medicinal chemistry and drug resistance mutations. In addition, the primitive nature of some viroporins often excludes approaches used to characterise cellular ion channels, where ion specificity and gating are usually far more selective. However, recent progress in some fields is beginning to bring these proteins into the drug discovery spotlight. Most notable, of course, is M2, where decades of research have culminated in atomic structures of the protein within membranes that represent ideal templates for drug design. M2 also represents a unique scenario where resistance is already commonplace amongst clinically relevant viruses, necessitating the search for novel compounds to overcome such mutations which will likely be chemically distinct from adamantane prototypes. The ongoing controversy surrounding adamantane binding to these channels merely serves to illustrate the need for improved inhibitors. Structural studies are also ongoing for many other viroporins, including HCV p7, HIV-1 Vpu,