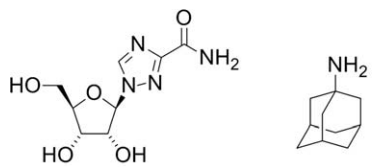
facilities.[7] Immunocompromised patients, especially lung transplant and bone marrow transplant patients, are a third, small, but significant patient population, with high mortality rates due to RSV-related complications.[8]

Despite the burden on the healthcare system in the developed world and the high mortality rates in certain high-risk groups, there is no treatment for RSV infection. Ribavirin (**1**, Scheme 2.1) was approved by the US Food and Drug Administration (FDA) but is rarely used owing to marginal efficacy and side effects for both patient and caregiver. Immunoprophylaxis against RSV infections with palivizumab (Synaggis) is only moderately effective and reserved for the highest risk preterm infants and those with conditions such as chronic lung disease and congenital heart disease due to the high cost of treatment. A cheap, effective and convenient RSV vaccine has not materialized yet and prospects seem rather slim after an early clinical trial with a formalin-inactivated RSV that exacerbated the disease course. Furthermore, the immune response that results after natural infection is modest and not highly protective, so multiple infections of the same individual within the same season have been reported.[9]

RSV is an enveloped virus with a negative single-strand RNA genome. The virus belongs to the family Paramyxoviridae that includes some other important respiratory pathogens such as parainfluenza virus and the closely related human metapneumovirus. RSV encodes for 11 proteins, including three surface glycoproteins (F, G and SH) and several proteins that comprise the viral RNA polymerase complex (N, P, L and M2-1). It replicates effectively in the upper and lower respiratory tract and can cause respiratory symptoms by directly damaging the integrity of the small airway epithelium and indirectly by inducing strong immune responses in lungs that lead to airway obstruction. Two major antigenic subgroups of RSV are known, RSV A and RSV B, that differ primarily in the genetic sequence of the G glycoprotein while maintaining a higher degree of homology across other parts of the genome. Both subgroups show comparable pathogenicity and can co-circulate in the same community during a seasonal epidemic, but their individual prevalence usually varies from season to season. A clinically effective RSV therapeutic therefore requires efficacy across a broad range of diverse isolates from both subgroups. Small molecule inhibitors identified to date, that are active against both subgroups,



Compound **1** Compound **2**

Scheme 2.1 Structures of ribavirin (**1**) and amantadine (**2**).