#### а

ABT-667, chemical structure 367 ABT-675 366-367 - inhibitor potency and oral bioavailability 367 acquired immunodeficiency syndrome (AIDS) - HIV as causative agent 51-52 - manageable chronic disease 73 - RNAi gene therapy 338-339 acute respiratory syncytial virus infection 337 ACV see acyclovir acyclic nucleoside phosphonates (ANPs) 231 - antiviral activity spectrum 96 - antiviral drugs 95 - human cytomegalovirus DNA polymerase inhibitor 244 - main classes 95-99 acyclic nucleoside phosphonates, oral prodrugs 189-198 acyclovir (ACV) 229 mechanism of action 232 adamantanamine-based M2 ion channel protein inhibitors, influenza treatment 352-353 adefovir see also acyclic nucleoside phosphonates - acyclic nucleoside phosphonates 95-97 - hepatitis B virus and HIV 11, 97-99 adefovir derivative, as prodrug of nucleoside phosphonates 197-198 adefovir dipivoxil, clinical application of nucleoside phosphonate 112-113 adenovirus acyclic nucleoside phosphonates 95–96, 191, 193, 195 - antiviral drugs 13 AIDS see acquired immunodeficiency syndrome

alkoxyalkyl ester of nucleoside 5'-monophosphates, prodrugs 185-189 alkoxyalkyl ester prodrugs - of nucleoside phosphates 185-189 - of nucleoside phosphonates 181-185 - of phosphonoformate 185 alkoxyalkyl esters - of (S)-HPMPA 191-196 - of tenofovir (HDP-(R)-PMPA) 196-197 alkylglycerol prodrugs, of phosphonoformate 185 alphaherpesviruses see herpes simplex virus; varicella zoster virus amantadine, influenza treatment 352-353 ambiguous base pairing, 5-aza-5,6-dihydro-2'-deoxycytidine 292-293 2-amino-7-[(1,3-dihydroxy-2-propoxy)methyl] purine (S2242), human cytomegalovirus DNA polymerase inhibitor 238–239 amphipathic DNA polymers, human cytomegalovirus entry inhibitor 237 amprenavir - brand name and manufacturer 5 - chemical structure 76 - comparison to darunavir 85-86 - discovery 3, 77-78 - HIV protease inhibitor 80 - in vitro resistance selection experiment 83-85 amprenavir monophosphate (fosamprenavir), amprenavir replacement 78 ANPs see acyclic nucleoside phosphonates antagonists - CCR5 38-40 - CXCR4 40-41 anti-cytomegalovirus agents see also anti-human cytomegalovirus compounds

– maribavir 209–221

391

- overview 209-210 anti-HIV drugs - lethal mutagenesis 283-284 - resistance 283, 295-296 anti-HIV evaluation 377 anti-human cytomegalovirus compounds 227-265 novel viral targets 235–260 anti-human cytomegalovirus drugs - classes 229-231 - clinical use 229-234 - need for new drugs 234-235 - prophylaxis and treatment 229 - resistance 233-234 - toxicity 231-233 anti-influenza agents, neuraminidase inhibitors 351-370 anti-influenza drugs 352 antiretroviral therapy, HIV 29, 52 see also highly active antiretroviral therapy antisense nucleotide, formivirsen 230 antiviral activities - benzimidazoles 1 - darunavir 81, 85-86 - iododeoxyuridine 1 - ribavirin 2 (see also ribavirin) - thiosemicarbazones 1 antiviral activity spectrum, of acyclic nucleoside phosphonates 96 antiviral compounds, oral activity 182-184 antiviral drug discoveries, milestones 3 antiviral drug era, overview and key events 1 - 4antiviral drugs against DNA viruses 13 - against hepatitis B virus 12 - against herpesviruses 4-8 - against retroviruses (HIV) 8-12 - alternatives 19 brand names 5–6 - first 1 (see also iododeoxyuridine) - for hepatitis C virus 15-17 - for influenza A virus infections 14 - 15- for poxviruses 17-18 - manufacturers 5-6 - milestones of discoveries 3 - resistance to (see drug-resistant mutations) antiviral RNAi, virus silencing 329-339 artemisinin 258 artesunate, human cytomegalovirus inhibitors 258, 260

2-aryl-2-hydroxyethylamine substituted 4-oxo-4.7-dihvdrothieno[2.3-b]pvridines. human cytomegalovirus DNA polymerase inhibitor 240 arylsulfone derivatives, human cytomegalovirus inhibitors 257-259 5-azacytidine (5AZC) - mechanism of action 291 - mutagenic HIV pharmaceutical 291-292 5-aza-5,6-dihydro-2'-deoxycytidine (KP-1212) - development 292-294 - mechanism of action 292 - mitochondrial toxicity 293 AZT see also zidovudine - brand name and manufacturer 5 – chemical structure 9 - enhancement of prodrugs 185

## b

BAY 38-4766 see phenylenediamine sulphonamides BCX-1812 see peramivir BDCRB see 2-bromo-5,6-dichloro-1-(β-Dribofuranosyl)benzimidazole benzimidavir, benzimidazole ribosides see maribavir benzimidazole compounds, anticytomegalovirus activity 210 benzimidazole ribonucleoside. maribavir 209-221 benzimidazole ribosides, human cytomegalovirus replication inhibitors 250-252 benzimidazoles, antiviral activity 1 4'-benzoyl-ureido-TSAO derivatives, human cytomegalovirus inhibitors 258-259 1-benzyloxycarbonylazetidines 250 berberine chloride, human cytomegalovirus inhibitors 257-259 bioavailability, oral 107-111 bioisosteres – cyclic nucleoside phosphonates 99-101 - nucleoside phosphonates 92 biological weapon, smallpox (variola virus) 17, 189 boceprevir 320-321 - binding to NS3 protease variants 316-318 brand names, antiviral drugs 5-6 (2-bromo-5,6-dichloro-1-(β-D-pyranosyl) benzimidazole) (GW275175X), cytomegalovirus inhibitor 210

2-bromo-5,6-dichloro-1-β-D-ribofuranosyl benzimidazole (BDCRB), human cytomegalovirus replication inhibitors 210, 252

#### С

caliciviridae, targeted by RNAi 333 carbocyclic nucleoside phosphonates, cyclic nucleoside phosphonates 105 CCR5 antagonists - HIV entry 38-40 - resistance to 39-40 CDK see cyclin-dependent kinase CDV see cidofovir chain terminators see also delayed chain terminators - blocking of viral replication 94 - 2-C-methylsubstituted ribonucleosides 4, 15 - 2',3'-dideoxynucleoside analogues 9 – entecavir 12 - obligatory and delayed 94 – RNA 105 chemokine receptors agonist, human cytomegalovirus-encoded receptors 256-258 chemotherapy era, antiviral 1 2-chloro-3pyridin-3-yl-5,6,7,8tetrahydroindolizine-1-carboxamide (CMV423), human cytomegalovirus inhibitors 258 8-chloro-TIBO (R86183) 378 cHPMP-5-azaC see cyclo-1-(3-hydroxy-2phosphonylmethoxypropyl)-5-azacytosine (cHPMP-5-azaC) chronic hepatitis C 307 cidofovir (CDV) 229-230 - alkoxyalkyl ester derivatives 244 - anti-cytomegalovirus agent 209 - broad-spectrum activity 231 - clinical application of nucleoside phosphonate 112 - Epstein-Barr virus 190 - human cytomegalovirus retinitis 231 - mechanism of action 231-232 - molluscivirus 112 - other double-stranded DNA viruses 190-191 – papillomavirus 112 - poxviruses 189-190 - toxicity 233 ciluprevir, hepatitis C virus 4 clinical applications, nucleoside phosphonates 111-115

clinical development - cyclophilin inhibitors 148, 149 - darunavir 86-87 clinical results in hepatitis C virus, cyclophilins 159-167 2-C-methylsubstituted ribonucleosides, chain terminators 4, 15 CMV see cytomegalovirus CMV423 see 2-chloro-3pyridin-3-yl-5,6,7,8tetrahydroindolizine-1-carboxamide CNPs see cyclic nucleoside phosphonates combination drug strategy, prevention of drug resistance 19-20 congenital cytomegalovirus see human cytomegalovirus congenital human cytomegalovirus infection 228-229 coreceptors, virus tropism and infectivity 33 coronaviridae, targeted by RNAi 333 covalent linear hepatitis C virus protease inhibitors - chemical structures 311 - enzyme-inhibitor interaction kinetics 311 - log octanol/water partition coefficient 311 - mechanism of action 310 - molecular weights 311 - pattern of resistance 316-318 - polar surface area 311 covalent linear protease inhibitors, resistance 316-318 cowpox - acyclic nucleoside phosphonates 190-194 - antiviral drugs 17-18 COX-2 see cyclooxygenase-2 CS-8958 see laninamivir CsA see cyclosporin A CXCR4 antagonists, HIV entry 40-41 cyclic nucleoside phosphonates (CNPs) - antiviral drugs 99 - examples of targeting viral RNA polymerases 104-107 - main classes 100-104 - oral prodrugs 189-198 cyclin-dependent kinase (CDK) 261 cyclin-dependent kinases inhibitors, human cytomegalovirus 261-262 cyclo-1-(3-hydroxy-2phosphonylmethoxypropyl)-5-aza-cytosine (cHPMP-5-azaC), human cytomegalovirus DNA polymerase inhibitor 241, 245 cyclooxygenase-2 (COX-2) 263 cyclooxygenase-2 inhibitors, human cytomegalovirus 262-263

cyclopentane and cyclopentene core phosphonates, cyclic nucleoside phosphonates 103-104 cyclophilin inhibitors – against HIV-1 151–152 - currently in clinical development 148, 149 - generation 168-169 - new noncyclosporine species 168 cyclophilins see also cyclosporin A activity against other viruses 167 - clinical results in hepatitis C virus 159-167 - hepatitis C virus 155-159 - HIV treatment 149-155 - overview 148 cyclopropavir, human cytomegalovirus DNA polymerase inhibitor 239-242 cyclosporin A, immunosuppression 147 cyps see cyclophilins cytomegalovirus (CMV) see also human cytomegalovirus – 2-bromo-5,6-dichloro-1-(β-D-ribofuranosyl) benzimidazole (BDCRB) 210 - chemical classes of inhibitors 210-211 - diseases 210, 215-220 - drugs 209-210 - inhibition of DNA maturation process and encapsidation 210 - inhibition of DNA polymerase 210 - inhibition of protein kinase pUL97 211 – (2,5,6-trichloro-1-(β-D-ribofuranosyl) benzimidazole (TCRB) 210 – unmet challenges 209–210 cytomegalovirus retinitis see also human cytomegalovirus retinitis - AIDS patients 227 - intraocular delivery 198-201 - maribavir treatment 214 - under highly active antiretroviral therapy (HAART) 217 Cytovene<sup>®</sup> see ganciclovir d DAA drugs see direct acting antiviral drugs DANA see 2-deoxy-2,3-didehydro-Nacetylneuraminic acid

dapivirine (R147681, TMC120) 380 DAPY see diarylpyrimidine darunavir – antiviral activities 81, 85–86 – brand name and manufacturer 5 – chemical structure 10, 76 – clinical development 86–87 – enfuvirtide 41

- hydroxyethylene scaffold 11

- ribbon structure of HIV-1 protease 79 - synthesis scheme 84 DATA see diaryltriazine delayed chain terminators see also chain terminators blocking of viral replication 94 dendrimers, human cytomegalovirus entry inhibitor 235-237 dengue virus, antiviral drugs 19 2-deoxy-2,3-didehydro-N-acetylneuraminic acid (DANA) – carbocyclic analogues 360–361 - carbocyclic scaffold 359 - inhibitor activity 356 deoxycytidine analogues - 5-aza-5,6-dihydro-2'-deoxycytidine 292 - 5-Hydroxy-2'-deoxycytidine 290-291 deoxyguanosine analogue, ganciclovir 229 deoxyribose nucleosides, lethal mutagens 287 diarylpyrimidine (DAPY) - analogues 381 - chemical structure 380 diaryltriazine (DATA) - analogues 381 - chemical structure 380 5,6-dichloro-1-β-D-ribofuranosyl benzimidazole (DRB), influenza virus multiplication 1 dideoxyfuranopyrimidines, human cytomegalovirus inhibitors 257-259 2',3'-dideoxynucleoside analogues, chain terminators 9 dihydroquinazolinyl-acetic acids, human cytomegalovirus replication inhibitors 252 diketo acids, HIV integrase inhibitors 4.12 direct acting antiviral (DAA) drugs 319 DNA binding inhibitors, HIV 59-60 DNA binding molecules, HIV 60 DNA cleavage inhibition, human cytomegalovirus 248-252 DNA packaging inhibition, human cytomegalovirus 248-252 DNA polymerase inhibitors - aciclovir 232 - cidovir 231 - ganciclovir 229 human cytomegalovirus 238–244 human cytomegalovirus diseases 232

– nucleoside analogues 238–242

- nucleotide analogues 244-245 DNA viruses see also adenovirus; Epstein-Barr virus; human herpesvirus type 6; mollusciviruses; papillomavirus; parapoxviruses; polyomavirus; poxviridae - antiviral drugs 13 - cidofovir 231 inhibition with nucleoside phosphonates 91 - miRNAs 332 DRB see 5,6-dichloro-1-ß- ribofuranosyl benzimidazole drug design - hepatitis C virus protease 310 - oseltamivir 359-364 - peramivir 366 structure-based (see structure-based drug) design) drug development see antiviral drugs drug-resistant mutations - helicase-primase inhibitors 142 - hepatitis C virus 158 - herpes simplex virus 95, 135-141 - HIV 19, 29, 41, 52, 77, 80, 151, 152 drugs see antiviral drugs

## е

EBV see Epstein-Barr virus elvitegravir - chemical structure 10 - discovery 3 - HIV integrase inhibitor 4, 12, 55-57.64 - integrase strand transfer inhibitor 57 endocytosis, HIV 33 enfuvirtide - brand name and manufacturer 5 - chemical structure 35 - discovery 3 - HIV treatment 11 - inhibitors of HIV fusion 41-42 interaction with other drugs 152 - protease inhibitors 41 entecavir, chain terminators 12 enterovirus, targeted by RNAi 333 entry inhibition, human cytomegalovirus 235-238 Epstein-Barr virus (EBV) - acyclic nucleoside phosphonates 191 - adefovir 97 - antiviral drugs 13 - cidofovir 190 error-prone replication, lethal mutagenesis 286-288

esterification, of alkoxyalkyl compounds 182–184 etravirine (R165335, TMC125), development 380 eye infection 198–201 – herpes simplex virus 1–2

# f

filoviridae, targeted by RNAi 333 flaviviridae, targeted by RNAi 333 flaviviruses see also hepatitis C virus - dengue virus 19 - west nile virus 15 - vellow fever 15 flavopiridol, cyclin-dependent kinases inhibitor 262 1-(3-fluoro-2-phosphonylmethoxypropyl) (FPMP) analogues, acyclic nucleoside phosphonates 97-98 FMDV see foot-and-mouth disease virus fomivirsen - chemical structure 230 - human cytomegalovirus infection 229 - mechanism of action 231 foot-and-mouth disease virus (FMDV), ribavirin 290 fosamprenavir, amprenavir monophosphate 78 foscarnet (FOS) - chemical structure 230 - human cytomegalovirus infection 229 - mechanism of action 231 - toxicity 233 foscarnet (PFA), anti-cytomegalovirus agent 209 Foscavir<sup>®</sup> see foscarnet FPMP see 1-(3-fluoro-2phosphonylmethoxypropyl)

## g

ganciclovir (GCV)
- anti-cytomegalovirus agent 209
- chemical structure 230
- human cytomegalovirus infection 229
- mechanism of action 229, 232
- resistance 232–233
- toxicity 231, 233
gefinitib 250
gene expression inhibitors, human cytomegalovirus 248
gene knockdown, RNA interference 329
gene silencing, RNA interference 329
generic names, antiviral drugs 5–6

genome replication inhibitors, human cytomegalovirus 238-248 glycoproteins, HIV see HIV-1 glycoproteins gp41, HIV-1 glycoprotein 31-32 gp120 - HIV-1 glycoprotein 30-31 - inhibition of CD4 interaction 36 GPCRs see G-protein-coupled receptors G-protein-coupled receptors (GPCRs), human cytomegalovirus 256 graft versus host disease (GvHD), human cytomegalovirus 228 GRID, neuraminidase inhibitor 355-358 GS4071 - C-3 side-chain analogues 362 - hydroxy, amino, and guanidino analogues 363 - inhibitor-active site interactions 361-362 - oral bioavailability 363 GS4104 see also oseltamivir – chemical structure 363 G-to-A hypermutations, HIV-1 285 guanosine analogues, ribavirin 289 GvHD see graft versus host disease GW1263W94, benzimidazole ribosides see maribavir GW275175X see (2-bromo-5,6-dichloro-1-(B-Dpyranosyl)benzimidazole) h

HA see hemagglutinin HAART see highly active antiretroviral therapy Hantaan virus, ribavirin 290 HBB, poliovirus and other enteroviruses see 2-(1-hydroxybenzyl)benzimidazole HBV see hepatitis B virus HCV see hepatitis C virus HDP-CDV see hexadecyloxypropyl-Cidofovir HDP-cidofovir nucleotide analogue prodrug, human cytomegalovirus 241 helicase inhibitors, human cytomegalovirus 245-246 helicase-primase complex - predicted structure 141 structure 130 helicase-primase inhibitors (HPIs) - cell culture and in vivo 133 - cross-resistance 136-139 – drug-resistant mutations 142 - frequency of mutation of herpesviruses 139-140 – helicase-primase complex 141 - inhibition of herpesvirus DNA 131-132, 134

- proposed mechanism of action 134-135 - replication of herpes simplex virus 130-131 - resistance of herpesviruses 135-136, 139-143 - resistance of herpesviruses (overview) 137 - varicella zoster virus 130-134 hemagglutinin (HA), influenza A viruses 351-352 hematopoietic stem cell transplant (HSCT), human cytomegalovirus infection 228 hepadnaviridae, targeted by RNAi 333 hepatitis B virus (HBV) - acyclic nucleoside phosphonates 196 - antiviral drugs 4, 6, 12, 15-17, 19-20, 109, 186 - clinical results of cyclophilin inhibitors 159-167 - coinfection 153 - cyclophilin inhibitors 155-158, 173 - esters of (S)-9-(3-hydroxy-2phosphonomethoxypropyl)-adenine 195 - genotype 1 162-166 - genotype 2 156-162 - genotypes 1-4 173 - inhibition by nucleoside phosphonates 91.115 - inhibition of polymerase 104-107 - nucleoside phosphonates 2, 92, 95, 97-99, 103, 107-109, 112-115, 193, 196-197 - nucleosides as antiviral drugs 181-182 - phosphatidyl-ddC 183 - protease inhibitors 3 - replication 148 - replication inhibition 4 tenofovir disoproxil fumarate 11 hepatitis C virus (HCV) - NS3·4A protease 308 - ribavirin 288-289 - therapy 307-316 hepatitis C virus genome - organization 308 - translation and polypeptide processing 308 hepatitis C virus genotype 1 - standard of care 307 - sustained viral response 307 hepatitis C virus protease - catalytic triad 315 - covalent linear, noncovalent linear, and noncovalent macrocyclic inhibitors bound to 315 - point mutations 316-318 – role of 308–310 hepatitis C virus protease inhibitors

- antiviral potency 316, 319-321 - classes 310 - clinical efficacy 319-321 - combination therapy 321 - design 310 - development 307-321 - emergence of resistance 316 - enzymatic mechanism of action 316 - future directions 321 - resistance 316-318 - roles 308 - similarities and differences 310-316 - threedimensional binding models 309-310 hepatitis C virus protease variants 317 N<sup>4</sup>-heptyloxycarbonyl-5,6-dihydro-5-aza-2'deoxycytidine (KP-1461), HIV treatment 292-294 hepsera see adefovir dipivoxil herpes simplex virus (HSV) - alphaherpesviruses 129 - antiviral drugs 4-8 - inhibitors (see helicase-primase inhibitors) - iododeoxvuridine 1 - latent infection 134 - resistance 135-142 herpes simplex virus infection, prophylaxis and treatment 209 herpesviridae - cytomegalovirus 209 - herpes simplex virus 209 - protein kinase inhibition 212 – targeted by RNAi 333 herpesvirus see also Epstein-Barr virus; herpes simplex virus; human herpesvirus type 6; varicella zoster virus - antiviral drugs 4-8 - maturation 248, 256 - replicative cycle 264 - resistance 135-142 2-(hexadecyloxy)ethyl ester of cHPMP-5-azaC, human cytomegalovirus 241 hexadecyloxypropyl adefovir, as prodrug of nucleoside phosphonates 197-198 hexadecyloxypropyl-cidofovir (HDP-CDV) - anti-cytomegalovirus agent 209 - human cytomegalovirus DNA polymerase inhibitor 244 HHV-5 see human herpesvirus 5 HHV-6 see human herpesvirus type 6 highly active antiretroviral therapy (HAART) - combination of drugs 29 - cytomegalovirus retinitis desease 217 - HIV-1 integrase 55-57 - human cytomegalovirus retinitis 227-228

- protease inhibitors 52, 75, 87 – treatment of HIV 52 HIV - antiretroviral therapy 52 (see also highly active antiretroviral therapy) - antiviral drugs 8-12 - integrase (see HIV-1 integrase) - lethal mutagenesis 283-297 - mutagenic 5-Hydroxy-2'deoxycytidine 290-291 - mutation rates 285 nonsynonymous mutations 286 - replication cycle 51-52 HIV-1 - allosteric site for binding NNRTIs 379 - cytomegalovirus retinitis desease treatment 214-217 - G-to-A hypermutations 285 - lethal mutagenesis 286-288 - mutagenic 5-Azacytidine 291-292 - mutagenic 5-Hydroxy-2'-deoxycytidine 291 - mutagenic deoxyribonucleosides 286-287 - mutagenic ribonucleosides 286-288 - mutation rates 285-286 - RNAi gene therapy 338-339 HIV DNA binding, inhibition 59-60 HIV entry - inhibition 34-42 - mechanism 32-33 HIV fusion, inhibitors 41-42 HIV-1 glycoproteins - structure of gp120 30-31 - structure of transmembrane gp41 31-32 HIV IN see HIV-1 integrase HIV inhibitation - cyclophilin 151-155 - DNA binding 59-60 - integrase (see HIV integrase inhibitors) - multimerization 60-62 HIV integrase - catalysis 53 - inhibition (see HIV integrase inhibitors) HIV-1 integrase (HIV IN) - as a target for HAART 55-57 - cofactor interactions 62-64 - enzymatic mechanism of the integration reaction 53 - mechanism of integration 53-54 - strand transfer reaction 12 - structural organization 54-55 HIV integrase inhibitors - diketo acid group 4, 12

- elvitegravir (see elvitegravir)
- first (see raltegravir)

- integrase binding 57-59 - integrase cofactor interactions 62-64 - integration step 53-59 - raltegravir 41 (see also raltegravir) - strand transfer 55-57 HIV integration reaction, enzymatic mechanism 53-59 see also HIV integrase inhibitors HIV multimerization, inhibition 60-62 HIV-1 replication, inhibitor 378 HIV-1 reverse transcriptase – fidelity 285 - mutation rate increasing 286-287 - role in the replication cycle 379 - TIBO binding site 378 HIV protease, as target for AIDS 73-74 HIV treatment, N4-heptyloxycarbonyl-5,6dihydro-5-aza-2'-deoxycytidine 292-294 HIV treatment drug classes - chemokine receptor antagonist 73 - entry and fusion inhibitor (see HIV entry) - integrase inhibitors (see HIV integrase inhibitors) nonnucleoside reverse transcriptase inhibitors (see reverse transcriptase) - nucleoside/nucleotide reverse transcriptase inhibitors (see nucleoside phosphonates) - overview 29, 73 - protease inhibitors (see protease inhibitors) host kinases, nucleoside phosphonates 92-94 host mechanisms, as target for antiviral drugs 147 HPIs see helicase-primase inhibitors HPMP see (S)-1-(3-hydroxy-2phosphonylmethoxypropyl) HPMP-5-azaC see (S)-1-(3-hydroxy-2phosphonylmethoxypropyl)-5-aza-cytosine HPMPA see (S)-9-(3-hydroxy-2phosphonomethoxypropyl)-adenine HPMPC see (S)-1-(3-hydroxy-2phosphonylmethoxypropyl)cytosine HSCT see hematopoietic stem cell transplant HSV see herpes simplex virus HTLV-III/LAV 377 see also HIV-1 human cytomegalovirus (HCMV) see also cytomegalovirus - antiviral drugs 229-234 – cellular targets inhibitors 260–265 - chemokine receptors agonist 256-258 – cyclin-dependent kinases inhibitors 261-262 - cyclooxygenase 2 inhibitors 262-263

- diseases 227-229 - DNA polymerase 246 - DNA polymerase inhibitors 238-245 - DNA replication 247-248 - gene expression inhibitors 248 - infection prophylaxis after transplantation 228-229 - infections (see specific infections) - inhibitors of viral genome replication 238-248 - inhibitors of virion assembly and egress 248-256 - inhibitors with a mechanism of action not fully unraveled 258-260 - manifestation of infection 227-228 - new inhibitors 256-258 - novel drug targets and strategies 264 - novel viral targets 235-260 - protease inhibitors 250, 256 - proteasome inhibitors 263-265 - protein kinase pUL97 229-230, 253 - replication inhibition 238-248 - viral entry inhibitors 235-238 - viral genome replication inhibitors 238-248 virion assembly and egress 248–256 human cytomegalovirus retinitis 227-228 see also cytomegalovirus retinitis - cidofovir 231 - fomivirsen 231 human herpesvirus 5 (HHV-5) see cytomegalovirus; human cytomegalovirus human herpesvirus type 6 (HHV-6) acyclic nucleoside analogue 238–240 - antiviral drugs 13 - human cytomegalovirus inhibitors 258 - nonnucleoside Analogues 243 - nucleotide Analogues 244 - phosphorothioated oligonucleotides 237 human immunodeficiency virus see HIV; retroviruses 2-(1-hydroxybenzyl)benzimidazole (HBB) 1 5-hydroxy-2'-deoxycytidine (5-OH-dC), mutagenic HIV pharmaceutical 290-291 hydroxyethylene scaffold, protease inhibitors 11 (S)-9-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), acyclic nucleoside phosphonates 95 (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl) (HPMP), acyclic nucleoside phosphonates 95 (S)-1-(3-hydroxy-2-

phosphonylmethoxypropyl)-5-aza-cytosine

(HPMP-5-azaC), human cytomegalovirus DNA polymerase inhibitor 241, 245

 (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl) cytosine (HPMPC) see also cidofovir
 human cytomegalovirus DNA polymerase

inhibitor 245 hypermutations, G-to-A 285

#### i

IDU see iododeoxyuridine imidazolylpyrimidines, human cytomegalovirus helicase/primase complex inhibitor 245-246 imidoylthiourea (ITU) - analogues 381 - chemical structure 380 immunocompromised patients, cytomegalovirus diseases 227 immunosuppression, cyclosporin A 147 IMPDH see inosine 5'-monophosphate dehydrogenase INBI see integrase binding inhibitors indolocarbazoles, human cytomegalovirus protein kinase inhibitors 250, 255 influenza, pandemics 351 influenza A infection 14-15 influenza neuraminidase, as a drug target 353-354 influenza neuraminidase inhibitors, resistance 368-369 influenza strain H1N1, neuraminidase inhibitors treatment 368-370 influenza strain H5N1, oseltamivir treatment 368 influenza vaccines 352 influenza virus - antiviral drugs 14-15 - parainfluenza 106 - research interest 143 - types and subtypes 351-352 – zanamivir 198 influenza virus multiplication, 5,6-dichloro-1β-D-ribofuranosyl benzimidazole 1 inhaled neuraminidase inhibitors 358-359 inosine 5'-monophosphate dehydrogenase (IMPDH), inhibition 288-289 INSTI see integrase strand transfer inhibitors integrase binding inhibitors, HIV 57-59 integrase cofactor interactions, HIV 62-64 integrase inhibitors, HIV see HIV integrase inhibitors integrase strand transfer inhibitors (INSTI),

HIV 55–57 *see also* HIV-1 Integrase; HIV integrase inhibitors

interferon cytokines, cyclophilins 155, 161, 173 intracellular metabolic pathways, nucleoside phosphonates 93 intraocular delivery, of antiviral prodrugs 198-201 intrinsic mutagenesis - retroviruses 284-286 - RNA viruses 284-286 iododeoxyuridine (IDU) - alphaherpesviruses 129 - discovery 3 - first antiviral drug 1 – herpes simplex virus 1–2 (2-isopropylamino-5,6-dichloro-1(β-Dribofuranosyl)benzimidazole (1263W94) see also maribavir

- cytomegalovirus inhibitor 210

ITU see imidoylthiourea

### k

KP-1212 see 5-aza-5,6-dihydro-2'-deoxycytidine KP-1461 see N<sup>4</sup>-heptyloxycarbonyl-5,6-dihydro-5-aza-2'-deoxycytidine

### I

laninamivir (CS-8958) 358-359 latency, of infection 134, 227 LBV see lobucavir leflunomide see also N-(4-trifluoromethylphenyl)-5methylisoxazole-4-carboxamide - human cytomegalovirus inhibitors 259-260 lethal mutagenesis - challenges and advantages 294-296 - fundamentals 286-288 - future perspectives 296-297 - HIV 283-297 - vs. conventional strategies (HIV) 294-296 lethal mutagens - deoxyribose nucleosides 287 - ribavirin 288-290 - ribonucleoside analogues 287 linear and macrocyclic HCV protease inhibitors, cross-resistance 318 lobucavir (LBV) - human cytomegalovirus DNA polymerase inhibitor 238 - structure 239

- lopinavir
- brand name and manufacturer 5
- chemical structure 76
- combination with ritonavir 77-78

comparison to darunavir 86
discovery 3
HIV protease inhibitor 80
loviride (R89439) 380–381

### m

mammalian viruses. RNAi mechanism 331-332 maraviroc, HIV treatment 38 maribavir see also benzimidazole ribosides - antiviral activity 210-212 - blood-brain barrier crossing 217 - clearance in animal species 215 - clinical development 215-217 - clinical phase I and II studies in treatment of cytomegalovirus retinitis desease 214-217 - clinical phase II study in prophylaxis of cytomegalovirus disease in transplant recipients 218 clinical phase III study with stem cell transplant recipients 218 - clinical studies phases I-III 254-255 - cytotoxicity in animal species 215 - failure of study with allogeneic stem cell transplant recipients 220 interactions with tacrolimus 219 - mechanism of action 212-214, 252-253 - metabolism 214, 218-219 - oral bioavailability in animal studies 214 pivotal study in liver transplant recipients 218-220 - preclinical studies 214-215 prevention and treatment of cytomegalovirus diseases 209-221 prophylaxis of cytomegalovirus diseases 218-221 - renal transplant recipients 219 - resistance 212-214, 220 - role of P450 enzymes 218-219 - selectivity 213 structure 210–211 - toxicology in animal studies 214 - transplant population 218-220 - treatment of cytomegalovirus diseases 215-217 - UL97 protein kinase (pUL97) inhibitor 252-255 viral protein kinase inhibition 212–213 maribavir pharmacokinetics - cytomegalovirus retinitis desease 216 – effect of hepatic impairment 218–219 - effect of renal impairment 219 mechanistic classes of HIV treatment drugs

- chemokine receptor antagonist 73 - entry and fusion inhibitor (see HIV entry) - integrase inhibitors (see HIV integrase inhibitors) - nonnucleoside reverse transcriptase inhibitors (see reverse transcriptase) nucleoside/nucleotide reverse transcriptase inhibitors (see nucleoside phosphonates) - overview 29, 73 - protease inhibitors (see protease inhibitors) metabolic pathways, nucleoside phosphonates 93 microRNA (miRNA), pathway 330-331 mollusciviruses - anti human cytomegalovirus 231 - antiviral drugs 13 - cidofovir 112 monkeypox - acyclic nucleoside phosphonates 99, 190 - antiviral drugs 17-18 Muller's ratchet 297 multimerization inhibitors, HIV 60-62 mutagenesis, lethal 286-288 see also lethal mutagenesis mutagenic deoxyribonucleosides, HIV-1 286-287 mutagenic pharmaceuticals - 5-azacytidine 291-292 5-Hydroxy-2'-deoxycytidine 290-291 - antiviral agents 288-292 - ribavirin 288-290 mutagenic ribonucleosides, HIV-1 incorporation 286-288 mutation rates - HIV 285-286 - RNA viruses 284 mutations - nonsynonymous 286 - viruses (see drug-resistant mutations) n NA see neuraminidase

NA see neuraminidase
narlaprevir, binding to NS3 protease
variants 316–318
Neu5Ac2en (DANA) see 2-deoxy-2,3-didehydro-N-acetylneuraminic acid
neuraminidase (NA) see also influenza neuraminidase
active site 354–355
aromatic inhibitors 364–365
crystal structure 354–355
cyclopentane-based inhibitors 364
influenza A viruses 351–352

- inhibitor binding 354-355

- oseltamivir-based inhibitors 364-365 - small-molecule inhibitors 355-364 - zanamivir-based inhibitors 364-365 neuraminidase active site, crystal structure 354-355 neuraminidase inhibitors 369 - ABT-675 366-367 - anti-influenza agents 351-370 - based on other scaffolds 364-367 - clinical use 367-369 - influenza 352-353 - inhaled (see inhaled neuraminidase inhibitors) - laninamivir 358-359 - oseltamivir 359-364 – peramivir 364–366 resistance 364 - zanamivir 355-358 nitropyrimidines, human cytomegalovirus helicase/primase complex inhibitor 245-246 NNRTIs see nonnucleoside reverse transcriptase inhibitors noncovalent linear hepatitis C virus protease inhibitors - chemical structures 312 – enzyme-inhibitor interaction kinetics 312 - log octanol/water partition coefficient 312 - molecular weights 312 - pattern of resistance 318 polar surface area 312 noncovalent macrocyclic hepatitis C virus protease inhibitors - chemical structures 313-314 - enzyme-inhibitor interaction kinetics 313-314 - log octanol/water partition coefficient 313-314 - molecular weights 313-314 - pattern of resistance and crossresistance 318 polar surface area 313–314 noncovalent protease inhibitors, resistance 318 noncyclosporine cyclophilin inhibitors, antiviral drugs 168-173 nonnucleoside analogues, human cytomegalovirus DNA polymerase inhibitor 240, 242-243 nonnucleoside antivirals 230 nonnucleoside inhibitors, phenylenediamine sulphonamides 248-251 nonnucleoside reverse transcriptase inhibitors (NNRTIs), HIV-1 377-379

NS3 protease 309-310 NS3 protease inhibitors, resistance and cross-resistance 316-318 NS3 protease variants, sensitivity to inhibitors 316-318 NS3-4A protease/helicase complex, threedimensional model 309-310 NS3-4A protease, hepatitis C virus 308-310 nucleoside 5'-monophosphates, prodrugs 185-189 nucleoside analogues - anti-cytomegalovirus drugs 209 - anti-HIV drug resistance 295-296 - antiviral activity 295 - ganciclovir 230 - human cytomegalovirus DNA polymerase inhibitor 238-243 - incorporation into HIV-1 genome 294 - mutagenic effects 288 nucleoside phosphonates - antiviral drugs (see acyclic nucleoside phosphonates; cyclic nucleoside phosphonates) - clinical applications 111-115 - examples 92 - metabolic pathways 93 - oral bioavailability 107-111 - prodrugs 107-111 (see also alkoxyalkyl ester prodrugs) - strategy for antiviral drugs 92-95 nucleotide analogues - cidovir 230 – human cytomegalovirus DNA polymerase inhibitor 241, 244-245 n

5-OH-dC see 5-hydroxy-2'-deoxycytidine oligodeoxyribonucleotides (ODNs), phosphorothioate-modified 237 olomoucine, cyclin-dependent kinases inhibitor 262 orf viruses - acyclic nucleoside phosphonates 191.195 - anti human cytomegalovirus 231 - antiviral drugs 13 orthomyxoviridae, targeted by RNAi 333 orthomyxoviruses see influenza virus orthopoxviruses see also smallpox studies of smallpox antivirals 191 oseltamivir - avian influenza strain H5N1 368 - chemical structure 353 - clinical use 367-368

- influenza treatment and prevention 352-353 - inhibitor design 359-364 - resistance 364, 368-369 oseltamivir (GS4104) 359-364 mechanism of resistance 364 4-oxo-1,4-dihydroquinoline (DHQ) carboxamides, human cytomegalovirus DNA polymerase inhibitor 240, 242 4-oxo-4,7-dihydrothieno[2,3-b]pyridine-5carboxamides, human cytomegalovirus DNA polymerase inhibitor 240, 243 7-oxo-4,7-dihydrothieno[3,2-b]pyridine-6carboxamides, human cytomegalovirus DNA polymerase inhibitor 240, 243 D papillomavirus - acyclic nucleoside phosphonates 95-97 – antiviral drugs 13 – cidofovir 112 – cyclosporin A and derivatives 167 - phosphonoamidates 110 papovaviridae, targeted by RNAi 333 parainfluenza, cyclic nucleoside phosphonates 106 paramyxoviridae, targeted by RNAi 333 parapoxviruses see also orf viruses – antiviral drugs 13 peptide aptamer technology 246-247 β-peptides 236 human cytomegalovirus entry inhibitor 235 peptides, generation of cyclophilin inhibitors 168-169 peptidyl-prolylisomerase, cyclophilins 168 peramivir (BCX-1812, RWJ-270201) 364-366 - inhibitor design 366 peramivir, chemical structure 366 PFA see phosphonoformic acid pharmacophores - antiviral drugs 7-8, 19 - cyclophilin inhibitors 171 - hepatitis C virus 15 - in antiretrovirus agents (overview) 9 – model 57 optimization and design of inhibitors 56-60 phenylenediamine sulphonamides (BAY 38-4766), human cytomegalovirus replication inhibitors 248-251

phosphonates, antiviral drugs see acyclic nucleoside phosphonates; cyclic nucleoside phosphonates; nucleoside phosphonates phosphonoamidates, as prodrugs of nucleoside phosphonates 107-111 phosphonoesters, as prodrugs of nucleoside phosphonates 107-109 phosphonoformic acid (PFA) 185 see also foscarnet 9-(2-phosphonylmethoxyethyl)adenine (PMEA), acyclic nucleoside phosphonates 95-97 9-(2-phosphonylmethoxypropyl) (PMP) analogues, acyclic nucleoside phosphonates 97-98 phosphorothioate-modified oligonucleotides, human cytomegalovirus entry inhibitor 237-238 picornaviridae, targeted by RNAi 333 PIs see protease inhibitors plaque reduction assays 132-133 helicase-primase inhibitors 132–133, 141 PMEA see 9-(2-phosphonylmethoxyethyl) adenine PMP see 9-(2-phosphonylmethoxypropyl) point mutations, resistance to protease inhibitors 316-318 poliovirus, infection 1 polyanions, as inhibitors of HIV attachment 34-36 polymerase, hepatitis C virus 104-107 polyomavirus - acyclic nucleoside phosphonates 96 - antiviral drugs 13 portal proteins 252 postattachment inhibitors, HIV entry 37 posttranscriptional gene silencing (PTGS) 329 - mammals 331 poxviridae see also poxviruses; vaccinia virus; variola virus – antiviral drugs 13 poxviruses see also variola virus - acyclic nucleoside phosphonates 194 - antiviral drugs 17-18 - antiviral effects of cidofovir derivatives 190 – cidofovir derivatives 189–190 primase inhibitors, human cytomegalovirus 245-246 pro-140, HIV treatment 39 prodrugs - of nucleoside phosphates (see alkoxyalkyl (ester) prodrugs)

- of nucleoside phosphonates (see alkoxyalkyl (ester) prodrugs) - of phosphonoformate (see alkoxyalkyl (ester) prodrugs) - oral 189-198 protease – HIV 73–74 - viral target for HIV therapy 29-30 protease inhibitors (PIs) - amprenavir (see amprenavir) - darunavir (see darunavir) - early developments 74-78 - first 2, 75 (see also saquinavir) – hepatitis C virus 3 - highly active antiretroviral therapy 52, 75, 87 - HIV 73-74 - human cytomegalovirus 250, 256 - hydroxyethylene scaffold 11 - lopinavir (see lopinavir) - medical need for next generation 78-85 - ritonavir (see ritonavir) - safety profile 321 - saguinavir (see saguinavir) - tipranavir (see tipranavir) proteasome inhibitors, human cytomegalovirus 262-265 protein kinase family, herpesviridae 212 protein kinase inhibitor, maribavir 212 protein-protein interactions inhibition, human cytomegalovirus 246-248 prusoff, iododeoxyuridine 1 PTGS see posttranscriptional gene silencing pUL84, human cytomegalovirus replication factor 247-248 pUL97 - cytomegalovirus protein kinase 211 - human cytomegalovirus protein kinase 253 purine cyclic nucleoside phosphonates, chemical structures 102 pyrimidine cyclic nucleoside phosphonates, chemical structures 100 pyrophosphate analogue, foscarnet 230 pyrrolidine-5,5-trans-lactams 250 q

 quinazolines, human cytomegalovirus protein kinase inhibitors 250, 255
 quinoxaline derivatives, design starting from cyclophilins structures 169–170

#### r

R89439 *see* loviride R147681 *see* dapivirine

R165335 see etravirine R278474 see rilpivirine R-125489 358-359 raltegravir - brand name and manufacturer 6 - chemical structure 10 - discovery 3 - first HIV integrase inhibitor 4, 12, 72 - HIV integrase inhibitor 41, 55-57, 64 - integrase strand transfer inhibitor 57 RBV see ribavirin Relenza<sup>®</sup> see zanamivir reoviridae, targeted by RNAi 333 replicative cycle, herpesviruses 264 respiratory syncytial virus (RSV), RNAi therapy 337 retroviridae, targeted by RNAi 333 retroviruses see also HIV - acyclic nucleoside phosphonates 96–99, 196-197 - antiviral drugs 8-12 - inhibition with nucleoside phosphonates 91 - intrinsic mutagenesis 284-286 - viral fitness 284-286 reverse transcriptase (RT) - HIV-1 378 - viral target for HIV therapy 29-30 rhabdoviridae, targeted by RNAi 333 ribavirin (RBV) - antiviral activity 2 - brand name and manufacturer 6 - chemical structure 7, 106 - chronic HCV genotype 1 162-165 - discovery 3 – hepatitis C 155–157, 173 - hepatitis C and cyclophilin 15 - influenza A 14 - mechanism of action 8, 289 - mutagenic pharmaceutical 288-290 - RNA virus 104 1-β-D-ribofuranosyl-1,2,4-triazole-3carboxamide see ribavirin 1-(β-L-ribofuranosyl)-2-isopropylamino-5,6dichlorobenzimidazole (GW1263W94) see maribavir ribonucleoside analogues - 5-Azacytidine 291-292 - 5-Hydroxy-2'-deoxycytidine 290-291 - lethal mutagens 287 - ribavirin 288-290 rilpivirine 377-385 - clinical proof of concept 383-384

- combination therapy 385

- development 380 - drug-drug interactions 383-384 - mechanism of action 381-383 - pharmacokinetics 383-384 - potency 384-385 resilience to NNRTI resistance 384–385 - resistance 385 rilpivirine (R278474, TMC278) 380-381 structure-activity relationship 381–383 rimantadine, influenza treatment 352-353 RISC see RNA-induced silencing complex ritonavir - body absorption 75 - brand name and manufacturer 5 - chemical structure 76 - combination with elvitegravir 56 - combination with lopinavir 77-78 - comparison to darunavir 86 - discovery 3 - HIV protease inhibitor 80 RNAi see also RNA interference - antiviral activity 331-332 - selecting optimal targets 332-334 RNAi gene knockdown, high-throughput screens 334 RNAi gene therapy – chronic infection 337–338 - future perspective 338-339 - HIV-1 infection 337-338 RNAi mechanism – mammalian viruses 331–332 therapeutic application 329–331 RNA-induced silencing complex (RISC) 331 RNA interference (RNAi) 248 see also RNAi – discovery 329 RNAi strategies, prevention of viral escape 334-335 RNAi therapy basic design 332 potential risks 336–337 RNA viruses - hepatitis C virus 92, 155 - intrinsic mutagenesis 284-286 - mutagenic nucleoside analogues 288 - mutation rates 284 - replication inhibitor 288-289 - viral fitness 284-286 roscivitine, cyclin-dependent kinases inhibitor 262 RSV see respiratory syncytial virus RT see reverse transcriptase RWJ-270201 see peramivir

#### S

S2242 see 2-amino-7-[(1,3-dihydroxy-2-propoxy) methyl]purine saquinavir - brand name and manufacturer 5 - chemical structure 10, 76 discovery 3 - first HIV protease inhibitor 2 - HIV protease inhibitor 80, 82 - HIV treatment 75, 80 - hydroxyethylene scaffold 11 SAR see structure-activity relationship second-generation HIV integrase inhibitors see HIV integrase inhibitors Selzentry<sup>®</sup> see maraviroc sequence-specific gene silencing 329 sialic acid analogues, neuraminidase inhibitor 355-358 sialidase, neuraminidase 352 siRNAs - delivery issues 335-336 - multiplexing 335-336 siRNA treatment, escape for several viruses 334 small interfering RNAs, human cytomegalovirus 248 small-molecule inhibitors, HIV entry 36-37 smallpox see also biological weapon; poxviruses; variola virus - orthopoxviruses 191 - vaccine 1, 17, 189 SOC see standard of care solid organ transplant (SOT), human cytomegalovirus infection 228 spontaneous mutations, HIV 286 standard of care (SOC), hepatitis C virus genotype 1 307 strand transfer inhibitors see integrase strand transfer inhibitors strand transfer reaction, HIV integrase 12 structure-activity relationship (SAR) 242 - acyclic nucleoside phosphonates 95-98 - cyclic nucleoside phosphonates 100-104 - rilpivirine//HIV-1 reverse transcriptase 381-383 structure-based drug design - hepatitis C virus protease inhibitors 234-238 - influenza neuraminidase inhibitors 369 - zanamivir 355-358 surface protein, viral 30 sustained viral response (SVR), hepatitis C virus therapy 307 SVR see sustained viral response

#### t

Tamiflu<sup>®</sup> see oseltamivir TCRB see (2,5,6-trichloro-1-(β-D-ribofuranosvl) benzimidazole TDF see tenofovir disoproxil fumarate telaprevir - binding to NS3 protease variants 316-318 - phase 2 clinical trials 319-320 tenofovir - acyclic nucleoside phosphonates 97-98 - alkoxyalkyl esters 196-197 tenofovir disoproxil fumarate (TDF) see also acyclic nucleoside phosphonates - clinical application of nucleoside phosphonate 113-115 - hepatitis B virus and HIV 11, 92, 97-99, 196 tetrahydrofuran core phosphonates - cyclic nucleoside phosphonates 100-103 - purine cyclic nucleoside phosphonates 102 pyrimidine cyclic nucleoside phosphonates 100 tetrahydro-imidazo[4,5,1-jk][1,4]benzodiazepin-2(1H)-one (TIBO) 378 4'-thiopyrimidine nucleosides 242 - human cytomegalovirus infection 242 thiourea derivatives, entry inhibitor 236-237 thymidine analogue, iododeoxyuridine 1 TIBO see also tetrahydro-imidazo[4,5,1-ik][1,4]benzodiazepin-2(1H)-one - chronicle of the discovery 377-385 - derivatives 378-379 TIBO R82150 378 TIBO R82913 378 TIBO R86183 378 tipranavir - brand name and manufacturer 5 - chemical structure 76 - development 78–79 – discoverv 3 - enfuvirtide 41 - HIV protease inhibitor 80 no hydroxyethylene scaffold 11 tivirapine, chemical structure 378 TMC120 see dapivirine TMC125 see etravirine TMC278 see rilpivirine transmembrane glycoprotein, HIV see HIV-1 glycoproteins transplant recipients – cytomegalovirus disease prophylaxis 218-220 - human cytomegalovirus infection and diseases 228

(2,5,6-trichloro-1-(β-D-ribofuranosyl) benzimidazole (TCRB), cytomegalovirus inhibitor 210, 251 N-(4-trifluoromethylphenyl)-5methylisoxazole-4-carboxamide, human cytomegalovirus inhibitors 259

## и

UL97 protein kinase (pUL97) inhibitors, human cytomegalovirus 250, 252-255 UL54-UL44 interaction, human cytomegalovirus 246

## ν

vaccines - poliovirus 1 - smallpox 1, 17, 189 vaccinia virus - acyclic nucleoside phosphonates 191-194 - antiviral drugs 17-18 - antiviral effects of cidofovir derivatives 190 - cyclosporin A and derivatives 167 - nucleoside phosphates and phosphonates 190 - thiosemicarbazones 1 valacyclovir (VACV), human cytomegalovirus 229 Valcyte<sup>®</sup> see valganciclovir valganciclovir (VGCV), human cytomegalovirus desease prophylaxis 229-230 varicella zoster virus (VZV) - alphaherpesviruses 129 - antiviral drugs 4-8, 104, 146, 191, 197 - helicase-primase inhibitors 130-134 - mutation 136, 181 variola virus (VARV) see also poxviruses; smallpox - acyclic nucleoside phosphonates 189-190 - antiviral drugs 17-18 VDA see viral decay acceleration VGCV see valganciclovir vicriviroc, HIV treatment 39 Vidaza<sup>®</sup> see 5-azacytidine viral decay acceleration (VDA) 292 viral fitness - retroviruses 284-286 - RNA viruses 284-286 viral surface protein, HIV entry 30 viral targets, earlier HIV therapy 29-30 Virazole<sup>®</sup> see ribavirin viread see tenofovir disoproxil fumarate

virion assembly and egress inhibition, human cytomegalovirus 248–256 virus attachment, inhibitors 34–37 virus-cell fusion, HIV entry 33 virus entry, HIV *see* HIV entry virus silencing, antiviral RNAi 329–339 virus tropism and infectivity, coreceptors 33 viruses

- enteroviruses 1
- hepatitis B (see hepatitis B virus)
- hepatitis C (see hepatitis C virus)
- herpes 4–8
- herpes simplex 1
- influenza 1
- polio 1
- smallpox 1
- varicella zoster 4–8
- Vistide<sup>®</sup> see cidofovir
- Vitravene<sup>®</sup> see formivirsen
- VZV see varicella zoster virus

#### w

- 1263W94 see (2-isopropylamino-5,6-dichloro-1 (β-D-ribofuranosyl)benzimidazole (1263W94) west nile virus – nucleosides 15
- ribavirin 290

#### x

- X-ray crystallography
- GS4071/neuraminidase complex 361, 369
- hepatitis C virus protease inhibitors 315, 318
- human cytomegalovirus protease inhibitors 256

- neuraminidase inhibitor 355-358

- peramivir/neuraminidase complex 369
- pyrollidine- and cyclopentane-based neuraminidase inhibitors 367
   zanamiyir/neuraminidase complex
- 361, 369
- X-ray diffraction
- NNRTI binding pocket within the HIV-1 reverse transcriptase 381
- rilpivirine/HIV-1 reverse transcriptase complex 381

#### γ

yellow fever, nucleosides 15

### z

- zanamivir
- C-6 carboxamide analogues 356–357
- C-6 carboxamide, ether, ketone, and hydroxy analogues 357
- chemical structure 353
- clinical use 367–368
- derivatives 198
- dimeric analogues 358
- glycerol side-chain analogues 358–359
- heterocyclic analogues 357-358
- influenza treatment and prevention 352–353
- inhibitor activity 356
- inhibitor design 355-358
- neuraminidase inhibitor 355-358
- resistance 368-369
- zidovudine see also AZT
- brand name and manufacturer 5