

Index

a

- abatacept 936, 943, 949, 1087, 2027
 abciximab
 – ALX-0081 624
 – CAPTURE study 2089
 – data supporting marketing approval 2088
 – EPILOG 2088–2089
 – GPIIb/IIIa receptor 2087
 – percutaneous coronary intervention (PCI) 2087
 – placebo 2088
 – treatment 2089
 AbGn-168 (Abgenomics) 1137
 ABT-122 (Abbvie) 991–992
 ABT-308 (RCP4046; Receptos and Abbvie) 1005
 ABT-981 (Abbvie) 982
 abYsis 208, 215
 ACCEPT (NCT00454584) 2073
 AD. *See* atopic dermatitis (AD)
 adalimumab (Humira®)
 – approved indications 1312–1313
 – BD 1313–1314
 – HS 1316–1318
 – principles, clinical use 1310
 – safety 1310–1312
 – sarcoidosis 1318
 – uveitis 1314–1316
 ADCC. *See* antibody-dependent cellular cytotoxicity (ADCC)
 ADCs. *See* antibody–drug conjugates (ADCs)
 ADEPT. *See* antibody-directed enzyme prodrug therapy (ADEPT)
 adipsin 1169–1170
 adjuvants 22, 1299, 1876–1877, 2042–2043, 2049–2050, 2053
 Administration of Radioactive Substances Advisory Committee (ARSAC) 1584
 ado-trastuzumab emtansine (T-DM1)
 – HER2-positive metastatic breast cancer 120
 – MTD 2059
 – and pertuzumab 1879
 – role 2060, 2061
 – structure 2060
 adoptive cellular immunotherapy 538–540
 adult non-renal transplantation
 – heart 1386–1387
 – liver 1383–1385
 – lung 1385–1386
 – pancreas 1387–1388
 adult T-cell leukemia (ATL)
 – and CTCL 2115
 – murine model 1356–1357
 – NHL 2115
 – tumor progression 2116
 adverse effects, omalizumab
 – anaphylaxis treatment 1803
 – immune complex diseases 1804
 – local reactions 1803
 – long-term treatment 1804
 – malignant neoplasms 1803–1804
 – systemic side effects 1803
 AEX. *See* anion-exchange (AEX) chromatography
 affinity chromatography
 – boronate 688
 – description 622
 – exemplified binding sequences, ligands 622
 – immobilized mannan-binding protein 31
 – and ion-exchange chromatography 1910
 – mAb purification 643
 – mouse monoclonal IgG antibodies 31
 – protein A/G 1301

- affinity maturation
 - enzyme activation-induced cytidine deaminase (AID) 20
 - and humanization 4
 - *in vitro*, 93, 107, 117–119, 313, 321, 908
 - *in vivo*, 115–117, 119, 317, 495
- afiibercept 836, 1177–1178, 1893–1894
- afutuzumab 754–755
- age-related macular degeneration (AMD) 944–945, 1394
 - aflibercept 1898–1894
 - ANCHOR and MARINA 1888, 1889
 - bevacizumab 1892–1893
 - clinical trials 1889
 - CNV development 1884
 - occult and classic neovascularization 1884, 1885
 - pathogenic mechanisms 1884, 1885–1886
 - wet form 1884
- aggressive B-cell lymphoma, rituximab
 - BL/BLL 1958
 - Cunningham study 1955
 - GELA LNH98-5 trial 1950, 1951
 - gemcitabine-based regimens 1955
 - HDT 1945
 - HOVON-46 study 1954
 - intergroup E4494 trial 1950, 1951–1952
 - MabThera International Trial (MInT) 1952–1953
 - monotherapy 1956–1957
 - PMBCL. *See* primary mediastinal B-cell lymphoma (PMBCL)
 - previously untreated 1945–1947, 1950
 - relapsed/refractory 1945, 1948–1949
 - retrospective population analyses, DLBCL 1953
 - RICOVER-60 trial 1954
- AGS-009 (Argos Therapeutics) 997, 998
- albumin binding
 - anti-RANKL (ALX-0141) 331
 - description 330
 - fusion with serum albumin 441
 - human PK data 332
 - pharmacokinetics, AlbuDabsT 330, 331
 - protein component, human serum 330
 - sdAbs 311
- ALCL. *See* anaplastic large cell lymphoma (ALCL)
- alemtuzumab
 - antibody features and production 1324–1325
 - B-CLL 1323–1324
 - blood lymphocyte 1338–1339
 - BMT 1329
 - Campath-1G 1324
 - CD52 antigen 1325–1326
 - CD52-subclones 1327
 - cell lysis. *See* cell lysis
 - chemotherapeutic agents 1339
 - CLL 1326–1327
 - consolidation therapy 1341–1342
 - CR 1340–1341
 - CTCLs. *See* cutaneous T-cell lymphomas (CTCLs)
 - fludarabine and alemtuzumab 1339–1340
 - grade 1/2 toxicities 1340
 - hematologic toxicities 1344–1346
 - hepatomegaly/splenomegaly 1338
 - IgM antibody 1324
 - immunogenicity and antiglobulin response 1328
 - immunosuppression and infectious events 1346–1347
 - immunotherapy combination 1342–1343
 - infusion-related adverse events 1343–1344
 - lymphocyte cell surface 1326
 - MRD. *See* minimal residual disease (MRD)
 - MS. *See* Multiple sclerosis (MS)
 - ORR 1341
 - serum concentrations 1329–1330
- alirocumab
 - LDL-C level reduction 858
 - phase III trials 859, 860–864
 - treatment 858–859
- allergic diseases
 - anti-immunoglobulin E treatment. *See* omalizumab
 - asthma 945–947
 - atopic dermatitis 948–949
 - rhinitis. *See* allergic rhinitis (AR)
- allergic rhinitis (AR)
 - anti-TSLP-R mAb 1009
 - clinical efficacy 1812, 1813
 - potential indications and contraindications 1805, 1806
 - randomized and double-blind clinical trials 1812,
- altered complement activation 157–158
- altered immunity 934
- ALX-0061 (Abylnx, Abbvie) 314, 506, 986
- Alzheimer's disease (AD)
 - active immunotherapy, A β 1218
 - disease and target 1217–1218
 - IL-4 and IL-5 role 948
 - and mini mental state examination (MMSE) 906
 - murine and human models 1011
 - mutation 908

- passive immunotherapy, A β 1218–1220
- pathology, APP transgenic mice 906
- pyroglutamate-3 A β 1220
- serum IgE 948
- treatment 906
- AMD. *See* age-related macular degeneration (AMD)
- AMG 139 (MEDI-2070; Amgen/Medimmune) 993
- AMG 157 (MEDI9929; Amgen/AZ-Medimmune) 1010
- AMG-317 (Amgen) 1002
- AMG 557 (Amgen/AZ-Medimmune) 1089
- AMG 729 (XmAb5871; Amgen from Xencor) 1117
- AMG 811 (Amgen) 1000
- amyloid β protein
 - bapineuzumab 906–907
 - cerebral plaques 906
 - gantenerumab 908–909
 - immunoconjugate approach 906
 - proteins and polypeptides 905
 - solanezumab 907–908
- amyotrophic lateral sclerosis (ALS)
 - active immunotherapy 1224
 - disease and target 1223–1224
 - and HD 1216
 - passive immunotherapy 1224
- anaplastic large cell lymphoma (ALCL)
 - and ALK 1432
 - brentuximab vedotin 1432–1433
 - CD30-positive hematologic malignancies 1435
 - chemotherapy 1436
 - chromosome translocation 1432
 - and Hodgkin lymphoma 344
 - primary cutaneous CD30-positive lymphoproliferative disorders 1433–1435
 - and TNF 759
- anastrozole plus trastuzumab 2047
- ANCA-associated vasculitis 1983–1984
- angiogenesis
 - angiopoietin type 2 836
 - angiotensin-2 receptor 837
 - anti-angiogenic antibodies 840, 841
 - anti-S1P inhibitors 1178–1181
 - anti-VEGF inhibitors 1177–1178
 - bevacizumab 795
 - cadherins 838
 - cancer development 764, 823–824
 - ECM 839, 841
 - endothelial and mural cells 824
 - HIF1- α 824
 - hypoxic and acidic tumor milieu 825
 - integrins 837–838
 - macrophages 825, 944
 - MET tyrosine kinase 838–839
 - molecular regulators 825–830
 - natural stimulators 827
 - organogenesis and wound healing 1177
 - p53 mutations 828
 - pleiotropin 828
 - PLGF 827
 - TAMs 828
 - TGF- β receptors 827
 - tumor cell accumulation 824
 - tumor-induced blood vessels 830
 - wound-healing processes 827
- anifrolumab 998
- anion-exchange (AEX) chromatography 624, 625
- ankylosing spondylitis (AS) 1605–1606
- anrukinzumab 1001, 1004
- anthrax bacillus 1200–1201
- anthrax toxin receptors (ATRs) 1899–1900
- anthrax toxins
 - *B. anthracis*, 1900
 - LF and EF 1900–1901
 - raxibacumab. *See* raxibacumab
- anti- α 4 β 7/MAdCAM-1
 - AMG 181 1129–1130
 - etrolizumab 1130
 - PF-00547659 (Pfizer) 1130–1131
 - vedolizumab 1129
- anti-C5/C5a/C5aR 1166–1169
- anti-CD22 (epratuzumab) 755–756
- anti-CD20 \times anti-CD3 lymphomun
 - adverse events 1486
 - allogeneic SCT 1484
 - diffuse large B cell lymphoma (DLBCL) 1485
 - graft vs. leukemia (GvL) effect 1484
 - HAMA response 1487
 - hematological remission 1487
 - mantle cell lymphoma (MCL) 1485
 - NHL 1484
 - in pediatric patients 1485, 1486, 1488
 - tumor progression 1485
- anti-EpCAM \times anti-CD3 catumaxomab
 - abdominal EpCAM-positive cancer diseases 1474
 - cancer stem cells (CSCs) 1477–1478
 - CASIMAS trial 1476
 - completed clinical trials 1475
 - gastric cancer treatment 1480–1481
 - locoregional administration 1478–1479
 - median antibody concentrations 1477

- anti-EpCAM × anti-CD3 catumaxomab (*contd.*)
 - in ovarian cancer patients 1481
 - peritoneal carcinomatosis 1479–1480
 - QoL Questionnaire-Core 30 items 1475–1476
 - SECIMAS study 1476
 - T cells adhesion 1477
 - vascular endothelial growth factor (VEGF) levels 1477
- anti-EpCAM antibodies
 - adecatumumab 761
 - description 760
 - edrecolomab, murine IgG2a antibody 760
 - European phase II trials, catumaxomab 761
- anti-GD2 × anti-CD3 ektomab 1488–1490
- anti-HER2/neu × anti-CD3 ertumaxomab 1482–1484
- anti-idiotypic antibody (Ab2)
 - Ab1/antigen-derived peptide and Ab1/Ab2 complexes 410
 - amino acid identity 408
 - antibody-antigen interaction 408
 - antigen-mimicking synthetic peptides 408, 410
 - B cell malignancies 415
 - in cancer. *See* cancer, Ab2
 - description 409
 - Fab mimicking 417
 - function and specificity 407
 - functional mimicry 410, 411
 - Guillain–Barré syndrome 417
 - homobodies 408
 - human hepatitis B surface antigen (HBsAg) 410
 - human immunodeficiency type 1 virus (HIV-1) 418
 - hydrogen bonds and solvent interactions 410
 - immunotherapeutic strategies 417
 - IVIg, autoimmune diseases 413
 - molecular mimicry, infectious agents and controversial theory 414
 - mouse Ab1 formulations, rodents immunization 414
 - mouse dams 417
 - Neu5Gc-gangliosides 412
 - normal γ -globulins 407
 - physiological significance and therapeutic potentials 407
 - racotumomab 774
 - recombinant fragments 414
 - with self-binding activity 408
 - self/non-self discrimination 412–413
- serogroup B *Neisseria meningitidis* capsular polysaccharide 418
- syngeneic and xenogeneic models 414
- vaccines, Ab2 β s 414
- anti-immunoglobulin E treatment, allergic diseases. *See* omalizumab
- anti-infectious monoclonal antibodies
 - anthrax bacillus 1200–1201
 - botulinum neurotoxins 1201
 - *Clostridium difficile*, 1197–1198
 - eculizumab 1200
 - HUS 1200
 - Inhibitex[®] 1198–1199
 - KaloBios[®] 1199–1200
 - pagimaximab BSYX-A110 1198
 - *Pseudomonas aeruginosa*, 1199
 - PVL 1199
 - SAR279356 1198
 - staphylococcal enterotoxins 1199
 - *Staphylococcus aureus*, 1198
- anti-inflammatory effects, omalizumab
 - B cells 1801
 - cytokines 1799
 - dendritic cell APCs 1800
 - eosinophils 1800–1801
 - Fc ϵ RI cell expression 1799
 - humoral and cellular parameters 1797, 1798
 - serum free IgE levels 1797, 1798
- anti-T-cell costimulators
 - anti-CD26 (DPPIV) 1095–1097
 - anti-CD28 1087–1088
 - anti-HVEM/LIGHT 1093–1095
 - anti-ICOSL (B7RP-1) 1088–1091
 - anti-NKG2A 1097–1098
 - anti-OX40/OX40L 1091–1093
- anti-TNF mAbs 1670
- antibody affinity
 - affinity maturation. *See* affinity maturation
 - antibody concentration 133
 - antigen binding and potency 120–121
 - biolayer interferometry (BLI) 129–132
 - cell-based titration experiment 133
 - *vs.* cell surface antigens 127–128
 - description 115
 - determination 128
 - ELISA 132–133
 - hybridoma cell lines 126
 - *in vitro* binding and potency. *See in vitro* binding and potency
 - *in vivo* binding and potency. *See in vivo* binding and potency
 - KinExA instruments 132
 - *vs.* soluble antigens. *See* soluble antigens

- SPR. *See* surface plasmon resonance (SPR)
- antibody-dependent cell-mediated cytotoxicity (ADCC)
 - ART621 506
 - CD20 receptor 789
 - and complement-dependent cytotoxicity (CDC) 17
 - D270A mutant 157
 - elotuzumab 757
 - FcγRIIIA 1117
 - glycoforms 181
 - glypican-3 790
 - in human lymphocytes 1324
 - K326W-E333S mutants 158
 - leukemic cells 186
 - SD1-Fc fusion protein 504
 - T-cell depletion capacity 1091
- antibody-dependent cellular cytotoxicity (ADCC)
 - aglycosylated/deglycosylated IgG molecules 609
 - and phagocytosis 278
 - approved mAbs with 670
 - chimeric antibodies 148
 - ensituximab (NPC-1C) 790
 - epratuzumab 756, 757–758
 - Fc receptors (FcRs) 1911, 1912
 - FcγRIIIa-F/F158 donor cells 153
 - GC-33 (RO5137382, RG7686) 790
 - GlymaxX technology 611
 - GM-CSF 1931
 - homodimers 1470
 - human immunological effector functions 17
 - human tumor xenografts *in vivo*, 290
 - humoral immune response 461
 - immune effector cells 789
 - K326W and K326W-E333S mutants 158
 - lenalidomide 1932
 - mAb-opsonized cells 1748
 - natural killer cells (NK cells) and macrophages 789
 - NK cell-mediated activity 156
 - obinutuzumab 1702
 - ocrelizumab 903–904
 - rituximab 789, 789–790
 - trastuzumab and pertuzumab 1874
 - tumor cell-bound antibodies 35
 - ublituximab (TGTX-1101, LFB-R603) 789–790
 - veltuzumab 1121
- antibody-directed enzyme prodrug therapy (ADEPT)
 - advantages 482
 - basic principle 476
 - carcinoembryonic antigen (CEA) 475
 - catalytic antibodies. *See* catalytic antibodies
 - CPG2 and benzoic mustard prodrugs 477–478
 - cytotoxic agents and toxins 475
 - drug molecules 476
 - *Enterobacter cloacae* beta-lactamase 327
 - F(ab) 2 fragments conjugated to CPG2 479
 - immunogenicity. *See* immunogenicity
 - indirect drug targeting 363
 - mammalian and non-mammalian origin 478
 - murine monoclonals 476
 - normal tissue toxicity 475
 - radiolabeled intact IgG 476
 - recombinant scFv-CPG2 fusion protein 479–480
 - tumor antigens 475
- antibody engineering
 - fluid-phase pinocytosis 158
 - human IgG₂ binding 159
 - M428L-N434S Fc variant 159–160
 - novel Fc variants 159
 - receptor (FcRn) 158
 - serum half-life 159
- antibody isotype
 - classical complement pathway 146
 - Fc region binding 146
 - FcαRI-transgenic mice 150
 - Gm allotype system 146
 - granulocyte colony-stimulating factor (G-CSF) 149
 - human Fcγ receptors 146, 147
 - human IgG₂ 148
 - human myeloid cells activation 149
 - in human serum 172
 - IgE molecule, allergic diseases 1778
 - immunoreceptor tyrosine-based inhibitory motif (ITIM) 146
 - isoforms, schematic representations 149
 - isotypes 149
 - mAbs, PK profiles 1253
 - neutrophil-expressed FcγRIIIb 148
 - polymeric immunoglobulin receptor (pIgR) 149
 - production 1297
 - ratio of activation to inhibition (A/I ratio) 145
 - subclasses 145, 146, 148
 - therapeutic applications 150
 - in tumor rejection 149

- antibody preparations
 - animal, choice of 1299
 - blood samples collection 1300
 - oligoclonal. *See* oligoclonal antibodies
 - polyclonal antibodies. *See* polyclonal antibodies
- antibody purification 1300–1301
- antibody selection
 - *in vitro*, 118
 - libraries 395–396
 - and maturation *in vitro*. *See* *In vitro* maturation and antibody selection
 - microarrays 393
 - phage, cell-surface and ribosome display 393–395
 - proteomic studies 393
 - recombinant systems 44
 - ribosome and mRNA display 398–399
 - ribosome display. *See* ribosome display
- antibody sequences
 - abYsis 215
 - antibody sequence databanks 210
 - databanks 210
 - germline components identification 214
 - germline sequence databases 211
 - “humanness” 214
 - subgroups assignment, tools 213
 - unusual features identification 214
 - web resources. *See* web resources
- antibody structure prediction
 - automated modeling tools 217–218
 - CDRs 216
 - data 213
 - light and heavy chains 216
- antibody-targeted drugs
 - antibody-directed enzyme prodrug therapy (ADEPT) 363
 - chemical immunoconjugates. *See* chemical immunoconjugates
 - cytotoxic payloads 363
 - recombinant cytotoxic fusion proteins. *See* recombinant cytotoxic fusion proteins
- antibody V domain humanization
 - amino acid interactions, FR-IMGT and CDR-IMGT 247
 - CDR-IMGT grafting 246, 247
- antibody–drug conjugates (ADCs)
 - ADC glembatumumab (CDX-011) 805–806
 - ado-trastuzumab emtansine 1236
 - bioanalysis 677
 - brentuximab vedotin 1236
 - for cancer treatment 344–346
 - chemically linked 369, 371, 374
 - cytotoxic compounds. *See* cytotoxic compounds, ADCs
 - description 341–344
 - first-generation 366
 - gemtuzumab ozogamicin 1236
 - HER2 inhibition 804
 - linkers. *See* linkers, ADCs
 - lorvotuzumab mertansine (IMGN-901, N901-DM1, BB-10901) 805
 - mesothelin 804–805
 - milatuzumab 805
 - vorsetuzumab mafodotin (SGN-75) 804
- antigen binding and potency 120–121
- antigen-presenting cells (APCs)
 - allergen presentation 1786
 - anti-CD4 1083
 - B cell and Th0 cells 1777
 - caveolin-1 1095
 - CD28 1087
 - CD40 1089–1090
 - CD4⁺ Th2 cells 1786
 - DCs 1786, 1800
 - FcεR expression 1809
 - T-cell activation 792
- APCs. *See* antigen-presenting cells (APCs)
- apoptosis
 - B cells 1162,
 - benralizumab 1006
 - CEA-positive cells 809
 - CTLs 279
 - CXCL10 1019
 - description 1175
 - eosinophil 1801,
 - gene insertions 531
 - HuM291 153
 - IL-18 983
 - infliximab 1600
 - mAbs 1175–1177
 - related genes 575
 - requiem 579
- applied genomics and cell line engineering
 - apoptosis 576–577
 - CHO cell lines 573–574
 - CHO-K1 genome 576
 - chromosome mapping 574
 - description 576
 - Fadd, Faim, Alg-2 and Requiem 575
 - FUT8 and guanosine diphosphate (GDP)-mannose 4,6-dehydratase 579
 - gene expression profile 575
 - gene knockout 577
 - gene silencing 576
 - LDH-C 574–575
 - miRNAs 575

- non CHO-derived DNA microarrays 574
- rAAV-based genome engineering 578
- RNAi-mediated knockdown/mRNA overexpression 578
- shRNAs 578
- siRNA knockdowns 579
- TALENs 577–578
- transcriptomics, proteomics and metabolomics 574
- ZFNs 577
- approved indications
 - abcximab 2088–2089
 - adalimumab 1312–1313
 - eculizumab 2102–2103
 - natalizumab 2105–2107
- AR. *See* allergic rhinitis (AR)
- arcitumomab (CEA-Scan™) 2124–2126
- ARG098 1176–1177
- arresten 829
- asialoglycoprotein receptor (ASGPR) 184
- ASKP-40 1090–1091
- asthma
 - anti-IgE mAb omalizumab 947
 - anti-TNFs 947
 - atopic 945
 - CNTO-3157 1149
 - description 945
 - TH17 and TH1 cells 946
 - therapies 946–947
 - TLR3 1148
 - TLR9 agonists 1149
 - TNF α blockers 947
- asymmetric heterodimerization domains.
 - See also* recombinant bispecific antibody molecules
 - CrossMab format 277
 - dock-and-lock (DNL) method 278
 - electrostatic steering effects 276–277
 - feasibility 278
 - jun-fos leucine zippers 278
 - knobs-into-holes approach 276
 - SEEDbodies 277
 - toxins 278
- atacept 941, 1119
- atopic dermatitis (AD) 876, 948–949, 1160
- ATTRACT trial 1601, 1604, 1610
- autoimmune disorders
 - ANCA-associated vasculitis 1983–1984
 - autoimmune cytopenias and hemophilia 1982–1983
 - CD22 antibodies 1555
 - chronic GVHD 1983
 - MG 1984–1985
 - OMS 1984

- RA 1980–1982
- SLE 1982
- automated modeling tools
 - MODELLER 217
- Molecular Operating Environment (MOE) 218
- Prediction of ImmunoGlobulin Structure (PIGS) 217, 218
- “RosettaAntibody3” 217
- SwissModel 217
- WAM Web site 217

b

- B-cell-activating factor (BAFF). *See* B-lymphocyte stimulator (BLyS)
- B-cell chronic lymphocytic leukemia (B-CLL) 91, 754, 1088, 1323, 1703
- B-cell inhibitors
 - anti-BAFF 1117–1119
 - anti-CD19 1115–1117
 - anti-CD20 1119–1121
- B-cell lymphoma
 - anti-CD20 antibody treatment 540
 - anti-CD20 monoclonal antibody rituximab 343
 - bispecific antibodies 288
 - BO20999 phase I 1715
 - BO21003 phase I 1715–1717
 - BO20999 randomized phase II 1717–1718, 1719–1720
 - BO21000 randomized phase II 1720, 1721
 - BO21003 randomized phase II 1718–1719
 - DLBCL 367, 1435
 - FBTA05 283
 - JO21900 1717
 - obinutuzumab 1716, 1721–1722
 - ofatumumab 754
 - phase III studies 1721–1722
 - redirected T cells 540
 - velutuzumab 1121
- B-cell lymphoma, rituximab
 - classification 1915
 - immune modulators 1931–1933
 - induction therapy 1917–1921
 - maintenance therapy 1937–1944
 - meta-analysis 1930–1931
 - mortality rates 1914–1915
 - phase II studies, chemotherapy 1922–1924
 - phase III studies, chemotherapy 1924–1927
 - relapsed/refractory indolent 1927–1930
 - rituximab monotherapy 1933–1935

- B-cell lymphoma, rituximab (*contd.*)
 - rituximab SC 1985–1994
- B-cellular non-Hodgkin's lymphoma
 - anti-CD20 antibody rituximab 758
 - description 753
 - elotuzumab (anti-CS1) 757–758
 - epratuzumab (anti-CD22) 755–756
 - galiximab (anti-CD80) 757
 - inotuzumab ozogamicin (anti-CD22) 756–757
 - obinutuzumab 754–755
 - ofatumumab 753–754
- B-CLL. *See* B-cell chronic lymphocytic leukemia (B-CLL)
- B-lymphocyte stimulator (BLyS) 898–899, 1117–1119, 1405
- Bacillus* species 562
 - *B. megaterium*, 565
 - *B. subtilis* and *B. brevis*, 564
 - intracellular and extra cytoplasmic molecular chaperones 564
 - polypeptide chains 565
 - signal peptides/secretion domains 564
- bapineuzumab 906–907, 1218
- basic fibroblast growth factor (bFGF)
 - angiogenesis stimulants 826
 - heparin 827
 - normal fibroblasts 827
 - tumor cells 824
- basiliximab and daclizumab
 - action mechanisms 1376
 - human organ transplantation. *See* human organ transplantation
 - IL-2R antibodies. *See* IL-2R antibodies
 - lymphocytes 1375
 - renal transplantation 1377
 - solid organ transplantation and IL-2R-based therapy 1377–1378
 - TAC 1376–1377
- BAX-69 (Baxter Healthcare Corp) 1018
- BD. *See* Behçet disease (BD)
- bDMARDs. *See* biological disease-modifying antirheumatic drugs (bDMARDs)
- BEGEDINA® 1096–1097
- Behçet disease (BD)
 - anti-TNF therapies 1313
 - phase 3 study 1314
- belimumab
 - BLISS-52 and BLISS-76 1405
 - BLISS-52 RCT outcome 1408
 - BLISS-76 RCT outcome 1409
 - BLISS-SC study 1411–1413
 - BLyS and autoimmunity 1406
 - hypersensitivity adverse events 1410
 - immunosuppression adverse events 1410
 - lupus patients 1409
 - malignancy adverse events 1410
 - mortality adverse events 1411
 - phase I clinical trial 1407
 - placebo-controlled trial 1408
 - psychiatric adverse events 1411
 - RA 937, 1115
 - RCT 1407
 - reproduction adverse events 1411
 - scFv 1406
 - side effects 1409
 - SLE 899, 942, 1115, 1405
 - standard-of-care (SOC) therapies 1118
 - steroid dosage reduction 1409
 - TNF homolog 1405–1406
- benralizumab 955, 1006–1007
- benzoic mustard prodrugs. *See* carboxypeptidase G2 (CPG2)
- bertilimumab 1017
- besilesomab (Scintimun®) 2131–2132, 2136
- best supportive care (BSC) 1861
- bevacizumab
 - in breast cancer 2091–2092
 - cervical cancer 2095
 - clinical trials 1893
 - EU-and US-approved indications 2090
 - Fc receptors 1892
 - in glioblastoma 2094–2095
 - marketing approval 2090
 - molecular weight 1892
 - in ovarian cancer 2092–2093
 - PRN protocol 1893
 - safety 2090–2091
 - second-line CRC treatment 1508
 - solid tumors 2089–2090
 - VEGF-A 2089
- bFGF. *See* basic fibroblast growth factor (bFGF)
- bi-specific T-cell engagers (BiTEs)
 - blinatumomab (MT-103, MEDI-538) 808
 - carcinoembryonic antigen (CEA) 808–809
 - defined 808
 - description 1466–1467
 - solitomab, EpCAMs 808
 - tandem scFv molecules 281
 - and trifunctional antibodies 804
- Biacore system 130, 654
- BIIB023 (Biogen-IDEC) 979
- BIIB033 (Biogen-IDEC) 1183
- bioinformatics tools, antibodies analysis
 - antibody sequence data. *See* antibody structure prediction
 - antibody structure 201–202

- CDRs and related regions 208–209
- Chothia numbering scheme 204–205
- enhanced Chothia (Martin) numbering scheme 206, 207
- Honegger and Plückthun (Aho) numbering scheme 206
- IMGT numbering scheme 206
- Kabat numbering scheme 203
- numbering schemes 202–208
- biolayer interferometry (BLI) 129–132, 131
- biological disease-modifying antirheumatic drugs (bDMARDs) 2027–2028
- Biologics Price Competition and Innovation Act (BPCI Act) 684, 1238
- biopsy-proven acute rejection (BPAR) 1378
- biosimilar monoclonal antibody
 - asparagine residues 691
 - biologics complexity and manufacturing process 687, 690
 - biosimilar candidate and RMP 687, 688
 - chemistry, manufacturing and controls (CMC) standards 685
 - chimeric/humanized recombinant mAbs 681
 - clinical development. *See* clinical development, biosimilar monoclonal antibodies
 - cysteine oxidation 691
 - disulfide bonds 687
 - drug development 685–686
 - in emerging markets 684–685
 - EU approach. *See* European Union (EU) approach, biosimilars
 - glycation 688
 - glycosylation 688
 - healthcare systems 681–682
 - immunoglobulin G (IgG) Fc fusion proteins 694
 - in living organisms 682
 - lysine-clipping results 688
 - manufacturing process development 691–692
 - physical stress 691
 - physicochemical and biological properties 685
 - preclinical development. *See* preclinical development
 - pyroglutamate formation 688
 - QTPP 686–687
 - regulatory authorities 682
 - “stand-alone” CMC part and comparability exercise 693
 - state-of-the-art methods 687, 689–690
 - “totality-of-the-evidence for biosimilar and innovator development” 693,
 - US 684
- bispecific antibodies
 - applications 268
 - B-cell lymphoma 288
 - catumaxomab (Removab) 1464–1465
 - chemical conjugation 269–271
 - CTLs, clinical trials 282
 - dual targeting strategies 289–291
 - effector cells retargeting. *See* effector cells retargeting and bispecific antibodies
 - effector molecules retargeting 285–289
 - Fc receptor, recombinant 285
 - generation 268
 - hapten-binding 289
 - recombinant. *See* recombinant bispecific antibody molecules
 - somatic gene therapy 291–293
 - somatic hybridization 268–269
- BL/BLL. *See* Burkitt’s and Burkitt-like lymphoma (BL/BLL)
- BLI. *See* biolayer interferometry (BLI)
- blisibimod 942, 1119
- BMS-981164 1011
- bone marrow transplant (BMT) 1329
- bone metabolism. *See* sclerostin
- botulinum neurotoxins 1201
- BPCI act. *See* Biologics Price Competition and Innovation Act (BPCI Act)
- branch retinal vein occlusion (BRVO) 1886, 1888, 1890–1891
- breast cancer
 - anastrozole plus trastuzumab 2047
 - eLEcTRA trial 2048
 - gemcitabine 2046
 - monoclonal antibodies 2048
 - TAnDEM trial outcome 2047
 - taxanes, trastuzumab in combination 2044–2046
 - TKI 2048
 - trastuzumab monotherapy. *See* trastuzumab monotherapy
 - triple combinations, trastuzumab 2047
- brentuximab vedotin
 - ALCL. *See* anaplastic large cell lymphoma (ALCL)
 - antibody-drug 1417–1418
 - CD30 1417–1418
 - description 1417
 - DLBCLs 1435
 - Hodgkin’s lymphoma 759–760
 - MMAE 1417
 - preclinical activity 1419

- brentuximab vedotin (*cont'd.*)
 - primary cutaneous CD30-positive lymphoproliferative disorders 1433–1435
- briobacept 1119
- BRVO. *See* branch retinal vein occlusion (BRVO)
- BSC. *See* best supportive care (BSC)
- BT-063 (Biotest AG) 1008
- BTT-1023 (Biotie) 1135
- Burkitt's and Burkitt-like lymphoma (BL/BLL) 1958
- c**
- C-chemokine receptor 4 (CCR4) 947, 1018–1019, 2115, 2116
- C-chemokine receptor 5 (CCR5) 1203
- C5 glycoprotein 1166–1168
- CA IX. *See* carbonic anhydrase IX (CA IX)
- calicheamicin conjugates
 - action mechanisms 1552
 - antibody-lysine site modification 357
 - cellular uptake and intracellular processing 1551
 - conjugate design/preclinical activity 1549–1550
 - DNA binding 1550
 - GO. *See* gemtuzumab ozogamicin (GO)
 - immunoconjugates 1555
 - IO. *See* inotuzumab ozogamicin (IO)
 - linker choice 1550–1551
 - resistance mechanisms 1552–1553
 - stable hydrazone linkage 356
- canakinumab
 - CAPS. *See* cryopyrin-associated periodic syndrome (CAPS)
 - cardiovascular risk. *See* cardiovascular risk
 - gouty arthritis 1450–1452
 - interleukin-1 (IL-1) 1445
 - marketed drug product 1446, 1447
 - production, pharmacology and pharmacokinetics 1446
 - RA. *See* rheumatoid arthritis (RA)
 - sJIA 1452–1454
 - type II diabetes 1456–1457
- cancer
 - drug targeting 503–504
 - eAds blocking, cell signaling 503
 - imaging 502–503
 - soluble ligands, irreversible removal 504–505
- cancer, Ab2
 - B cell malignancies 415
 - carcinoembryonic antigen (CEA) 416
 - CeaVac and TriAb 416
 - Ep-CAM 416
 - phase II clinical trials 417
 - protein and non-protein tumor-associated antigens 415
 - racotumomab and TriGem vaccines 415–416
 - sialic acid-containing glycosphingolipids 415
 - tumor-associated antigens 416
- cancer therapy
 - hybridomas 787
 - immunoconjugates. *See* immunoconjugates
 - innate immunity. *See* innate immunity
 - intracellular signaling. *See* intracellular signaling
 - rituximab, anti-CD20 antibody 787
 - unclear/unknown mechanisms 809–811
 - unique mechanisms 811–812
- canonical residues
- CDR-grafting 93
- light-and heavy-chain variable regions 102
- canstatin 829
- capromab (ProstaScint™) 2126–2129
- carbonate linkers 356
- carbonic anhydrase IX (CA IX) 543, 767–768
- carboxypeptidase G2 (CPG2)
 - CC3 xenograft model 477
 - dimethyl sulfoxide (DMSO) 477
 - drug-resistant ovarian xenograft model 478
 - *Pseudomonas* species 477
 - radioimmunoassay 477
 - xenograft-bearing mice, CEA 477
- cardiac adverse events
 - cardiotoxicity 2055
 - clinical trial data 2054
 - HERCULES multicenter phase II trial 2057
 - left ventricular ejection fraction (LVEF) 2055
 - symptomatic cardiac events 2056–2057
- cardiovascular risk
 - atherosclerosis 1457
 - CRP 1457
 - phase III outcome 1457
- CARs. *See* chimeric antigen receptors (CARs)
- Castleman's disease 2032
- catalytic antibodies
 - bispecific anti-tumor/abzyme molecules 479
 - description 478
 - synthetic antibody libraries 478–479
- catalytic protease. *See* pro-protein convertase subtilisin kexin (PCSK)-9

- cation-exchange (CEX) chromatography 624
- catumaxomab (Removab). *See also* Triomab® trAb family
 - anti-EpCAM × anti-CD3. *See* anti-EpCAM × anti-CD3 catumaxomab
 - bispecific antibodies 1464–1465
 - CTLs 283
 - gastric cancer treatment 1480–1481
 - ovarian cancer patients 1481
 - peritoneal carcinomatosis 1479–1480
 - systemic treatment outcome 1478–1479
 - trAb. *See* trifunctional antibodies (trAb)
 - tumor treatment 1469, 1471
- C5b-9 MAC 1166
- CD6
 - 105–130-kDa surface glycoprotein 901
 - CD6-positive T cells 902
 - itolizumab 902
 - ligands 901
 - mature thymocytes 2113
 - positive effects, alloHSCT without GvHD 1096
 - T cell activation 2114
- CD20
 - 33–37-kDa non-glycosylated phosphoprotein 902
 - ADCC and ADCP activity 1697
 - ADCC potency 1706
 - B-cell expression 1115–1116, 1702
 - on B cells 1749–1752
 - B-cellular non-Hodgkin’s lymphoma 753
 - in bloodstream 1748
 - CDC and ADCC 903
 - characteristics 1696, 1698–1699, 1748–1752
 - chimeric murine/human mAb 1342
 - complement exhaustion, killing impact 1750
 - cynomolgus monkeys 376
 - cytotoxicity mediated, type I mAbs 1735
 - exhaustion, two-step *in vitro* model 1751
 - expressing Z138 tumor cells 1702–1703
 - FDA, cancer treatment 1733
 - humoral immunity 902
 - hypothetical model 1698
 - *in vitro* action mechanism 1695–1697
 - *in vitro* trogocytosis 1751
 - interactions 1735–1736
 - internalisation 1707, 1752
 - intravenous infusion 1749
 - MS4a family, integral membrane proteins 1737–1738
 - next-generation 1735–1736
 - obinutuzumab 754–755, 1698–1699
 - ocrelizumab 903–904
 - ofatumumab 753–754, 791, 903
 - rituximab and ofatumumab 143
 - rituximab mechanisms 1912
 - tetramers 1696
 - therapeutic target 1910–1911
 - type I and II 1695–1697, 1696
 - with ⁹⁰Y-ibritumomab tiuxetan 1583
- CD22
 - ADCs with uncleavable linkers 371
 - B-cell lineage restricted transmembrane glycoprotein 371
 - epratuzumab 904–905
 - expression, B-cell neoplasias 1547–1548
 - SIGLECs 904
 - targeting inotuzumab ozogamicin 353
- CD30
 - HDACs 1419
 - mutations 1419
 - preclinical activity 1419
 - TRAF 1418–1419
- CDC. *See* complement-dependent cytotoxicity (CDC)
- CDP7657 (UCB and Biogen-IDEC) 1091
- CDR-grafting
 - anti-Tac antibody 92
 - B-cell chronic lymphocytic leukemia (B-CLL) 91
 - 3D computer modeling, antibody structure 95–97
 - design cycle 92
 - donor anti-hapten antibody B1–8, murine 90
 - human framework sequences. *See* human framework sequences, CDR-grafting
 - identification, putative backmutations. *See* putative backmutations
 - P67.6 antibody 1550
 - source (donor) sequence analysis 92–95
 - stability 104
 - VL and VH, rat antibody Campath-1R 91
- CDR-IMGT grafting 246, 247
- CDRs. *See* complementarity determining regions (CDRs)
- cell culture
 - “continuous” processes 615, 616
 - culture medium and aeration 615
 - disadvantages 615
 - feeder 30
 - feeding strategies 617
 - fully disposable manufacturing, drug substance 615, 616
 - growth characteristics 615, 616
 - *in vitro* cultivation systems 614–615

- cell culture (*contd.*)
 - inoculum phase 615
 - mammalian 571
 - media 614
 - media and tailor-made process design 604
 - nonoptimal agitation/aeration 641
 - perfusion 616–617
 - recombinant Sp2/0 murine myeloma cell line 2069
- cell distribution, IgE
 - APCs 1786
 - physiologic and pathophysiologic significance 1786–1787
 - surface of effector 1785–1786
- cell fusion
 - bacterial and viral infections, rodents 24
 - hybridoma production 18
 - immunized mice 23
 - monoclonal antibodies generation 23, 24
 - nonproducing variants 23
 - poly ethylene glycol (PEG) 23
 - time course, hybridoma development 24–25
- cell lysis
 - ADCC 1328
 - alemtuzumab 1327–1328
 - apoptosis 1328
- cell surface antigens 127–128, 341, 791
- cell-surface receptors
 - CD6 901–902
 - CD20 902–904
 - CD22 904–905
- central retinal vein occlusion (CRVO) 1886, 1890
- certolizumab pegol
 - CD 2096, 2097
 - description 2095
 - investigational indications 2100–2101
 - marketing applications 2096
 - methotrexate (MTX) 2096
 - and RA 2098–2100
 - safety 2096
- cetuximab (Erbix)
 - advanced pancreatic cancer 1511
 - in cancer 1502
 - carboplatin and 1511
 - chimerization 1503
 - in clinics 1511–1512
 - colon cancer, clinical results. *See* colon cancer
 - epidermal growth factor receptor (EGFR) 1501–1502
 - KRAS and 1505
 - mechanism of action 1503–1505
 - monoclonal antibody 225 1503
 - NSCLC, clinical results. *See* non-small-cell lung cancer (NSCLC)
 - preclinical results 1506
 - production 1511
 - SCCHN, clinical results. *See* squamous cell carcinoma of head and neck (SCCHN)
- CEX. *See* cation-exchange (CEX) chromatography
- chaperonin 10 1150
- CHD. *See* congenital heart disease (CHD)
- chemical immunoconjugates
 - ADCs first-generation, within phase I/II clinical trials 364, 366
 - clinical efficacy 364
 - cross-linkage heterogeneity. *See* cross-linkage heterogeneity
 - cytotoxic drugs 363–364
 - effector moieties. *See* effector moieties
 - GPNMB glembatumumab vedotin 364
 - hybridoma technology 364
 - infusional and hypersensitivity reactions 364
 - ITCs first-generation, within phase I/II clinical trials 364, 365
 - linker stability 364, 367–368
 - target antigens, characteristics 370–371
- chemokine inhibitors
 - anti-CCR4 1018–1019
 - anti-CXCL10 1019–1021
 - anti-CXCR5 1017–1018
 - anti-eotaxin-1 1015–1017
 - anti-MIF 1022–1023
 - anti-RANTES 1021–1022
 - bertilimumab 1017
- chimeric antigen receptors (CARs)
 - adoptive cellular immunotherapy 520, 538–540
 - antibodies and T cell receptors 521–522
 - autologous tumor-specific T cells 519
 - capping, shedding/endocytosis 519
 - CAR-modified T lymphocytes 540–545
 - double chain CARs 523–524
 - extracellular spacer domains 528–529
 - first signal 525–526
 - immunoglobulin T cell receptors 522–523
 - immunological effector lymphocytes 519
 - monoclonal antibodies 519
 - neovascularization, solid tumors 546
 - preclinical studies. *See* preclinical studies, CARs
 - receptor gene-modified effector lymphocytes 546

- redirected T cells/alternatively T-bodies 520–521
- second and third signals 529–530
- signal domains, downstream signal molecules 526–528
- single-chain CARs 524–525
- TAA 520
- transmembrane domain 528
- tumor taxis and CAR⁺ effector cells 545–546
- CHOP. *See* cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP)
- choroidal neovascularization (CNV)
 - choroidal vessels 1887
 - development 1884
 - macrophages 944
 - PDT treatment 1891
 - prevalence 1886
 - pro-angiogenic cytokines 1885
 - REPAIR clinical trial 1891
 - right eye 1888
 - S1P levels 1179
- Chothia numbering scheme 204–205, 207
- chronic lymphocytic leukemia (CLL)
 - alemtuzumab 86, 1330–1331
 - FC chemotherapy 1971
 - FCR therapy 1968
 - fludarabine 1333, 1334–1336
 - FR-based regimens 1970–1971
 - grade 3/4 hematologic toxicities 1335–1336
 - hematologic toxicities 1334
 - infections 1334
 - infusion-related and hematological toxicity rates 1964, 1968
 - malignant cells 87, 1331, 1334–1335
 - monotherapy 1753
 - non-CHEMO agents 1971–1973
 - ORR 1335
 - p53 abnormalities 1336
 - R-chlorambucil vs. chlorambucil alone 1970
 - R-FC vs. FC 1968–1969
 - rituximab monotherapy 1964, 1965–1967
 - rituximab retreatment 1973–1974
 - rituximab SC 1985–1994
 - salvage therapy 1331
 - and SLL 1936
 - symptoms 1917
 - thrombocytopenia 1331
 - treatment 1333–1334
- cixutumumab (IMC-A12) 766–767, 799
- clazakizumab 869, 987–988
- clinical development, biosimilar monoclonal antibodies
 - efficacy and safety 699–700
 - pharmacokinetics and pharmacodynamics 697, 698–699
 - pharmacovigilance and risk management 701
- CLL. *See* chronic lymphocytic leukemia (CLL)
- CMV. *See* Cytomegalovirus (CMV)
- CNOP. *See* cyclophosphamide, mitoxantrone, vincristine and prednisone (CNOP)
- CNTO-3157 1149
- CNV. *See* choroidal neovascularization (CNV)
- colon cancer
 - bevacizumab 1508
 - COIN and NORDIC-VII trails 1508
 - combination therapy 1507–1509
 - CRYSTAL phase III trial 1508
 - EGFR on tumor tissue 1506
 - grade 3/4 adverse events 1507
 - II/III clinical trials 1507–1508
 - KRAS mutation status 1508
 - NORDIC-VII study 1508
 - toxicity 1507
- commercial manufacturing processes
 - biosimilar mAb 682
 - description 639–640
 - downstream manufacturing 643–645
 - economy of scale 645–646
 - harvest 642–643
 - large-scale unit operations and systems 639
 - process characterization and validation 646–647
 - upstream manufacturing 640–642
- comparability and risk assessment 653–652
- complement-dependent cytotoxicity (CDC)
 - antibodies, indirect effects 143
 - CD20-positive lymphoma cells elimination 144
 - C1q binding capacity 146
 - description 791
 - Fc-mediated Mo 145
 - Fcy receptor polymorphisms 145
 - ofatumumab, human mAb 791
 - rebmab 100 (hu3S1932) 791–792
 - rituximab 1911–1912
 - veltumumab (IMMU-106) 791
- complement inhibitors
 - anti-C5/C5a/C5aR 1166–1169
 - anti-factor D 1169–1170
 - CD55 1913
- complement system
 - activation 157–158

- complement system (*contd.*)
 - CDC. *See* complement-dependent cytotoxicity (CDC)
 - as confounding factor 1745–1746
 - IgG antibodies, classical complement pathway 146
 - monoclonal antibodies, MoA 143
 - ofatumumab 1735, 1750
- complementarity determining regions (CDRs)
 - “abbreviated CDRs” 105
 - antibody engineering, chimeric and CDR-grafted mAbs 91
 - antibody structure prediction 216, 217
 - antigen binding and specificity 668
 - bioinformatics tools, antibodies analysis 208–209
 - chimeric/humanized antibodies 36
 - Chothia definitions 92–93
 - description 92
 - error-prone PCRs 118
 - murine 107
 - murine complementary regions 665
 - obinutuzumab (GA101, GAZYVA) 1697
 - structure, antibody 26–2F FAB 93
- conditionally replicative adenoviruses (CRAds) 293
- congenital heart disease (CHD)
 - children, RSV hospitalization 1838–1839
 - mechanical ventilation 1837
 - motavizumab 1845
 - prevalence 1841
- congestive heart failure
 - adalimumab 1311
 - cardiac adverse events 2055
 - safety 1613
 - trastuzumab trials 2056
- contiguous hypervariable loop region
 - adnectins 451
 - Anticalins[®] 452
 - CTLA-4 450
 - fynomers 451
 - human fibronectin type III (FN3) 450–451
 - lipocalins 451–452
 - natural immune system 450
 - neutrophil gelatinase-associated lipocalin (NGAL) 453
 - phagemid display library 451
 - 174-residue bilin-binding protein (BBP), *Pieris brassicae*, 452
 - tendamistat, soluble 74 amino acid inhibitor 450
- Contract Research Organisation (CRO) 729–730
- costimulatory molecules 1086, 1087, 1090, 1093
- CPG2. *See* carboxypeptidase G2 (CPG2)
- CQA. *See* critical quality attribute (CQA)
- CRAds. *See* conditionally replicative adenoviruses (CRAds)
- critical quality attribute (CQA)
 - non-human glycan patterns 692
 - physicochemical and biological properties 685
- CRO. *See* Contract Research Organisation (CRO)
- Crohn’s disease (CD)
 - CERTIFI (NCT00771667) 2077
 - infliximab 1602–1603,
- cross-linkage heterogeneity
 - drug antibody ratio (DAR) 369
 - EU and Kabat numbering 369
 - maleimide-linked payloads 370
 - “naked” IgG contaminations 369
 - SMCC and SMPT 369
- CRS. *See* cytokine release syndrome (CRS)
- CRVO. *See* central retinal vein occlusion (CRVO)
- cryopyrin-associated periodic syndrome (CAPS)
 - canakinumab 1448, 1449
 - and FCAS 1448
 - inflammatory markers 1448
 - NLRP3 gene 1448
 - treatment 1450
- cryptic and conformational epitopes
 - amyloid fibrils 323
 - chemokine receptor (CXCR4) 323
 - enzyme active sites and viral clefts 323
 - inhibition, fibril formation 323
- CSF2 (GM-CSF) 1025–1026
- Cunningham study 1955
- cutaneous T-cell lymphomas (CTCLs)
 - CD52 expression 1353
 - CMV reactivation 1355
 - mycosis fungoides/Sézary syndrome 1353
 - PTCL 1355
 - response rates, alemtuzumab 1353–1355
- CVP. *See* cyclophosphamide, vincristine, prednisone (CVP)
- CXCL10 990, 1019–1020, 1021, 1148
- CXCR5 1017–1018
- cyclophosphamide-based regimens 1922
- cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP)
 - DLBCL 1955
 - failure-free survival (FFS) rate 1951–1952
 - HIV-associated lymphomas 1977

- MCL. *See* mantle cell lymphoma (MCL)
 - median PFS 1942
 - MInT 1952–1953
 - ORR and CR rates 1930, 1950
 - PMBCL. *See* primary mediastinal B-cell lymphoma (PMBCL)
 - sequential rituximab 1923
 - VNCOP-B 1945
 - cyclophosphamide, mitoxantrone, vincristine and prednisone (CNOP) 1922, 1930
 - cyclophosphamide, vincristine, prednisone (CVP)
 - CLL. *See* chronic lymphocytic leukemia (CLL)
 - CT 1941–1942
 - R-CVP 1924–1925
 - SABRINA 1992
 - cytokine inhibitors
 - anti- α V β 6 integrin 1013–1014
 - TGF β inhibitors 1011–1013
 - TH1 cytokines 970–1000
 - TH2 cytokines 1000–1011
 - cytokine release syndrome (CRS)
 - anti-TNF mAbs 1670
 - *in vitro* cytolytic assays 1662
 - indomethacin 1669
 - M-CD3 and 1665–1666
 - management 1666
 - methylprednisolone 1666–1668
 - pathophysiology 1662–1663
 - pentoxifylline 1668–1669
 - recombinant human soluble tumor necrosis factor receptor 1669–1670
 - symptoms 1663–1664
 - T cell function 1662
 - cytomegalovirus (CMV)
 - antigenemia 1343
 - IgG 1203
 - infection 1342
 - MSL-109 resistance 1203
 - pneumonitis and oral candidosis 1338
 - reactivation 1343
 - cytotoxic compounds, ADCs
 - DNA-/DNA-topoisomerase-targeted cytotoxic agents 352–353
 - microtubule-targeted cytotoxic agents 346–352
 - cytotoxic T-lymphocyte antigen 4 (CTLA-4)
 - B7 ligands binding 1620
 - CD4+ 1620
 - immunomodulatory cytokines 1620
 - MYPPPY sequence 1620
 - cytotoxic T lymphocytes (CTLs)
 - anti-CD3 antibody TR66 281
 - bispecific antibodies, clinical trials 282
 - catumaxomab 283
 - CD28 binding to monoclonal antibodies 281–282
 - ertumaxomab 283
 - major histocompatibility complexes (MHCs) 279
 - monoclonal antibodies, chemical heteroconjugation 283
 - TriomAbs 283
 - tumor cells 280
 - 3D computer modeling, antibody structure
 - *ab initio* methods 96–97
 - cocaine-binding antibody 97
 - humanized antibody 95–96
 - putative backmutations 96
 - QUANTA and CHARMm 96
 - SCRs 96
 - stereochemical verification model 97
 - Swiss PDB Viewer and academic servers 97
 - V and C domains 97
- d**
- dacarbazine (DTIC)
 - adverse events 1640
 - melanoma patients 1622
 - patients without brain metastasis 1628–1629
 - phase II open-label trial (MDX010-08) 1625
 - dalotuzumab (MK-0646) 766, 800
 - Data Bank of Japan (DDBJ) 233
 - Db. *See* diabodies (Db)
 - DC-SIGN. *See* dendritic cell-specific intercellular adhesion molecule 3-grabbing nonintegrin (DC-SIGN)
 - dekavil 1185
 - dendritic cell APCs 1800
 - dendritic cell-specific intercellular adhesion molecule 3-grabbing nonintegrin (DC-SIGN) 184
 - denosumab (Prolia®)
 - diseases and targets 775–776
 - FDA guidelines 1526–1527
 - FREEDOM (phase 3 study) 1524–1525
 - HALT (phase 3 study) 1526
 - osteoporosis 1521
 - osteoprotegerin-immunoglobulin Fc segment complex (OPG-Fc) 1521
 - phase 1 study 1522–1523
 - phase 2 study 1523–1524
 - RANK/RANKL signaling pathway 1522
 - RANKL 1521

- denosumab (Prolia[®]) (*cont'd.*)
- STAND (phase 3 study) 1525–1526
 - urinary NTX/creatinine 1523
- dermatology life quality index (DLQI) 1317, 1539, 2072, 2074
- diabetes
- type I 152, 413, 876, 949–950, 1080, 1886
 - type II 853, 873, 875, 950–951, 1095, 1456–1457
- diabetic macular edema (DME)
- blood-retinal barrier 1886
 - definition 1886
 - FDA approval 1889
 - macular laser procedures 1890
 - retinal hemorrhages, intraretinal cysts and microaneurysms 1887
- diabodies (Db) 272, 273–274
- diffuse large B-cell lymphoma (DLBCL)
- CD30-positive 1435
 - CR rates of R-ICE 1955
 - DA-EPOCH 1950
 - GELA LNH98-5 trial 1950, 1951
 - intergroup E4494 trial 1950, 1951–1952
 - MInT 1952–1953
 - and relapsed MCL 1973–1974
 - retrospective population analyses 1953
- dipeptidyl peptidase IV (DPPiV) 1095–1096
- direct cell death induction, obinutuzumab
- ability 1702
 - B-cell malignancies 1703
 - CD20, B-cell cycle progression 1702
 - CD40-induced resistance mechanisms 1703
 - fluorescence-activated cell sorting (FACS) analysis 1703
 - HLA-DR 1702
 - host immune response 1704
 - murine type II CD20 antibody B1 1702
 - primary B-cell chronic lymphocytic leukemia (B-CLL) cells 1703
 - ROS in human B-lymphoma cell lines 1703
 - in Z138 MCL cells 1702
- disease-modifying antirheumatic drugs (DMARDs) 505, 936–937, 986, 1120, 1567, 1571, 1980, 2027, 2029, 2030, 2096
- disk stack centrifugation system 642–643
- disulfide linkers 355–356
- DLBCL. *See* diffuse large B-cell lymphoma (DLBCL)
- DLQI. *See* dermatology life quality index (DLQI)
- DLX105 ESBA-105 974
- DME. *See* Diabetic macular edema (DME)
- double chain CARs
- antibody V regions 524
 - chimeric TCR variants 523
 - Fab fragments 524
 - functional antigen-binding Fv/Fab fragment 524
- downstream processing. *See also* commercial manufacturing processes
- AEX 624
 - affinity chromatography 622–623
 - antibody's purity and monomer content 623
 - automation/miniaturization 627,
 - binding proteins 440
 - biotherapeutic molecules 619,
 - CEX 624
 - description 618
 - development concepts 628
 - disposable and single-use concepts 627, 628
 - drug substance manufacturing 625
 - efficacious and safe therapeutic antibodies 620
 - HIC 623
 - IEC 623–624
 - microfiltration 1833
 - monoclonal antibodies 620–622
 - process-related impurities 619–620
 - product-related impurities 620
 - and production, antibody 1833–1835
 - resins and ligands 626
 - separation technologies 626–627
 - small-scale and large-scale processes 643
 - stress conditions 620
 - ultra/diafiltration (UF/DF) 622
 - validation, DNA removal 624–625
 - virus clearance 625,
 - virus filters 644
- dromedary IgG2 and IgG3 247–248
- DTIC. *See* dacarbazine (DTIC)
- dual targeting strategies, bispecific antibodies 289–291
- dupilumab 948, 1002–1003
- e**
- E. coli* S30 399–400
- eAds. *See* engineered antibody domains (eAds)
- early breast cancer (EBC)
- adjuvant trastuzumab 2049–2050
 - adjuvant treatment 2053
 - disease-free survival, EBC trials 2052
 - docetaxel 2054
 - FinHer trial 2052
 - HERA trial 2050, 2051

- infusion-related reactions 2054
- MBC 2049
- and PST 2048
- response rate 2049
- trastuzumab monotherapy/combination therapy 2053–2054
- trastuzumab treatment, tumor types 2053
- eculizumab 1167
 - adverse reactions 2101
 - approved indications 2102–2103
 - C5 2101
 - IgG2 sequences 2101
 - investigation use 2103–2104
- efalizumab (Raptiva)
 - absorption 1537
 - action mechanism 1535
 - administration, psoriatic plaques 1536
 - anti-mouse CD11a antibodies 1535–1536
 - antibody, development and characterization 1531–1532
 - biotransformation 1537
 - chimpanzees, immunization 1536
 - dose-dependent nonlinear pharmacokinetics 1537
 - elimination 1537
 - health-related quality of life (HRQoL) 1539
 - *in vitro* studies 1535
 - long-term efficacy 1538–1539
 - psoriasis treatment. *See* psoriasis
 - randomized controlled clinical trials (RCTs) 1540–1541
 - randomized, placebo-controlled, double-blind studies 1538
 - safety and tolerability 1539–1540
 - single-dose intravenous study 1536
 - subcutaneous effects 1537
- effector cells retargeting and bispecific antibodies
 - CTLs 279, 279–283
 - Fc receptor 283–285
 - phagocytosis 278
- effector moieties
 - calicheamicins and microtubule inhibitors 372
 - cytostatic drugs 372
 - diphtheria toxin (DT) 372
 - onconase (ONC) 373–374
 - pancreatic RNase A family 373
 - proapoptotic proteins 374
 - *Pseudomonas* exotoxin (PE) 372
 - ribosome-inactivating proteins (RIPs) 373
- EGFR. *See* epidermal growth factor receptor (EGFR)
- elidelumab 1020–1021
- elotuzumab (anti-CS1) 757–758
- endostatin
 - anticancer spectrum 829
 - Down syndrome 828
 - functions 828
 - integrin deficiency 828
 - NSCLC 829
 - proteolytic cleavage 828
 - wnt-signaling pathway 828
- engineered antibody domains (eAds)
 - cancer, targeting. *See* cancer
 - clinical/preclinical development 489, 490–491
 - HCABs 489
 - hematological disorders. *See* hematological disorders, eAds
 - vs. HIV-1. *See* human immunodeficiency virus type 1 (HIV-1)
 - human IgG CH₂ 495
 - inflammation. *See* inflammation, eAds
 - libraries. *See* libraries
 - VH and VL 494
 - V_HH 492, 493
 - VNAR 492, 493
 - X-ray and NMR structures 489
- enhanced Chothia (Martin) numbering scheme 206, 207
- envelope (env) proteins 1183–1184
- enzyme-linked immunosorbent assay (ELISA)
 - ADA measurement against antibodies 672
 - HCPs 648
 - heavy-and light-chain subclasses, hybridoma antibodies 27
 - hybridoma supernatants 27
 - microtiter plates and binders 126
 - polyclonal phage preparations 46
 - RSV replication 1832
 - solid phase 27, 28
 - SPR, BLI and KinExA 132
- eotaxin-1 1015–1017
- epidermal growth factor receptor (EGFR)
 - acne-like skin rash 761
 - drug hypersensitivity reactions 762
 - necitumumab 762
 - nimotuzumab 762–763
 - ramucirumab (VEGF-R) 764
 - signaling proteins, K-RAS/N-RAS 761
 - squamous cell carcinoma 761–762
 - trastuzumab emtansine (Her2/Neu) 763–764
 - tumor cell proliferation and neoangiogenesis 761
 - zalutumumab 762

- epithelial cell adhesion molecule (EpCAM).
 See anti-EpCAM antibodies
- epitope recognition
- avidity and bivalent binding 1699
 - binding properties and 1699
 - ofatumumab 1737–1739
 - rituximab and 2H7 binding 1701
 - Scatchard analysis 1699
 - type II and crystal structure 1700
- epratuzumab 904–905
- error-prone PCRs
- amino acid exchange 118
 - and mutated sequences 153
 - PCR-based mutagenesis and DNA shuffling 118
- ERVWE1 env (syncytin-1) 1184
- ESBA1008 1178
- ESBA-105 Novartis 973–974
- Escherichia coli*
- aglycosylated IgG antibodies 562
 - BAC purification 79, 80
 - *Campylobacter jejuni*, 563
 - conventional expression systems 440
 - cyclodextrin glycosyl transferase 564
 - genetic modifications 563
 - prokaryotic cell expression 374
 - protease-deficient strains 563
 - proteins purification 563
 - random mutagenesis 563
 - recombinant protein expression 562
 - redox mutant (*trxB gor*) strains 563
 - S30 cell-free lysate 399
 - Sec-secretion pathway 563
- esophageal and gastric cancer 1684–1685
- etrolizumab 1130
- eukaryotic expression systems
- filamentous fungi 569–570
 - hosts 565
 - insect cells 570–571
 - mammalian cells. See mammalian cells
 - plants 579–580
 - protein secretion 565
 - transgenic animals 580–581
 - yeast 565–569
- European Organization for Research and Treatment of Cancer (EORTC) 1475, 1930, 1942
- European Union (EU) approach, biosimilars
- CHMP 684
 - Epoetin alfa 683
 - European Medicines Agency (EMA) guidelines 682
 - marketing approvals 683
 - regulated markets 684
- evolocumab (AMG 145)
- GAUSS trial 853
 - human monoclonal immunoglobulin G2 (IgG2) antibody 853
 - phase III trials with 854–857
 - RUTHERFORD trial 853
- expression systems
- ADCC and CDC 609
 - ammonia 607
 - antibody-derived formats and scaffold proteins 605–606
 - biopharmaceuticals 612
 - cell engineering strategies 609
 - cell variance, host cell lines 610
 - cis-active elements 608
 - clone-screening platforms 610–611
 - co-transfection 608
 - endogenous DHFR/GS activity 607
 - *Escherichia coli*, 613
 - Fc-linked N-glycans 609
 - fundamental problems 613
 - gene expression 606
 - glycostructures 609
 - GlymaxX technology 610, 611
 - high-mannose-type O-glycosylation 612
 - internal ribosomal entry site (IRES) 608
 - mammalian-cell-based systems 606
 - metabolic selectable marker genes 607
 - mRNAs 606
 - nonviral DNA delivery methods 607
 - post-translational modifications, protein 609
 - recombinant biopharmaceuticals 605
 - recombinant proteins 605
 - redominant mammalian host cell line 606
 - targeted integration systems 608–609
 - transient 607
- extracellular spacer domains, CARs 528–529
- f**
- fanolesomab (LeuTech®, NeutroSpec®) 2132–2134
- farletuzumab (MORAb-003) 769
- Fc engineering
- ADCC 156
 - bacterial-based screening system 157
 - 113F variant 156
 - Fc-attached carbohydrate structures 156
 - Fc variants harboring amino acid exchanges 156
 - FcγRIIIa binding affinity 156
 - lacking Fc glycosylation 156
- Fc-fusion
- anti-EGFR sdAb 329

- anti-TNF Fc-fusion molecule ART621 330
- and approved mAbs 1234–1235, 1237
- description 329
- neo-epitopes 677
- proteins 1234–1235, 1237, 1238
- Fc receptor. *See* also protein-engineered antibodies
 - CD16 284
 - granulocyte colony-stimulating factor (G-CSF) 284
 - NK cell-mediated cytotoxicity 284
 - recombinant bispecific antibodies 285
 - toxicity 284
- FcεRI (high-affinity IgE receptor)
 - cell activation 1782–1783
 - expression, basophils and mast cells 1783, 1784
 - IgE binding 1781–1782
 - mast cells, basophils and DCs 1781,
- FcεRII (low-affinity IgE receptor)
 - activation 1784
 - CD23 functions 1784–1785
 - IgE binding 1784
 - transmembrane polypeptides 1783, 1784
- FFP-102 1091
- figitumumab (CP-751,871) 767
- filamentous fungi
 - antibody fragments 569
 - *Aspergillus* species 570
 - description 569
 - fungal high-mannose glycans 570
 - IgG antibodies, fungal expression 570
 - KexB cleavage site 569
 - recombinant heterologous products 569
 - *T. reesei* cellobiohydrolase I (CBHI) 569
- first-in-man (FIM) safety
 - clinical trial authorization 1277–1278
 - comparability investigations 1275–1276
 - modes of action 1273
 - post-marketing activities 1279–1280
 - pre-authorization interactions 1276–1277
 - risk management plan 1278–1279
 - Tegenaro case 1272–1273
- first signal, CARs
 - effector mechanisms, CAR⁺ cytotoxic lymphocytes 525
 - signaltransduction, T cells 526, 527
 - TCR complex and FcεRIγ chain 526
- FL. *See* follicular lymphoma (FL)
- fludarabine 1333, 1334–1331
- follicular lymphoma (FL)
 - CD80 expression 757
 - DLBCL 1485
 - inotuzumab ozogamicin 367–368
 - monotherapy 1753–1756
 - ocrelizumab 903
 - ofatumumab 380
 - rituximab, phase I/II study 903
 - ⁹⁰Y-ibritumomab tiuxetan 1585
 - follow-on monoclonal antibody 684–685
 - foralumab 1083
 - Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM)
 - denosumab efficacy 1524–1525
 - hypocalcemia 1525
 - nonvertebral fractures 1525
 - free serum IgE concentration, rhuMAB-E25 1790, 1791
 - freedom to operate analysis
 - CDR sequences 714
 - divisional applications 714
 - Europe and United States 713
 - “infringement” 711, 712–713
 - licensing negotiations 711
 - parameters 713
 - specialist skills 713
 - therapeutic antibodies 711
 - freeze-dried protein formulations 638
 - fresolimumab 794–795, 1013
 - fucose and bisecting *N*-acetylglucosamine
 - anti-epidermal growth factor receptor (EGFR) 181
 - complement-dependent cytotoxicity (CDC) 182
 - “knockout” CHO cell line 181
 - neutrophil-mediated ADCC 181
 - Potelligent technology 181
 - fusion peptide 1827
 - fusion protein. *See* recombinant scFv-CPG2 fusion protein

g

 - gag*-encoded protein 1183
 - galactosylation
 - DC-SIGN 184
 - dendritic cells 183
 - glycoforms 182
 - hydrogen/deuterium exchange 183
 - mannan binding lectin (MBL) 183
 - recombinant IgG antibody therapeutics 183
 - rheumatoid arthritis (RA) 182
 - tumor necrosis factor receptor 183
 - galiximab 757, 1087–1088
 - ganitumab (AMG 479), 765–766
 - gantenerumab 908–909, 1219–1220

- GELA LNH98–5 trial 1950, 1951
- gemcitabine
- and bleomycin 1437
 - and carboplatin 2092
 - and nimotuzumab 1685
 - and placebo group 1685–1686
 - regimens 1955
 - and rituximab 1979
- gemtuzumab ozogamicin (GO)
- allogeneic stem cell transplantation 1555
 - CD33-positive leukemic cells 1553
 - CMA-676 1553
 - composition 1548
 - conjugate design/preclinical activity 1548
 - dose and schedule 1554–1555
 - French ALFA trial 1555
 - IgG4 moiety 1549
 - Italian GIMEMA assessed 1554
 - myeloid cells 1553
 - relapsed AML patient 1554
 - single-agent phase II evaluations 1553–1554
 - target antigen selection, ADC therapy. *See* target antigen selection, ADC therapy
 - veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) 1554
- GenBank/European Nucleotide Archive (ENA)/DNA 233
- German Multicenter acute lymphoblastic leukemia (GMALL) regimen 1958
- germline components identification 214
- germline sequence databases 211
- gevokizumab 875–876, 877
- girentuximab (CA IX) 767–768
- glioma
- high-grade 836, 2094
 - malignant 377, 1683
 - pediatric 1684
 - recursive partition analysis (RPA) 1683
 - types 1682–1683
- glycoengineering, obinutuzumab
- antibody glycoengineering 1704
 - carbohydrate and Fc region 1705
 - in Chinese hamster ovary (CHO) cells 1706
 - Fc receptors 1704
 - “GlycoMab technology” 1704
 - human glycosylphosphatidylinositol (GPI) anchored FcγRIIIb 1706
 - mogamulizumab 1705
 - posttranslational modifications 1704
- glycosylation
- aglycosylated IgG-Fc 186–187
 - cetuximab (Erbix) 188
 - CHO cells 189
 - direct simulation Monte Carlo (DSMC) 188
 - fucose and bisecting *N*-acetylglucosamine 180–182
 - galactosylation, IgG-Fc activities. *See* galactosylation
 - IgG-Fc glycans, chemo-enzymatic synthesis 185
 - IgG-Fc oligosaccharide moiety 176–177
 - IgG-Fc protein/oligosaccharide interactions 177–179
 - IgG-Fc, quaternary structure 174–175
 - IgG glycoforms, in cellular FcγRs recognition 180
 - IgG molecule 172–173
 - *N*-linked glycosylation 187
 - polyclonal human IgG-Fab, analysis 187
 - protective mechanisms activation 180
 - recombinant antibodies 188
 - sialylation, IgG-Fc oligosaccharides 184–185
 - VH deglycosylated molecule 189
 - X-ray crystallographic studies 188
- GM-CSF. *See* granulocyte-macrophage cerebrospinal fluid (GM-CSF)
- GMALL regimen. *See* German Multicenter acute lymphoblastic leukemia (GMALL) regimen
- GnbAC1 (GeNeuro Innovation SAS) 1184
- GO. *See* gemtuzumab ozogamicin (GO)
- golimumab
- adverse events (AEs) 1569
 - arthritis 1567
 - binding affinity 1568
 - cynomolgus macaques 1568,
 - DMARDs 1567
 - full-length human IgG1 antibody 1568
 - market competitors 1575
 - pharmacokinetic (PK) properties 1568
 - phase 3 studies 1566
 - recommended SIMPONI dose regimen 1565
 - rheumatoid arthritis. *See* rheumatoid arthritis
 - TNF levels reduction 1567
- gouty arthritis
- canakinumab 1451
 - colchicine vs. canakinumab groups 1451
 - joint inflammation 1450
 - NSAIDs 1452
 - treatment 1452, 1453
- graft-versus-host disease (GVHD)
- chronic 1983

- donor T cells 1360
- and graft rejection 1361
- immunosuppression 1096
- and nephrotoxic serum models 979
- pathogenic role 1096
- prophylaxis 1361
- granulocyte-macrophage cerebrospinal fluid (GM-CSF) 1931, 1971
- growth factor inhibitors
 - anti-CSF1 (M-CSF) 1023–1025
 - anti-CSF2 (GM-CSF) 1025–1028
 - GS-5745 (Gilead Sciences Inc.) 1182
 - GSK-1070806 (GSK) 984
 - GSK-1995057 (GSK) 975–976
 - GSK-2434735 1003
 - guselkumab 993
 - GVHD. *See* graft-versus-host disease (GVHD)
- h**
- HACA. *See* human antichimeric antibodies (HACA)
- hairy cell leukemia (HCL) 1978–1979
- HALT. *See* hormone ablation therapy (HALT)
- hapten-binding bispecific antibodies 289
- HBsAg. *See* human hepatitis B surface antigen (HBsAg)
- HCL. *See* hairy cell leukemia (HCL)
- HD. *See* Hodgkin's disease (HD)
- HDT. *See* high-dose therapy (HDT)
- head and neck, nimotuzumab
 - advanced carcinomas 1680
 - CRT treatment 1682
 - inclusion criteria 1680
 - ionizing radiation 1680
 - irradiation, CR 1681
 - nasopharyngeal tumor 1681
 - pharmacodynamic effect 1680
 - radical surgery 1681–1682
- health-related quality of life (HRQoL) 1539
- heart transplantation
 - basiliximab 1386–1387
 - daclizumab 1387
- hematological disorders, eAds
 - ALX-0081, bivalent humanized V_HH 507–508
 - von Willebrand disease type 2B (VWD2B) 507
 - von Willebrand factor (VWF) 507
- hemolytic uremic syndrome (HUS)
 - drug designations 2103
 - eculizumab 1200
 - pathophysiology 1200
 - treatment 1200
- hepatomegaly/splenomegaly 1338
- HESs. *See* hypereosinophilic syndromes (HESs)
- heterobifunctional cross-linkers 270
- HIC. *See* hydrophobic interaction chromatography (HIC)
- hidradenitis suppurativa (HS) 1316–1318
- HIF1- α . *See* hypoxia-inducible factor 1 alpha (HIF1- α)
- high-dose therapy (HDT)
 - ASCT and allogeneic SCT 1959
 - beneficial effect 1976
 - *in vivo* purging process 1974
 - immunochemotherapy 1975–1976
 - PFS and OS rates 1975
 - posttransplant maintenance 1975
- HIV-1. *See* human immunodeficiency virus type 1 (HIV-1)
- HIV-associated lymphomas 1977
- Hodgkin's disease (HD) 1979
- Hodgkin's lymphoma
 - ABVD 1429
 - allogeneic transplant 1427
 - anaplastic large cell lymphoma 1420
 - before/after auto-SCT 49, 1427
 - brentuximab vedotin 759–760, 1429
 - CD30-positive hematologic malignancies 1429, 1432
 - combined modality therapy 1421
 - SCT 1421,
 - treatment 1421
- Honegger and Plückthun (Aho) numbering scheme 206
- hormone ablation therapy (HALT) 1526
- HOVON-46 study 1954
- HRQoL. *See* health-related quality of life (HRQoL)
- HS. *See* hidradenitis suppurativa (HS)
- human and chimeric IgH loci
 - anti-human κ anti-human λ L-chain affinity matrix 84
 - B-cell numbers 83
 - description 83
 - IgM and IgG titers 83
 - immunization, antigens 85
 - in OmniRat 84
- human anti-human antibody (HAHA) responses 2078
- human antichimeric antibodies (HACA) 1909, 1910, 1973, 1984
- human epidermal growth factor receptor 2 (Her2)
 - adjuvant treatment 2042–2043
 - age considerations 2058

- human epidermal growth factor receptor 2 (Her2) (*contd.*)
 - breast cancer. *See* breast cancer
 - cardiac adverse events. *See* cardiac adverse events
 - dosing/scheduling 2059
 - FDA approval 2062
 - infusion-related reactions 2057–2058
 - intracellular signaling 2042
 - natural killer (NK) cells 2042
 - patients considerations 2058
 - safety and side effects 2061–2062
 - trastuzumab 2041–2042
 - human family chronology
 - heavy chain variable genes (V_H) 219
 - light chain variable genes (V_L and V_K) 219, 220
 - human framework sequences, CDR-grafting
 - affinity, specificity and activity 97
 - biopharmaceuticals, FDA 97, 98–99
 - database search 101–102
 - donor sequence (homology) matching 100
 - donor VH and human frameworks 100
 - germline 101
 - subgroup consensus/expressed 101
 - VL/VH 100–101
 - 10th Human Genome Mapping Workshop (HGM10) 233
 - human heavy-chain diseases (HCD) 248
 - human hepatitis B surface antigen (HBsAg) 410
 - human Ig transloci construction
 - BAC and YAC libraries 78
 - IgH 78–80
 - Ig κ 80
 - Ig λ 80–81
 - in transgenic animals 78
 - human IgG CH₂ 495
 - human immunodeficiency virus type 1 (HIV-1)
 - CD4bs, HIV-1 gp120 500
 - CoRbs, HIV-1 gp120 499–500
 - coreceptors 501
 - implications 501
 - MPER, HIV-1 gp41 500–501
 - MPER of gp41 499
 - vital immune cells 498
 - human organ transplantation
 - adult non-renal transplantation. *See* adult non-renal transplantation
 - BPAR 1378
 - renal. *See* renal transplantation
 - humanization
 - CDR-grafting. *See* CDR-grafting
 - defined 89
 - engineered mAb 89
 - history 89–90
 - phage libraries. *See* phage libraries
 - removal, T- and B-cell epitopes 106
 - resurfacing/veneering 104–105
 - SDR-transfer. *See* specificity-determining residue (SDR)-transfer
 - Huntington's disease (HD)
 - active immunotherapy, DNA vaccines 1223
 - disease and target 1222
 - passive immunotherapy, intrabodies 1222–1223
 - HUS. *See* hemolytic uremic syndrome (HUS)
 - hydrazone linkage 356
 - hydrophobic interaction chromatography (HIC) 623
 - hyper-CVAD 1958, 1959, 1962
 - hypereosinophilic syndromes (HESs) 876, 877
 - hypoxia-inducible factor 1 alpha (HIF1- α) 824
- i**
- IBD. *See* inflammatory bowel disease (IBD)
 - ibrutinib 1972–1973
 - IEC. *See* ion-exchange chromatography (IEC)
 - IgA antibodies, antibody isotype. *See* antibody isotype
 - IgE. *See* immunoglobulin E (IgE)
 - IGF-1R. *See* insulin-like growth factor type I receptor (IGF-1R)
 - IgG antibodies, antibody isotype. *See* antibody isotype
 - IgG-Fc oligosaccharide moiety
 - galactose residues 176
 - glycoforms 176, 177
 - heterogeneity 176
 - plasma cell clone 177
 - polyclonal IgG 176
 - soluble and cell-surface-expressed receptor 176
 - IgG-Fc protein/oligosaccharide interactions
 - glycosidases and glycosyl transferases 178
 - inter-heavy chain disulfide bridge 179
 - PNGase F enzyme 178
 - sugar residues, interactions 178
 - X-ray crystallographic analysis 177, 179
 - IGHG CH amino acid positions
 - IGHG1 alleles and G1m allotypes 251, 252, 253, 257
 - interface ball-and-socket-like joints 251, 253

- knobs-into-holes methodology 249, 251, 253
- N-linked glycosylation site 249, 250
- Ig κ , human Ig transloci construction 80
- Ig λ , human Ig transloci construction
 - description 80
 - endogenous 81
 - YAC, 17 V λ and all J-C λ s 80–81
- IgM. *See* immunoglobulin M (IgM)
- IL-2R antibodies
 - ADM 1394
 - ATL. *See* adult T-cell leukemia (ATL)
 - GVHD 1394–1395
 - MS. *See* multiple sclerosis (MS)
 - TSP/HAM 1393
 - uveitis 1393–1394
- IMGT Collier de Perles
 - C domain 241
 - graphical 2D representation 237
 - V domain 239, 241
- IMGT-ONTOLOGY concepts
 - genes and alleles 233–236
 - *Homo sapiens* IG chain labels 235
 - IMGT Collier de Perles 237–241
 - IMGT unique numbering concept 236–237
- immunogenetics and immunoinformatics 231
- labels 233
- standardized keywords 232–233
- IMGT unique numbering concept
 - CDR-IMGT length 237
 - IG and TR gene allelic polymorphisms 237
 - IG and TR V-DOMAIN 236
 - MH superfamily (MhSF) 237
 - structural level 237
- imicromab (MyoScint™) 2129–2130
- immune-complex-mediated arthritis (ICA) model 1150
- immune library generation 317
- immune modulators, B-cell lymphoma
 - GM-CSF 1931
 - IFN- α -2 α 1931–1932
 - lenalidomide 1932
 - ORR and CR rates 1932–1933
- immune system
 - adjuvants 22
 - antibody molecules 18
 - CD100 1085–1086
 - CDC 791–792
 - disorders 1639
 - immunocompetent cells 934
 - and immunogenicity 667–668
 - inflammatory diseases 934–935
 - killer cells 279
 - network theory 412
- immune thrombocytopenia purpura (ITP) 1350
- immunization, monoclonal antibody
 - adjuvants 22
 - antibody response outcome 21
 - factors 21
 - *in vitro*, 22
 - KLH/BSA 22
- immunoconjugates
 - ADCs. *See* antibody–drug conjugates (ADCs)
 - bispecific antibodies 807–808
 - bispecific mAbs 803–804
 - BiTEs. *See* bi-specific T-cell engagers (BiTEs)
 - brentuximab 803–794
 - mAbs/mAb fragments 802–803
 - RAIT. *See* radioimmunoconjugates (RAIT)
 - SWOG S0106 803
- immunogen
 - animals 1299
 - carrier proteins, preparation 1298–1299
 - definition 1298
 - immunogenicity 1298
 - properties and preparations 1298
- immunogenicity
 - of Abs 668, 669
 - ADAs bioanalytical assessment *vs.* therapeutic antibodies 671–673
 - ADCC and/or CDC function 669, 670
 - advantages 482
 - AEC 482
 - antibody-based drugs 667, 675, 676
 - approved mAbs, USA and Europe 665, 667
 - B-cell modification approach 480
 - bispecific antibodies 677
 - chimeric ADCs 677
 - clinical 1256–1257
 - clinical consequences, Abs 671
 - Fc γ Rs 669
 - Food and Drug Administration (FDA) 677
 - fragments 675
 - glycoengineering 671
 - hexa-histidine tag (His-tag) to C-terminus 480
 - and immune system 667–668
 - insufficient tumor penetration 677
 - mAbs development 668, 669
 - murine, chimeric and humanized mAbs¹ 668
 - murine monoclonal antibody, bacterial enzyme 480
 - nonclinical 1255–1256

- immunogenicity (*contd.*)
 - nonimmunogenic enzymatic activities 481
 - prediction tools 673–674
 - recombinant-DNA technology 665
 - risk assessment, antibodies 670
 - T-cell epitope modification strategy 480–481
 - T-cell proliferation assays and *in silico* analysis 481
 - of therapeutic antibodies 674–675
 - tools 482
- immunoglobulin E (IgE)
 - allergen-binding site 1778–1779
 - allergic and nonallergic conditions 1778
 - anti-IgE inhibitors 1161–1162
 - anti-IgE M1' inhibitors 1162
 - cell distribution 1785–1786
 - distribution and blood concentration 1779
 - distribution of FcεR 1780
 - early and late-phase allergic reactions 1776–1777
 - FcεRI (high-affinity IgE receptor) 1781–1783
 - FcεRII (low-affinity IgE receptor, CD23) 1783–1785
 - physiologic and pathophysiologic significance 1786–1787
 - serum concentration, asthma and rhinitis 1775–1776
 - synthesis and regulation 1779–1780
- immunoglobulin heavy (IgH)
 - BACs with human V_H, D, J_H segments and rat C-region locus 79,
 - cis-acting control sequences 79
 - cYAC/BAC vector 79, 80
 - description 78–79
 - XenoMouse animals 79
- immunoglobulin M (IgM) 1197
- immunoglobulin T cell receptors
 - CARs 522–523
 - extracellular spacer domains 523
- immunological responses
 - antitumor immune 770
 - checkpoint blockade/vaccination 770
 - eradication, equilibrium and escape 770
 - ipilimumab (anti-CTLA4) 771–772
 - nivolumab (anti-PD1) 772
 - PD-1 and CTLA-4 ligands 770
 - tumor regression 770
- immunoreceptor tyrosine-based activation motif (ITAM)-containing the FcRγ-chain 143
- immunotherapeutics, neurological disorders
 - active vs. passive 1216–1217
 - AD. *See* Alzheimer's disease (AD)
 - advantages and challenges 1215–1216
 - ALS. *See* amyotrophic lateral sclerosis (ALS)
 - antibody-based therapies 1216
 - HD. *See* Huntington's disease (HD)
 - PD. *See* Parkinson's disease (PD)
 - transmissible spongiform encephalopathies. *See* transmissible spongiform encephalopathies
 - in vitro* affinity maturation
 - anti-2-phenylloxazol-5-one (phOx) antibody Fv fragment 118
 - biotinylated and non-biotinylated antigen 119
 - CDRs 119
 - error-prone (PCRs) 118
 - panning 117
 - physical/chemical parameters 118
 - site-directed mutagenesis 118
 - in vitro* binding and potency
 - cell-based bioassays 121
 - monoclonal antibodies target, cytokines 122
 - simulated effect, antibody–antigen mixture 123
 - in vitro* maturation and antibody selection
 - *de novo* design 397
 - DNA mutagenesis and display technologies 397
 - guided selection 397
 - off-rate selection 397
 - post-selection populations 398
 - in vivo* affinity maturation
 - antibody diversity and germinal center 116
 - “germlinized”/“superhumanized” antibody 117
 - hypermutation and clonal deletion 116
 - naive cells 115
 - single B-cell clones 116
 - somatic hypermutation 117
 - VDJ rearrangements 115
 - in vivo* binding and potency
 - affinities 123
 - tumor penetration 124
 - unbound concentrations 124, 125
 - individual extended loops
 - bacterial TEM-1 β-lactamases 456–457
 - charybdotoxin 456
 - cysteine-knot motifs 455
 - human plasma kallikrein (pKAL) 454
 - knottins 455–456
 - Kunitz-type scaffold, DX-890 454–455
 - protease inhibitors 454
 - thioredoxin (TrxA) 455

- indomethacin 1669
- inducible T cell costimulator (ICOS)
 - 1088–1089
- infectiology, mAbs
 - anti-infectious mAbs. *See* anti-infectious monoclonal antibodies
 - antimycotic 1207
 - antitoxinic activity 1196–1197
 - and clinical trials 1196
 - IgM 1197
 - infectious diseases 1195
 - viral diseases and anti-infectious mAbs 1201–1207
- infectious disease
 - cancer 1295
 - virology 1295
 - XOMA3AB antitoxin 1295
- inflammation, eAds
 - IBD 507
 - RA 505–506
- inflammatory bowel disease (IBD)
 - acute flares 938
 - eAds 507
 - mAbs 939
 - mild 938–939
 - natalizumab 939
 - systemic immunosuppressive drugs 939
- inflammatory diseases
 - allergic diseases 945–949
 - arthropathies 953
 - diabetes 949–951
 - IBD 938–939
 - MS 939–941
 - ocular diseases 943–945
 - organ transplantation–graft rejection 951–953
 - psoriasis and psoriatic arthritis 937–938
 - RA 936–937
 - SLE 941–943
- infliximab
 - ankylosing spondylitis (AS) 1605–1606
 - antibody characteristics 1599
 - antibody formation against 1611
 - autoantibody formation 1612
 - CD 1602–1603
 - congestive heart failure 1613
 - hepatic events and pregnancy outcome 1613
 - hepatotoxicity 1639
 - infusion reactions/delayed hypersensitivity reactions 1611–1612
 - malignancies/lymphoma 1612–1613
 - marketing 1618
 - neurological disorders/demyelinating disease 1612
 - pediatric Crohn’s disease 1603
 - pediatric ulcerative colitis 1609
 - pharmacokinetics 1600–1601
 - preclinical characterization 1600
 - psoriasis 1607–1608
 - psoriatic arthritis (PsA) 1606–1607
 - RA 1603–1605
 - serious infections 1609–1610
 - ulcerative colitis 1608–1609
- infringement 711, 712–713
- infusion reactions/delayed hypersensitivity reactions 1611–1612
- injection-site reactions (ISRs) 1338
- innate immunity
 - ADCC. *See* antibody-dependent cellular cytotoxicity (ADCC)
 - BMS-936559 (MDX-1105) 794
 - CDC. *See* complement-dependent cytotoxicity (CDC)
 - conventional methods 788
 - effector cells, targeting 789
 - ipilimumab 792–793
 - MPDL3280A, PD-L1 targeting compound 794
 - nivolumab 793–794
 - pidilizumab (CT-011, hBAT-1) 793
 - programmed death 1 (PD-1) receptor 793
 - rituximab, anti-CD20 antibody 789
 - transforming growth factor-beta (TGFβ) 794
 - tremelimumab 793
- inotuzumab ozogamicin (IO)
 - B-cellular non-hodgkin’s lymphoma 756–757
 - calicheamicin conjugates. *See* calicheamicin conjugates
 - CD22 antibodies 1555
 - conjugate design/preclinical activity 1549
 - DLBCL 367
 - IgG4 moiety 1549
 - relapsed/refractory follicular lymphoma (FL) 367
 - rituximab and 1556
 - side effects 1555
- insect cells
 - disadvantages 570
 - N-glycosylation patterns 571
 - recombinant antibody expression 570
 - research and development 570
 - secretory proteins 570–571
- insulin-like growth factor type I receptor (IGF-1R)

- insulin-like growth factor type I receptor (IGF-1R) (*contd.*)
 - cixutumumab (IMC-A12) 766–767
 - dalotuzumab (MK-0646) 766
 - description 765
 - figitumumab (CP-751, 871) 767
 - functional hybrid receptors 765
 - ganitumab (AMG, 479) 765–766
 - tumorigenesis 765
- $\alpha 1\beta 1$ integrin (VLA-1 (Cd49a))
 - binding, monomeric collagens 1131
 - collagen recognition 1131
 - dysregulation 1132
 - macrophages 1132
 - SAN-300 1132–1133
 - T cells 1132
- $\alpha 2\beta 1$ integrin (VLA-2)
 - binding to collagen 1133
 - and ECM ligands interaction 1133
 - expression 1133
 - vatelizumab 1134
- $\alpha 4\beta 7$ integrin
 - immunosurveillance 899–900
 - MAdCAM-1 expression 1128
 - memory T lymphocytes 900
 - natalizumab, humanized IgG4 antibody 2104
 - tissue tropic migration 900
 - vedolizumab 900–901
- integrin-mediated TGF- $\beta 1$ activation 1014
- interface packing residues
 - 1B4 humanization 94
 - residues at VL/VH interface 93, 94
- intergroup E4494 trial 1950, 1951–1952
- interleukin-5 (IL-5)
 - anti-IL-5 mAbs 1006
 - bone marrow CD34⁺ progenitor cells 877
 - eosinophil trafficking 1005
 - eosinophils 876, 1005, 1006
 - HESs 876, 877
 - IL-5 KO mice 1006
 - IL-5R expression 1005
 - mepolizumab 877–881
 - reslizumab 879–881, 882–883
- interleukin 6 (IL-6)
 - biological activities and signaling 2023–2024
 - *cis*- and *trans*-signaling 869
 - description 866, 984, 985
 - functions 866, 869
 - hyperlipidemia 2035
 - IL-6 KO mice 985
 - immunogenic potential 2036
 - infections 2033–2034
 - inflammatory diseases 985
 - liver function abnormalities 2034–2035
 - malignancies 2033
 - monoclonal antibodies 2024–2025
 - sarilumab 869–870, 871–872
 - sirukumab 870, 873, 874
 - tocilizumab 869
- interleukin 10 (IL-10) 1007–1008
- interleukin-13 (IL-13)
 - cytokine and receptor-directed inhibitory antibodies 883
 - lebrikizumab 884–885
 - in lungs, adult mice 883
 - monocytes and macrophages 883
 - Th2 T helper cells 883
- interleukin-18 (IL-18) 982–984
- interleukin-20 (IL-20) 993, 994
- interleukin-21 (IL-21) 994–995
- interleukin-23 (IL-23) 992–993
 - BLys 898–899
 - cytokine family 897
 - IL-23p19 mRNA expression 897
 - Merck–Schering-Plough 897–898
 - tabalumab 899
- interleukin-31 (IL-31) 1010–1011
- interleukin-17A (IL-17A)
 - anti-IL-17 mAb 990
 - brodalumab 892, 895–896
 - description 989
 - expression and dysregulation 990
 - granulopoiesis and neutrophil mobilization 885
 - heterodimer 989
 - ixekizumab 891–892, 893–894
 - principal activities 989
 - proinflammatory effects 989
 - secukinumab 885–891
 - T helper cells 885
- interleukin-1 β (IL-1 β)
 - gevokizumab 875–876, 877
 - interleukin-1 receptor type I (IL-1RI) 875
 - over-expression of 873
 - Th17 cells 873, 875
- The international ImMunoGeneTics information system® (IMGT®)
 - antibody engineering 231
 - antibody humanization 231
 - database 206, 230
 - IMGT/Collier-de-Perles tool 241
 - IMGT data 212
 - IMGT/DomainGapAlign 244–245
 - IMGT/2Dstructure-DB 244
 - IMGT/3Dstructure-DB 241, 243
 - IMGT/HighV-QUEST 246

- IMGT/mAb-DB 231, 232
- IMGT numbering scheme 206
- IMGT-ONTOLOGY. *See* IMGT-ONTOLOGY concepts
- IMGT/V-QUEST 245, 246
- immunoinformatics 229, 230
- web resources. *See* web resources
- WHO-International Nonproprietary Names (INN) program 230
- International Nonproprietary Name (INN) Working Group Meeting 1283
- intracellular signaling
 - bevacizumab 795–796
 - cetuximab 795
 - description 795
 - ligand-dependent cell receptor inhibition 798–800
 - ligand inhibition 796–797
 - and signal propagation 796
 - signal transduction, ligand-independent alteration 800–802
 - TGF β 795
- intravenous immunoglobulins (IVIg) 413
- IO. *See* inotuzumab ozogamicin (IO)
- ion-exchange chromatography (IEC) 623–624
- ipilimumab
 - action mechanism 1621–1622
 - adverse events 1636–1641
 - anti-CTLA-4 antibody doses 1624–1625
 - biomarkers 1630–1631
 - BRAF mutation status 1630
 - chemotherapy-naive patients 1625
 - in combination with chemotherapy 772
 - cytotoxic T-lymphocyte antigen 4 (CTLA-4) 1620
 - grade III/IV autoimmunity 1624
 - immune-related adverse events (irAE) 1636–1641
 - immune-related response criteria (irRC) 1634–1636
 - initial phase II trials 1623–1625
 - lactate dehydrogenase (LDH) 1630–1631
 - long responders 1629–1630
 - lung cancer 1633–1634
 - maximum tolerated dose (MTD) 1622
 - melanoma 771–772, 1622
 - nonimmunogenic treatment 1625
 - NSCLC 772
 - pharmacokinetics 1622
 - phase II studies 1625–1628
 - phase III trial 1628–1629
 - plasma peak concentration 1622
 - prostate cancer 772, 1631–1633

- “total tumor burden” 1634
- toxicity profile 771
- transfectoma and hybridoma-derived 1622
- tumor flare reaction 1636
- WHO criteria 1634–1636
- itolizumab (Alzumab[®])
 - CD6 2114
 - description 902
 - humanization 2113
 - plaque psoriasis 2114
 - RA 2115

k

- Kabat data 203, 210, 211–212
- Kabat numbering scheme 203
- KB003 1028
- keyhole limpet hemocyanin (KLH) 126

l

- lampalizumab 1170
- LBL. *See* lymphoblastic lymphoma (LBL)
- lebrikizumab 884–885, 1001
- lenalidomide
 - combined chemotherapy 1758–1759
 - lymphomun applications 1486
 - and rituximab 1933, 1964, 1971
 - second treatment cycle 1486
 - tumor volume reduction 757–758
 - in untreated FL 1937
- leucine-rich repeat and Ig domain containing Neurite outgrowth inhibitor (NOGO) receptor interacting protein-1 (LINGO-1) 1182–1183
- leukocyte adhesion and migration inhibitors
 - anti- α 1 β 1 integrin (VLA-1) 1131–1133
 - anti- α 2 β 1 integrin (VLA-2) 1133–1134
 - anti- α 4 β 7/MAdCAM-1 1128–1131
 - anti-CD162 1136–1137
 - anti-VAP-1 1134–1135
- LFG316A (Novartis, Morphosys) 1168
- libraries
 - CDRH3 59
 - description 495
 - “designer” properties 59
 - with grafted *in vivo* formed CDRs 497–498
 - HCabs 495–496
 - human “single-pot”/universal phage display libraries 59, 60–64
 - immune libraries 57
 - lambda subfamilies V λ 4–V λ 10 58
 - naive 57–58
 - semi-synthetic and synthetic 58, 496–497
 - VH and VL genes 58–59

- library generation
 - immune 317
 - naïve 317
 - synthetic 317–318
 - ligand-dependent cell receptor inhibition
 - cixutumumab 799
 - colony stimulating factor 1 (CSF-1) 798
 - dalotuzumab 799–800
 - insulin-like growth factor receptors (IGFRs) 799
 - “target-able” mutations 798
 - VEGF pathway 798–799
 - LIGHT 1093–1095
 - linkers, ADCs
 - carbonate 356
 - description 353–354
 - disulfide 355–356
 - hydrazone linkage 356
 - noncleavable thioether 354–355
 - peptide 356
 - site of 357–358
 - liquid protein formulations 635–638
 - liver
 - elimination of IgG 1790, 1791
 - function abnormalities 2034–2035
 - liver transplantation
 - basiliximab 1383
 - daclizumab 1384–1385
 - lung transplantation
 - basiliximab 1385–1386
 - daclizumab 1386
 - LY2382770 (Eli Lilly) 1013
 - lymphoblastic lymphoma (LBL) 1958
 - lymphomun. *See* anti-CD20 × anti-CD3 lymphomun
 - lymphotoxin-alpha (LT α) 976–977, 1662
- m**
- M-CD3. *See* muromonab cluster of differentiation 3 (M-CD3)
 - mAb-resistant mutants (MARMs) 1829
 - mAbs. *See* monoclonal antibodies (mAbs)
 - MabThera International Trial (MInT) 1952–1953
 - macrophage migration inhibitory factor (MIF) 1022–1023
 - mammalian cells
 - acceptor cell lines 572
 - advantages 571
 - batch/fed-batch bioreactor processes 573
 - CpG islands, promoter regions 572
 - Cre (cyclization recombination) 572
 - designer substrates 572
 - folding and secretion machinery 571
 - genomics and cell line engineering 573–579
 - human IgG 573
 - IRES 573
 - transfection, HEK293 cell lines 573
 - mammalian expression technology. *See* applied genomics and cell line engineering
 - mantle cell lymphoma (MCL)
 - description 1916
 - immune modulators 1963–1964
 - relapsed 1963
 - rituximab monotherapy 1963
 - untreated, rituximab plus chemotherapy 1959–1963
 - manufacturing process development
 - Chinese hamster ovary (CHO) cells 603–604
 - commercial. *See* commercial manufacturing processes
 - comparability and risk assessment 653–652
 - description 603
 - downstream processing. *See* downstream processing
 - drug product development 631–634
 - formulation designing 628–629
 - freeze-dried protein formulations, excipients 638
 - LCLF to HCLF 638–639
 - liquid formulation and freeze-dried formulations 629–630
 - liquid protein formulations, excipients 635–638
 - monoclonal antibodies (mAbs) 603
 - novel IgG-derived molecule formats 604
 - protein characterization. *See* protein characterization
 - quality control testing 651, 652–653
 - quality parameters 604
 - rapid formulation 635
 - resulting drug substance 604
 - stability testing 651, 653
 - upstream processing. *See* upstream processing
 - marginal zone lymphomas (MZLs)
 - chlorambucil arm 1935
 - description 1935
 - retrospective analysis, SMZL 1935–1936
 - MARMs. *See* mAb-resistant mutants (MARMs)
 - mast cell activation syndrome (MCAS) 1814
 - matrix metalloproteinases (MMPs) 824, 826, 828, 1181–1182
 - matuzumab 832

- mavrilimumab 1026–1027
- maximum tolerated dose (MTD)
 - BR96-doxorubicin 353
 - brentuximab vedotin 1426
 - lenalidomide 1964
 - and low immunogenic responses 377
- MCAS. *See* mast cell activation syndrome (MCAS)
- MCL. *See* mantle cell lymphoma (MCL)
- mean fluorescence intensity (MFI) values 1474
- mechanisms of action (MoA), mAbs
 - complement system 143
 - concentrations, direct growth inhibition 144
 - epidermal growth factor receptor (EGFR) 141
 - Fc-mediated effector functions 143
 - FcγRIIa-H131 144
 - FcγRIIIa-V158 alloform 144
 - IgG, structure and function 142
 - *in vitro* assays 142
 - “immune checkpoints” 141
 - immunogenicity 141
 - lymphoma patients, rituximab therapy 144
 - “naked” antibodies 141
 - polymorphonuclear (PMN) cells 143
 - radioimmunoconjugates generation 141
 - rituximab therapy, FcγRIIa and FcγRIIIa allotypes 144
 - tumor-directed immune responses 144
 - tumor necrosis factor (TNF) 141
 - VEGF 141
- MEDI551 (Medimmune) 1117
- MEDI4212 (Medimmune) 1162
- MEDI5117 (Medimmune) 988
- MEDI7814 (AZ-Medimmune) 1168
- MEDI8968 981–982
- mepolizumab
 - GlaxoSmithKline (GSK) 877, 878
 - *in vitro* and *in vivo*, 877
 - phase III trials 878, 879–881
- Merck–Schering-Plough
 - mAb development 897
 - phase II clinical trial 897–898
- metastatic colorectal cancer (mCRC). *See* panitumumab, mCRC
- minimal residual disease (MRD)
 - blood and bone marrow 1336–1337
 - CLL 1337
 - ISRs 1338
 - NCIWG 1336
- MInT. *See* MabThera International Trial (MInT)
- MODELLER 217
- MOE. *See* Molecular Operating Environment (MOE)
- mogamulizumab (Poteligeo)
 - allergic rhinitis 2115–2116
 - asthma 1019, 2115–2116
 - ATL and CTCL 2115
 - CCR4 expression 2115
 - clinical trials 1019
 - defucosylated Fc 1019
 - description 2115
 - relapsed/refractory ATL 2116
 - side effects 2116
- Molecular Operating Environment (MOE) 218
- molecule generation and *in vitro* pharmacology
 - mechanism of action, raxibacumab 1901
 - raxibacumab generation 1901
- monoclonal anti-IgE molecule
 - formation and tissue distribution, rhuMAB-E25 1788, 1790–1791
 - humanization 1788, 1789
 - IgE-Fcε3 1788
 - interactions with IgE 1792
 - rhuMAB-E25, molecular model 1788, 1789
- monoclonal antibodies (mAbs)
 - ADC/radionucleotides 751
 - agencies, clinical review 1266–1267
 - anti-EpCAM antibodies. *See* anti-EpCAM antibodies
 - anti-neoplastic therapy 751
 - antigen–antibody binding 26
 - antigenic determinants 21
 - approval timelines 1267–1268
 - B-cellular non-Hodgkin’s lymphoma. *See* B-cellular non-Hodgkin’s lymphoma
 - B lymphocyte 18
 - blockage, immunological responses. *See* immunological responses
 - cell fusion 23–25
 - chimeric (mouse/human) rituximab antibody 17
 - clinical development 1264–1265
 - clinical developments 752
 - cloning 30
 - cytotoxicity assays 29
 - denosumab 775–776
 - description 737, 738–744
 - drawbacks 17
 - drug selection, hybridomas 25–26
 - efficacy and safety 954–956
 - vs. EGFR. *See* epidermal growth factor receptor (EGFR)

- monoclonal antibodies (mAbs) (*contd.*)
 - ELISA. *See* enzyme-linked immunosorbent assay (ELISA)
 - epitope and affinity 21
 - expansion and freezing, hybridoma clones 30–31
 - fast approval 1268–1270
 - FDA and/or EMEA 751
 - FIM clinical studies 1272–1280
 - flow cytometry 27, 28
 - fragmentation, monoclonal IgG antibodies 32
 - function screening 30
 - Hodgkin’s lymphoma 759–760
 - hybridoma technology 18–19
 - ¹²⁵I-iodine-labeled second-step antibodies/protein A 26
 - IGF-1R. *See* insulin-like growth factor type I receptor (IGF-1R)
 - immunization. *See* immunization, monoclonal antibody
 - immunohistology and immunocytology 28–29
 - investigator sponsored trials, academic settings 753
 - labeling 32
 - “magic bullets” 17
 - mass culture and purification 31
 - membrane-bound and secreted forms 19–21
 - myeloma cell lines. *See* myeloma cell lines
 - onartuzumab 773–774
 - oregovomab 753
 - ovarian cancer. *See* ovarian cancer
 - pentumomab 775
 - pharmaceutical trials, oncology 752
 - phase 3 clinical trials 737
 - phase 1 clinical trials, immunological disease 929–930
 - phase 2 clinical trials, immunological disease 931–933
 - pivotal trials 1271–1272
 - racotumomab 774
 - rapid market access 1270–1271
 - RCC. *See* renal cell carcinoma (RCC)
 - regulatory validation, development program 1266
 - rilotumumab 773
 - scientific advice, EU 1264
 - T-cellular non-Hodgkin’s lymphoma 758–759
 - target modulation mechanisms 954
 - transgenic mouse and phage display technologies 751
 - for tumor therapy. *See* tumor therapy
 - UMIN-CTR and WHO 752
 - Western blotting/immunohistology 21
- mononuclear phagocytic system (MPS) 1744
- monosome vs. ribosome display 401
- MOR103 1027, 1028
- MORAB-022 1027
- mouse family chronology
 - heavy chain variable genes (V_H) 220
 - light chain variable genes (V_λ and V_κ) 220
- MPS. *See* mononuclear phagocytic system (MPS)
- MS. *See* multiple sclerosis (MS)
- mucosal addressin cell adhesion molecule-1 (MadCAM-1) 939, 1127, 1128–1131
- multiple myeloma and acute leukemias 1359
- multiple sclerosis (MS)
 - alemtuzumab 940–941
 - CARE-MS I and II 1351–1352
 - description 939–940, 1377
 - IFN beta-1a 1350–1351
 - ITP 1350
 - lymphocyte repertoire 1349
 - mAbs 941
 - mitoxantrone treatment 940
 - MSFC 1351
 - natalizumab 940
 - ocrelizumab 941
 - primary progressive 1347
 - progressive relapsing 1347
 - relapsing remitting 1347
 - secondary progressive 1347
 - T-cell pool 1349
 - TNFR1 inhibition 940
 - transitional 1 B cells 1348–1349
 - treatments 1347
- multiple sclerosis functional composite (MSFC) 1351
- muromonab cluster of differentiation 3 (M-CD3)
 - action mechanisms 1648
 - cardiac transplant recipients 1659, 1660–1661
 - cytokine release syndrome. *See* cytokine release syndrome (CRS)
 - diagrammatic representation 1646
 - efficacy 1654–1655, 1657–1658
 - human T cells activation 1650
 - immunogenicity 1650–1651
 - immunosuppression, infections 1670–1671
 - interactions 1651–1652
 - liver transplant recipients 1659
 - mAbs production 1646–1647

- murine mAb 1646
- neoplasia 1671
- pharmacodynamics 1649
- pharmacology 1647
- plasma concentrations 1648–1649
- renal–pancreas transplant recipients 1656
- surface antigens 1648
- therapeutic use 1652–1656
- withdrawal from market 1672
- myasthenia gravis (MG) 1984–1985
- myeloma cell lines
 - antibody without antigen 22
 - LOU/C strain, rat myeloma 23
 - mouse interspecies hybridomas 23
 - nonproducer lines 23
- MZLs. *See* marginal zone lymphomas (MZLs)

- n**
- N-/O-glycosylation sites
 - β -sheet structure, antibodies 95
 - consensus pattern
 - asparagine-X-serine/threonine 95
 - drug/radionuclides 95
- “naked” gene delivery systems 750
- namilumab 1027
- naptumomab estafenatox (5T4) 768–769
- natalizumab
 - approved indications 2105–2107
 - description 2104
 - multiple sclerosis (MS) 2104
 - safety 2105
- natural killer cell group 2A (NKG2A) 1097–1098
- NCT00747344 (Pearl) 2074
- necitumumab 762
- Neisseria meningitidis* infection 1167
- neoplasia 1671
- neovascularization. *See* angiogenesis
- neurological disorders/demyelinating disease 1612
- neutrazumab 1168, 1169
- neutrophil gelatinase-associated lipocalin (NGAL) 453
- NGAL. *See* neutrophil gelatinase-associated lipocalin (NGAL)
- NI-0101 (Novimmune) 1150–1151
- NI-0501 (Novimmune) 1000
- NI-0701 (Novimmune) 1021, 1022
- NI-0801 (Novimmune) 1021
- NI-1401 (Novimmune/Roche-Genentech) 991
- nimotuzumab
 - allergic reactions 832
 - description 1679
- EGFR 762–763
- esophageal and gastric cancer 1684–1685
- glioma 1682–1683
- head and neck 1679–1682
- immunoglobulin G 832
- NSCLC. *See* non-small-cell lung cancer (NSCLC)
- pancreatic cancer 1685–1686
- pediatric glioma 1684
- nivolumab (anti-PD1) 772
- NN-8210 1169
- NN-8226 994
- NN-8765 (IPH2201; Novo Nordisk licensed from Innate Pharma) 1098
- NN-8828 Novo Nordisk from BMS (Zymogenetics) 995
- nomenclature
 - application information 1287
 - elements, name 1283
 - stems and infixes 1284
 - target/disease class infix 1284–1286
 - USAN modified designations 1286–1287
- non-antibody scaffolds
 - advanced mammalian expression systems 437
 - artificial binding proteins 441, 442
 - artificial binding proteins vs. antibodies 438, 439
 - bacterial expression systems 437
 - biomolecular characteristics, medical use 442, 443
 - biopharmaceutical drug development programs 436
 - bivalency 441
 - clinic 461–463
 - in clinical development 442, 446–447
 - companies, commercial performance since 2006 442, 444–445
 - conventional *Escherichia coli* expression systems 440
 - dense and complex IP issues 437
 - genetic libraries 435
 - *in vivo* and *in vitro*, 439–440
 - innovative biopharmaceutical compounds 436
 - non-Ig scaffold proteins 438
 - poly-ethylene glycol (PEG) 441
 - *Pseudomonas* exotoxin 441
 - scaffold proteins. *See* scaffold proteins
 - sequence-/consensus-guided design 435
 - single domain immunoglobulins. *See* single domain immunoglobulins
 - size comparison 438, 439
 - therapeutic application 442

- non-approved diseases
 - AR 1811–1812, 1813
 - MCAS 1814
 - urticaria/angioedema 1812, 1813
 - VIT 1813–1814
 - non-Hodgkin's lymphoma (NHL)
 - aggressive (DLBCL) 1588
 - CD20-targeted immunotherapy 1580–1581
 - epidemiology 1579
 - response rates, alemtuzumab 1357–1358
 - responses classification 1359
 - rituximab 1357
 - standard therapy 1580
 - non-small-cell lung cancer (NSCLC)
 - aflibercept 836
 - combination therapy 1510–1511
 - figitumumab 767
 - HGF–MET pathway 838
 - IGFs 799
 - ipilimumab 772
 - monotherapy 1510
 - necitumumab 762
 - non-squamous 833
 - optimal duration of therapy 1688–1689
 - patient selection 1687–1688
 - pharmacodynamic evaluation 1689–1690
 - progression-free survival (PFS) 829
 - racotumomab 774
 - safety 1690
 - noncleavable thioether linkers 354–355
 - nonclinical testing, mAbs
 - components 1250–1251
 - pharmacology and pharmacokinetic studies 1252–1253
 - test species 1251–1252
 - toxicology 1254–1255
 - nonmyeloablative conditioning regimens
 - allogeneic engraftment 1363
 - CMV reactivation 1362
 - GvHD prophylaxis 1362
 - total body irradiation (TBI) 1361–1362
 - nonsteroidal anti-inflammatory drugs (NSAIDs) 942, 945, 1452, 1567, 1571, 1572, 2031, 2033
 - novel antibodies 707–708
 - NSCLC. *See* non-small-cell lung cancer (NSCLC)
 - nurse shark IgN 248–249
- O**
- obinutuzumab
 - B-cellular non-Hodgkin's lymphoma 754–755
 - CDC activity 1701–1702
 - CDRs 1697
 - chemotherapy, Bcl-2 and MDM2 inhibitors 1712–1713
 - clinical experiences 1715
 - in CLL 1722
 - CLL11 trial 1722–1723
 - in cynomolgus monkeys, B-cell depletion 1713–1714
 - direct cell death induction 1702–1704
 - elbow-hinge engineering 1698
 - epitope recognition 1699–1701
 - *ex vivo* whole blood B-cell depletion 1708–1709
 - flow cytometry, reagents 1697
 - glycoengineering 1704–1706
 - *in vitro* NK cell and neutrophil ADCC and macrophage ADCP activity 1706–1708
 - nonclinical pharmacology studies 1714
 - putative mechanism of action 1696
 - type II CD20 antibody 1698–1699
 - in xenograft models 1709–1712
 - ocrelizumab 903–904, 941, 1120
 - ocular diseases
 - AMD 944–945
 - uveitis 943–944
 - ofatumumab
 - anti-CD20 constructs development 1734,
 - apoptosis 1748
 - B-cellular non-Hodgkin's lymphoma 753–754
 - C3b deposition and complement receptors 1745
 - CD20 interactions 1735–1736
 - cell lines and CLL cells 1739–1742
 - CLL monotherapy 1753
 - complement control proteins 1735
 - as confounding factor 1745–1746
 - development and characterization 1737
 - dose requirements 1743–1744
 - epitope characterization 1737–1739
 - FC for CLL, combined chemotherapy 1757–1758
 - FL monotherapy 1753–1756
 - lenalidomide, combined chemotherapy 1758–1759
 - mononuclear phagocytic system (MPS) 1744
 - mouse models 1746–1747
 - neutrophils 1745
 - O-CHOP for FL, combined chemotherapy 1758
 - physical, immunochemical and functional characteristics 1736

- pivotal trial for CLL 1756–1757
- rheumatoid arthritis 1760–1761
- RTX-refractory FL 1759–1760
- type I CD20 mAbs, cytotoxicity mediated 1735
- oligoclonal antibodies
 - cocktail formulations 1292
 - effector functions 1292
 - FDA/regulatory considerations 1295–1296
 - fragment combinations 1293
 - *in vivo* oligoclonal immune response 1292
 - natural immune response 1291–1292, 1293
 - preparations 1292
 - quality control issues 1292
 - uses/applications 1293–1294
 - varieties 1292
- olokizumab 869, 987, 2024
- omalizumab
 - administration 1806, 1807
 - adverse effects. *See* adverse effects, omalizumab
 - allergic asthma 1159
 - anti-IgE mAb, humans 1787
 - assessment, therapeutic response 1809–1810
 - beneficial effects 1796, 1797
 - cell distribution 1785–1786
 - contraindications 1804, 1805, 1806
 - cost 1811
 - dosage 1806, 1807–1808
 - drug interactions 1810
 - early and late-phase asthmatic responses 1793–1794
 - exacerbation rate 1796, 1797
 - IgE affinity 1160
 - indications 1804, 1805
 - monitoring of therapy 1810
 - onset of action, anti-immunoglobulin E effect 1808
 - pharmacodynamics 1802
 - pharmacokinetics 1802
 - phase III randomized double-blind clinical trials 1794–1796
 - pregnancy and lactation 1810–1811
 - preparation 1805
 - safety and efficacy, rhuMAb-E25 1792–1793
 - treatment duration 1808–1809
- OMS. *See* opsoclonus myoclonus syndrome (OMS)
- onartuzumab 773–774

- OPN-305 (Opsona) 1146–1147
- opsoclonus myoclonus syndrome (OMS) 1984
- oregovomab 769–770
- organ transplantation–graft rejection 951–953
- Orthoclone OKT3. *See* muromonab cluster of differentiation 3 (M-CD3)
- otelixizumab 1082, 1083
- ovarian cancer
 - farletuzumab (MORAb-003) 769
 - oregovomab 769–770
- oxelumab (Genmab) 1093
- ozoralizumab 314, 505–506, 972–973

p

- palivizumab, RSV disease
 - adverse events (AEs) 1843–1845
 - Alaska native infants 1842
 - amino acids A105 1830–1831
 - antigenic sites and neutralization epitopes 1829
 - cell-line stability 1834, 1835
 - CHD. *See* congenital heart disease (CHD)
 - cotton rats, lungs 1832–1833
 - description 1825
 - downstream processing 1833
 - FDA approval 1834
 - immunoaffinity-purified F protein 1831–1832
 - indications and usage 1839–1840
 - mAb1129 1829–1830
 - MARMs 1829
 - MCB and WCB 1833
 - mortality 1825
 - motavizumab 1845
 - newborns 1840–1841
 - pathogenesis 1825–1826
 - phase 3 trials 1835–1836
 - plaque-reduction assay 1832
 - population demographics 1840
 - premature infants. *See* premature infants, palivizumab
 - preventive treatment 1202
 - REACH program 1841
 - risk factors 1825
 - RSV-IVIG 1829
 - scale-up comparability tests 1834, 1835
 - serum concentration 1842–1843
 - serum neutralizing antibodies 1828
 - Swedish recommendations 1841–1842
 - virion, proteins and genome 1826–1827
- pancreas transplantation 1387–1388

- pancreatic cancer
 - cetuximab 797
 - ganitumab 766
 - MT-110 808
 - MUC5AC 790
 - nimotuzumab 763
- panitumumab, mCRC
 - antibody combination therapy 1863–1864
 - approval 1858
 - clinical trials 1860
 - description 1855
 - development 1856–1857
 - EGFR 1855–1856
 - first-line therapy with FOLFOX 1862
 - head and neck cancer 1864
 - KRAS, BRAF and PIK3CA 1857–1858
 - monotherapy 1859, 1861–1862
 - production, galenics and pharmacokinetic properties 1858–1859
 - safety, pharmacokinetics and activity 1859
 - second-line therapy with FOLFIRI 1862–1863
 - xenograft mouse model 1857
- panning
 - phage display and monoclonal binders 46, 47
 - protease digestion 48
- Panton-Valentine leukocidin (PVL) 1199
- Parkinson's disease (PD)
 - active immunotherapy–clinical 1221
 - active immunotherapy–preclinical 1221
 - description 1220–1221
 - passive immunotherapy, full-length antibody 1221
 - passive immunotherapy, intrabodies 1221–1222
- pateclizumab 977–978
- patents
 - academic institutions, inventors 722
 - annual renewal fees 722
 - antigen and antibody format 717–718
 - attacking 726
 - claims 706
 - commercial success 705
 - dominant 716
 - drug companies 705
 - due diligence 732
 - exclusivity 724–725
 - fee for service, CRO 729–730
 - freedom to operate. *See* freedom to operate analysis
 - functional enhancements 718
 - funding 731–732
 - generation, antibodies 716
 - generic and biosimilar producers 731
 - innovative companies 730–731
 - intellectual property rights 706
 - investment 705
 - methodology 710
 - modifications, antibody 709–710
 - monitoring 725
 - National Phase stage, costs 722
 - novel antibodies. *See* novel antibodies
 - out-licensing 731
 - overlapping 710–711
 - ownership 723
 - partnered discovery 730
 - Patent Cooperation Treaty (PCT) 720–721
 - prior art 718
 - priority year 720
 - production systems 718
 - provisional/priority applications 719, 720
 - public disclosures 720
 - “regional phase” route 721
 - royalty stacking 715
 - specification 720
 - start-up companies 716
 - term extensions 723–724
 - therapeutic applications 708–709
 - third-party observations 725–726
 - time scales and costs 719
 - transactions. *See* transactions, patents
 - unitary 722
 - unsolved patent issues and litigation threat 715
- PCNSL. *See* primary central nervous system lymphoma (PCNSL)
- PD-0360324 (Pfizer) 1024, 1025
- pediatric Crohn's disease 1603
- pediatric glioma 1684
- pediatric ulcerative colitis 1609
- pegaptanib 1178
- PEGylation
 - anti-TNF nanobodies 329
 - description 328
 - lysine/cysteine amino acids 328
 - microbial expression levels 329
 - renal and hepatic pathways 329
- pentumomab 775
- pentostatin 1922–1923
- pentostatin, mitoxantrone, rituximab (PMR) 1923
- pentoxifylline 1668–1669
- peptide linkers 356
- peripheral T-cell lymphoma (PTCL) 1426
- pertuzumab
 - ADCC pathway 1874
 - adjuvant chemotherapy 1876–1877

- adverse events 1877
- anthracyclines 1878
- biomarkers 1877–1878
- Calu-3 and KPL-4 xenograft models 1874
- cardiac dysfunction 1876
- cardiac safety profile 1879–1880
- dimerization inhibitors 1874
- efficacy and safety 1875
- HER2-positive breast cancer 1871
- mAbs trastuzumab 502, 2048
- mechanisms, trastuzumab resistance 1871–1873
- pathological complete response (pCR) 1878
- PI3K/Akt inhibition 1874
- single-agent 1875–1876
- trastuzumab emtansine (T-DM1) 1878–1879
- pexelizumab 1167
- PF-04236921 (Pfizer) 988, 989
- phage display
 - comparison, recombinant antibody selection systems 43, 44
 - human hybridomas 43
 - hybridoma technology 43
 - *in vitro* selection process 45
 - *in vitro* technologies 43
 - libraries. *See* libraries
 - panning rounds, M13K07 46
 - peptide::pIII fusion protein 45
 - phage T7 and phage Lambda 45
 - phagemid system 45
 - sdAbs 319
 - selection and screening 46–47
 - vectors. *See* vectors, phage display
- phage libraries
 - combinatorial antibody libraries 107
 - guided selection 107
 - HFS and HFA 107
 - murine CDRs 107
- phagemid system 45, 48
- phagocytosis 278
- pharmacodynamic evaluation, NSCLC 1689–1690
- PHOENIX-1 (NCT00267969) 2072–2073
- PHOENIX-2 (NCT00307437) 2073
- pitracinra (Aerovance) 947, 1002
- placental growth factor (PLGF)
 - breast cancer progression 823–826
 - signal transduction 827
 - VEGF 1177
- PMBCL. *See* primary mediastinal B-cell lymphoma (PMBCL)
- PMR. *See* pentostatin, mitoxantrone, rituximab (PMR)
- PMX-53 1167
- polyclonal antibodies
 - adjuvants 1299
 - description 1296
 - FDA/regulatory considerations 1295–1296
 - immunogen 1298–1299
 - production 1297–1298
 - recombinant 1302–1303
 - route of injection 1300
 - therapeutics 1301–1302
- posttransplant lymphoproliferative disorder (PTLD) 1976–1977
- preclinical development
 - anti-drug antibodies (ADAs) 696
 - CMC comparability exercise 694
 - FDA biosimilar draft guidelines 696
 - *in vivo* non-clinical strategy 695
 - non-human primates 696
 - stepwise approach 694, 695
- preclinical studies, CARs
 - animal models 755–756
 - CAR transfected effector cells 750–751
 - effector functions, CAR gene-modified effector lymphocytes 751
 - memory function, redirected T cells 752–755
 - “naked” gene delivery systems 750
 - retroviral gene transfer into T lymphocytes 748–750
- Prediction of ImmunoGlobulin Structure (PIGS) 217, 218
- premature infants, palivizumab
 - prevention, recurrent wheeze 1837–1838
 - RSV-related hospitalization 1836–1837
- primary central nervous system lymphoma (PCNSL) 1978
- primary cutaneous CD30-positive lymphoproliferative disorders
 - brentuximab, treatment 1435
 - lymphomatoid papulosis (LyP) 1433
- primary mediastinal B-cell lymphoma (PMBCL)
 - CHOP-like CT 1957
 - DA-EPOCH-R 1957–1958
 - description 1916
 - MACOP-B and VACOP-B 1957
 - primary systemic therapy (PST) 2048
- pro-protein convertase subtilisin kexin (PCSK)-9
 - alirocumab 858–859
 - description 852
 - evolocumab 853–857

- pro-protein convertase subtilisin kexin (PCSK)-9 (*contd.*)
 - knock-out (KO) mouse studies 853
 - LDL-C 853
 - production systems
 - antibody fragments 561
 - eukaryotic expression systems. *See* eukaryotic expression systems
 - examples, expression systems 582, 583
 - functional immunoglobulin G (IgG) antibodies 561
 - glycosylation sites 561
 - prokaryotic expression systems. *See* prokaryotic expression systems
 - progression-free survival (PFS) 1426
 - prokaryotic expression systems
 - advantages and disadvantages 562
 - *Bacillus* species 564–565
 - cell-wall-less L-form, *Proteus mirabilis* 562
 - *Escherichia coli* 562–564
 - *Pseudomonas fluorescens* 564
 - prophylactic trimethoprim/sulfamethoxazole 1922
 - protein characterization and quality control testing
 - carbohydrate heterogeneity 648
 - contaminants 650
 - impurities 648–650
 - overall structural confirmation 648
 - physicochemical properties 647
 - potency 650
 - purity 647–648
 - protein-engineered antibodies
 - clinical toxicity 152
 - combined protein-and glycoengineering. *See* Fc engineering
 - computational design algorithms and high-throughput screening 154
 - engineered Fc portions 155
 - FcγRs activation 153–156
 - hOKT3γ1(Ala-Ala) 152
 - human IgG isotypes to cellular Fc receptors 151
 - mutant Fc library 153
 - mutating amino acid 297 (N297A) 152
 - mutations 152–153
 - rat anti-human CD3 antibody (YTH 12-5) 152
 - selected engineered IgG1 Fc variants 154
 - solvent-exposed amino acid residues 153
 - unmodified human IgG₄ 151
 - Xmab5574 (MOR208) 156
 - yeast display system 153
 - pseudogene (P) 211, 233, 245
 - Pseudomonas fluorescens* 564
 - psoriasis
 - characteristics 937, 1533
 - experimental autoimmune encephalomyelitis (EAE) 2071
 - IL-12 and IL-23 role 2071
 - infliximab 1607–1608
 - keratinocytes, overproduction and immature migration 2071
 - plaque 1533
 - and psoriatic arthritis 937–938
 - systemic agents 2071
 - T-cell activation 1533–1534
 - T-cell migration and extravasation 1534
 - T-cell reactivation 1534–1535
 - psoriatic arthritis (PsA) 1571–1572, 1606–1607, 2074–2075
 - PTLD. *See* posttransplant lymphoproliferative disorder (PTLD)
 - putative backmutations
 - anti-Tac humanization 102
 - CDR residues 102–103
 - description 102
 - “hybrid variable” regions 103
 - VH of antibody ABL364 103
 - PVL. *See* Panton-Valentine leukocidin (PVL)
- q**
- QAX576 (Novartis) 1004–1005
 - QBX258 (Novartis) 1003
 - QGE031 (Novartis, Roche–Genentech) 1161–1162
 - quality control testing 651, 652–653
 - Quality Target Product Profile (QTPP) 686–687
 - quaternary structure, IgG-Fc
 - inflammatory cascades activation 175
 - “overlapping nonidentical sites” 175
 - polyclonal IgG cleavage 174
 - rheumatoid factor (RF)-like autoantibody 174
 - staphylococcal protein A (SpA) 174
 - streptococcal protein G (SpG) 174
 - X-ray crystal analysis 174–175
- quilzumab 1162
- r**
- RA. *See* rheumatoid arthritis (RA)
 - rabbit reticulocyte 400
 - racotumomab 774
 - radioimmunoconjugates (RAIT)
 - lintuzumab-radiolabeled (huM195-radiolabeled) 806–807
 - therapeutic radioisotopes 806

- ⁹⁰Y-epiratuzumab (IMMU-102) 806
- radioimmunotherapy (RIT)
 - bispecific antibodies and 286–288
 - clinical studies using 1590
 - in mantle cell lymphoma 1588–1589
 - primary adverse event 1586–1587
 - principles 1581
 - therapeutic advantages 1582
- radiolabeled antibodies
 - arcitumomab 2124–2126
 - besilesomab 2131–2132
 - ¹¹¹In-capromab 2126–2129
 - fanolesomab 2132–2134
 - ¹¹¹In-imicromab 2129–2130
 - satumomab 2123–2124
 - sulesomab 2134–2137
- RAIT. *See* radioimmunoconjugates (RAIT)
- ramucirumab (VEGF-R) 764
- ranibizumab
 - AMD. *See* age-related macular degeneration (AMD)
 - anti-VEGF effect 1891–1894
 - CDR 1883
 - CRVO and BRVO 1886
 - DME 1886, 1889
 - molecular weight 1883–1884
 - myopic CNV. *See* choroidal neovascularization (CNV)
 - recombinant antibodies 1883
- RANTES 1021
- rapid automated protein purification technology (RAPPT) 627
- rapid formulation development 635
- raxibacumab
 - animal models 1902–1903
 - animal rule 1901–1904
 - anthrax attacks 1899
 - anthrax toxins. *See* anthrax toxins
 - antibiotic combination studies 1904
 - ATRs 1899–1900
 - description 1899
 - dosing 1906
 - health and human services (HHS) 1899
 - HGS 1902
 - human safety 1905–1906
 - indication 1906–1907
 - molecule generation and *in vitro* pharmacology 1901
 - monotherapy studies 1903–1904
 - nonclinical safety 1905
 - safety and anthrax 1900
- RCC. *See* renal cell carcinoma (RCC)
- REAL. *See* Revised European American Lymphoma (REAL)
- receptor gene-modified effector lymphocytes 546
- receptor tyrosine kinase (RTK) 830
- recombinant antibody selection systems 43, 44
- recombinant bispecific antibody molecules
 - antigen-binding site and IgG fusion 275–276
 - asymmetric heterodimerization domains 276–278
 - diabodies (Db) 272–274
 - genetic engineering 271
 - single-chain diabodies (scDb) 272, 274
 - single-chain variable fragment 272
 - single-domain antibodies and alternative scaffolds 272
 - tandem scFv molecules (taFv) 272, 273
 - therapeutic applications 274
 - variable domain 272–274
- recombinant cytotoxic fusion proteins
 - advantages 375
 - anti-Lewis Y-directed immunotoxins 375
 - anti-mesothelin SS1P (SS1-dsFv-PE38) 377
 - BL22 (RFB4(dsFv)-PE38) 377
 - cytokine release syndrome 375
 - cytotoxic T and NK cells 378
 - disulfide-stabilized Fv fractions (dsFvs) 374–375
 - immunoRNases 377–378
 - immunotoxins, within phase I/II clinical trials 375, 376
 - LMB-2 375–377
 - single chain Fv (scFv) fragments 374
- recombinant human soluble tumor necrosis factor receptor 1669–1670
- recombinant scFv-CPG2 fusion protein
 - description 479
 - MFCEP1 and bis-iodo phenol prodrug 480
 - MFCEP, *Pichia pastoris* 480
 - phage antibody technology 479–480
 - SW1222 colon carcinoma xenografts 480
- regorafenib 832–833
- regulatory considerations, mAbs development
 - ADCs 1236
 - approved mAbs and Fc-fusion proteins 1234–1235, 1237, 1238
 - cell line qualification 1240–1242
 - chimeric mAbs 1235
 - comparability 1247–1248
 - human mAbs 1236
 - immunogenicity 1255–1257
 - nonclinical testing 1249–1255
 - product stability 1245

- regulatory considerations, mAbs development
 - (*cont'd.*)
 - quality by design 1248–1249
 - quality control testing 1242–1244
 - reference standard 1245–1246
 - safety test, feasibility clinical trials 1246–1247
 - statutory authorities 1237–1239
 - TSE 1244–1245
 - viral clearance and inactivation studies 1246
- relapsed/refractory indolent B-cell lymphoma 1927–1930
- renal cell carcinoma (RCC)
 - girentuximab (CA IX) 767–768
 - naptumomab estafenatox (5T4) 768–769
- renal transplantation
 - basiliximab vs. daclizumab 1382
 - basiliximab vs. lymphocyte-depleting agents 1379
 - calcineurin inhibitor-sparing protocols 1381–1382
 - daclizumab 1379–1380
 - IL-2R monoclonal antibodies vs. placebo 1378–1379
 - steroid-sparing protocols 1380–1381
- renal–pancreas transplant recipients 1656
- resins and ligands 626
- reslizumab 879–881, 882–883
- respiratory syncytial virus (RSV)
 - MEDI-493 1152
 - palivizumab. *See* palivizumab, RSV disease
 - sdAbs 324
 - TLR4 1149
- restin 829
- resurfacing/veneering, humanization 104–105
- Revised European American Lymphoma (REAL) 1915
- rheumatoid arthritis (RA)
 - ACR20 2025
 - ACT-RAY trial 2026–2027
 - alemtuzumab 1359–1360
 - ankylosing spondylitis 1572–1573
 - anti-TNF α V_HHs, Ablynx 505–506
 - Arana Therapeutics 506
 - bDMARDs 2027–2028
 - biologic therapy 2025, 2026
 - canakinumab 1454
 - DMARDs 936–937
 - GlaxoSmithKline 506
 - GO-FORWARD, GO-AFTER and GO-BEFORE studies 1570–1571
 - inflammatory biomarkers 1569
 - infliximab 1603–1605
 - initiation 936
 - interleukin 6 (IL-6) signaling 506
 - juvenile idiopathic arthritis, clinical studies 1574–1575
 - monotherapy long-term extensions 2028
 - MTX treatment 1569, 2027
 - NI-0101 (Novimmune) 1150–1151
 - ofatumumab (OFA) 1760–1761
 - phase 3 studies 1569
 - propagation 936
 - psoriatic arthritis 1571–1572
 - radiographic progression 2030
 - synoviocytes 936
 - TCZ 2025, 2026
 - TLR signaling 1146
 - TNF antagonist 2029–2030
 - TNF α 505
 - TNF α -blocking drugs 936
 - tocilizumab combined therapy 2028, 2029
 - ulcerative colitis 1573–1574
- ribosome display
 - advantages 399
 - antibody generation 402
 - construction 400–401
 - eukaryotic, rabbit reticulocyte 400
 - vs. monosome 401
 - prokaryotic, E. coli S30 399–400
- RICOVER-60 trial 1954
- rilotumumab 773
- RIT. *See* radioimmunotherapy (RIT)
- rituximab
 - autoimmune disorders 1979–1985
 - B-cell lymphoma. *See* B-cell lymphoma, rituximab
 - CD20 antigen, properties 1910–1911
 - in combination with bendamustine 1926–1927
 - mechanism of action 1911–1913
 - pharmacokinetic (PK) studies 1913–1914
 - production, design and structure 1909–1910
 - subcutaneous (SC) rituximab formulation. *See* rituximab SC
 - rituximab in combination with CHOP (R-CHOP) 1925
 - rituximab in combination with CHVP-IFN 1926
 - rituximab in combination with CVP (R-CVP) 1924–1925
 - rituximab in combination with ifosfamide and etoposide (R-IE regimen) 1978
 - rituximab in combination with MCP (R-MCP) 1925–1926

- rituximab maintenance therapy
 - chemotherapy induction 1941–1942
 - description 1937, 1938–1939
 - monotherapy induction 1937, 1940–1941
 - overall survival hazard ratios (HRs) 1943–1944
 - previously untreated FL patients 1943
 - relapsed/refractory follicular lymphoma 1942
 - relapsed/refractory indolent B-cell lymphoma 1942–1943
 - rituximab monotherapy
 - relapsed indolent B-cell lymphoma 1934–1935
 - untreated patients with FL 1933–1934
 - rituximab SC
 - development 1993
 - PK bridging 1986
 - PK, safety and efficacy results 1986, 1987–1989
 - research questions 1986, 1990
 - SABRINA (BO22334) 1992
 - SAWYER (BO25341) 1992–1993
 - SparkThera (BP22333) 1986, 1991
 - romosozumab
 - CTX and P1NP 866
 - phase III studies 866, 867–868
 - postmenopausal osteoporosis 865
 - treatment 865
 - rontalizumab 997
 - “RosettaAntibody3” 217
 - RSV. *See* respiratory syncytial virus (RSV)
 - RTK. *See* receptor tyrosine kinase (RTK)
- S**
- SA237 986, 987
 - SABRINA (BO22334) 1992
 - salvage therapy 1331
 - SAN-300 1132–1133
 - SAR156597 (Sanofi) 1003
 - SAR252067 (Sanofi, licensed from KHK) 1095
 - SAR-113244 (Sanofi) 1018
 - sarcoidosis 1318
 - sarilumab
 - cytokine-mediated inflammatory signaling 869
 - MTX 870
 - phase III studies 870, 871–872
 - satumomab (OncoScint®) 2123–2124
 - SAWYER (BO25341) 1992–1993
 - scaffold proteins
 - contiguous hypervariable loop region. *See* contiguous hypervariable loop region
 - individual extended loops. *See* individual extended loops
 - rigid secondary structure interface 457–461
 - SCCHN. *See* squamous cell carcinoma of head and neck (SCCHN)
 - scFv. *See* single chain Fv (scFv)
 - sclerostin
 - animal models 859–865
 - bone density measurement 865
 - osteoblastogenesis, inhibitor 859
 - romosozumab 865–866
 - SOST gene complex 859
 - SCRs. *See* structurally conserved regions (SCRs)
 - sdAbs. *See* single-domain antibodies (sdAbs)
 - SDR. *See* specificity-determining residue (SDR)-transfer
 - second and third signals, CARs 529–530
 - selectins 1136–1137
 - semaphorins
 - expression 1086
 - humoral and cellular immunity 1085
 - inflammatory disease therapy 1085
 - plexins 1085
 - VX-15 1086
 - sequence families
 - heavy chain variable genes (V_H) 221
 - human family chronology. *See* human family chronology
 - light chain variable genes (V_L and V_κ) 221–222
 - mouse family chronology. *See* mouse family chronology
 - subgroups and 218–219
 - sequential rituximab
 - CHOP CT 1923
 - fludarabine 1964
 - FND 1923
 - sialic acid binding immunoglobulin-type lectins (SIGLECs) 904
 - sialylation, IgG-Fc oligosaccharides
 - amino acid residues 184
 - ASGPR 184
 - autoantibody-initiated inflammation 185
 - galactose residues 184
 - inflammatory cascades 185
 - sifalimumab 996
 - SIGLECs. *See* sialic acid binding immunoglobulin-type lectins (SIGLECs)
 - single-chain CARs 524–525
 - single-chain diabodies (scDb) 272, 274

- single chain Fv (scFv)
 - antibody format 46
 - assembly PCR 58
 - V gene subfamilies 58
 - Yol linker and Gly-Ser linker 48
- single-domain antibodies (sdAbs)
 - ability and stability 324
 - affinity maturation 321
 - albumin binding. *See* albumin binding
 - albumin-binding 311
 - bi-/tri-specific molecules 311
 - bi-specifics and targeted payloads 326–328
 - biopharmaceuticals 312
 - *Camelidae* (nanobodies)/human frameworks 314
 - clinical assets 314, 315–316
 - companies 312, 313
 - conventional mAbs/HCAbs/IgNARs 312, 313
 - cryptic and conformational epitopes 323
 - diagnostic application 325–326
 - Fc-fusion. *See* Fc-fusion
 - HCAbs 311
 - HIV-1-integrase, TVNH and GFP 320
 - *in vitro* compartmentalization and ribosome display 320–321
 - imaging 332–334
 - immune library generation 317
 - immune repertoires 320
 - modularity 324
 - naïve library generation 317
 - natural immunoglobulin repertoire, camels 312
 - PEGylation. *See* PEGylation
 - phage display 319
 - pharmacokinetics/biodistribution 328
 - polyethylene glycols (PEGs) 311
 - pulmonary administration 324
 - radioisotope-based imaging 311
 - structural differences 322
 - synthetic library generation 317–318
 - target space 321
 - tissue penetration 325
 - transgenic animals 318–319
 - yeast and bacterial display 319–320
- single domain immunoglobulins
 - Bence–Jones dimers 449
 - CDR loop 448
 - “heavy-chain” antibodies 449
 - Ig novel antigen receptors (IgNARs) 449
 - light and heavy chains 448
 - research tools and protein therapeutics 448
 - single-chain (sc) F_v fragments 448–449
 - X-ray structural analysis 449
- sirukumab (CNT0136)
 - human anti-IL-6 mAb 870
 - MTX therapy 870, 873
 - phase III trials 873, 874
- sJIA. *See* systemic-onset juvenile idiopathic arthritis (sJIA)
- Sjögren’s syndrome 1984
- Skin toxicity 1861
- SLE. *See* systemic lupus erythematosus (SLE)
- small lymphocytic lymphoma (SLL)
 - 1915–1916, 1936
- SMZL. *See* splenic marginal zone lymphoma (SMZL)
- solanezumab 907–908
- solid organ transplantation
 - alemtuzumab immunosuppressive properties 1364
 - and IL-2R-based therapy 1377–1378
 - kidney and pancreas 1364
 - MMF 1365
- soliris (eculizumab)
 - clinical efficacy data 1269
 - clinical package 1269
- soluble antigens
 - antibody characteristics 126
 - ELISA 126
 - epitopes 126–127
 - keyhole limpet hemocyanin (KLH) 126
 - methods and technologies 127
- soluble mediators
 - chemokine inhibitors 1015–1023
 - cytokine inhibitors 969–1015
 - growth factor inhibitors 1023–1028
- somatic gene therapy, bispecific antibodies
 - adenoviral vectors 292
 - bispecific chemical conjugates 292
 - conditionally replicative adenoviruses (CRADs) 293
 - DNA *in vivo* transfer 291
 - gene transfer vehicle 292
 - recombinant 292
- somatic hybridization
 - antibody-secreting cells 268, 269
 - enzyme-linked immunosorbent assay (ELISA) 269
 - fluorescence-activated cell sorting (FACS) 269
 - heavy and light chain pairing 269
 - heterologous heavy chain pairing 269
- sonenpcizumab 810–811, 1179, 1180–1181
- source (donor) sequence analysis
 - canonical residues 93
 - CDRs. *See* complementarity determining regions (CDRs)

- interface packing residues. *See* interface packing residues
 - N-/O-glycosylation sites 95
 - rare framework residues 94–95
 - SparkThera (BP22333) 1986, 1991
 - specificity-determining residue (SDR)-transfer
 - anti-V-region antibodies 106
 - CDR-grafted mAbs 105
 - murine mCOL-1 105
 - sphingosine 1-phosphate (S1P) 1178–1180
 - splenic marginal zone lymphoma (SMZL)
 - rituximab therapy 1935–1936
 - splenectomy 1916
 - SPR. *See* surface plasmon resonance (SPR)
 - squamous cell carcinoma of head and neck (SCCHN)
 - cetuximab 1509
 - combination therapy 1509–1510
 - grade 3 toxicities 1509
 - monotherapy 1509
 - panitumumab 1864
 - radiotherapy 1509
 - structurally conserved regions (SCRs)
 - average α -carbon coordinates 96
 - and templates 96
 - Study of Transitioning from Alendronate to Denosumab (STAND)
 - BMD and bone turnover 1525
 - CTX-I levels 1525
 - side effects 1525–1526
 - STX-100 1014–1015
 - subcutaneous (SC) rituximab formulation. *See* rituximab SC
 - subgroups assignment, tools 213
 - sulesomab (Leukoscan[®]) 2134–2137
 - surface plasmon resonance (SPR)
 - antibody affinity 129
 - “avidity effects” 130
 - Biacore system 130
 - charge-coupled device (CCD) camera 131
 - evanescence wave 129
 - physical process 128
 - sensors 129–130
 - total internal reflection (TIR) 129
 - synthetic library generation
 - description 317
 - human antibody scaffolding 318
 - natural antibody repertoires 318
 - negatively charged solubilizing amino acids 318
 - risks, immune response 317–318
 - submicromolar affinity, sdAbs 317
 - systemic juvenile idiopathic arthritis (sJIA)
 - ACR50 response 1454, 1456
 - characterization 1452
 - IL-1 and IL-6 1452
 - phase III trials 1453–1454
 - treatment 1454, 1455
 - systemic lupus erythematosus (SLE)
 - AMG 729 1117
 - BAFF levels 1118
 - belimumab 1405
 - rituximab 1116, 1120, 1982
 - systemic-onset juvenile idiopathic arthritis (sJIA)
 - designed international trial 2031–2032
 - intention-to-treat analysis 2031
 - radiologic evaluation 2031
 - TCZ treatment 2030
- t**
- T-and B-cell epitopes 106
 - T-cell depletion and graft rejection prevention
 - campath-1 family 1360
 - lymphocytes 1361
 - T cell inhibitors
 - anti-CD3 1081–1083
 - anti-CD4 1083–1085
 - anti-CD100 1085–1086
 - anti-T cell $R\alpha\beta$ 1079–1081
 - T-cell prolymphocytic leukemia (T-PLL) 1355–1356
 - T cell receptors
 - and antibodies 521–522
 - antigen-specific 1086
 - immunoglobulin 522–523
 - mAbs 1080
 - MHC-restricted CD4⁺ T helper cells 1079
 - $\alpha\beta$ TCR 1080, 1081
 - T-cellular non-Hodgkin’s lymphoma 758–759
 - TAB-08 1088
 - tabalumab 899, 1119
 - TALENs. *See* transcription activator-like effector nucleases (TALENs)
 - TAMs. *See* tumor-associated macrophages (TAMs)
 - tandem scFv molecules (taFv) 272–273
 - target antigen selection, ADC therapy
 - CD22 expression in B-cell neoplasias 1547–1548
 - CD33 in AML 1546–1547
 - target/disease class infix
 - single letter 1284
 - source infix 1285–1286
 - tumor-specific infixes 1285
 - USANC 1284

- taxanes, trastuzumab in combination
 - docetaxel monotherapy 2045–2046
 - paclitaxel 2045
 - phase III trial 2047
- TGF β inhibitors
 - anti- α V β 6 integrin 1014–1015
 - antiproliferative and proapoptotic effects 1011, 1012
 - description 1011
 - fresolimumab 1013
 - immunosuppressive role 1013
 - isoforms 1011
 - LY2382770 (Eli Lilly) 1013
 - metelimumab (CAT-192) 1012
- TH1 cytokines
 - anti-IFN- α 996–998
 - anti-IFN- α β R 998
 - anti-IFN- γ 998–1000
 - anti-IL-1 979–982
 - anti-IL-6 987–989
 - anti-IL-17 989–991
 - anti-IL-18 982–984
 - anti-IL-20 993–994
 - anti-IL-21 994–995
 - anti-IL-23 992–993
 - anti-IL-6R 986–987
 - anti-LT α 976–978
 - anti-TNF α 970–974
 - anti-TNFR1 975–976
 - anti-TWEAK 978–979
 - IL-6 inhibitors 984–986
- TH2 cytokines
 - anti-IL-10 1007–1008
 - anti-IL-13 1003–1005
 - anti-IL-31 1010–1011
 - anti-IL-4 and anti-IL-13 1000–1002
 - anti-IL-5R/IL-5 1005–1007
 - anti-IL-4R α 1002–1003
 - anti-TSLP 1008–1010
- therapeutic antibodies
 - anti-CD3 antibody 4
 - antibody structure 2–3
 - biosimilar antibodies 10
 - cancer and immune-mediated disorders 2
 - cell surface markers and soluble molecules 7
 - clinical studies 2012 7
 - combination therapies 11
 - in European Union/United States 7, 8
 - immune defense 1
 - lateral chain theory 2
 - mogamulizumab, afucosylated IgG1 11
 - molecular and immunological processes 10
 - molecular cloning and recombinant expression 4
 - natalizumab (Tysabri[®]) 10
 - new therapeutic agents 6
 - novel alternative production systems 6
 - novel molecular designs 11
 - passive and active vaccination 1, 2
 - recombinant human IgG therapeutics 5
 - specificity issues 6
 - systems employed, human antibodies 4, 5
 - thrombocytopenia 1331
 - thrombospondin 1 (TSP-1)
 - HIF-1 α 830
 - p53 tumor suppressor gene 830
 - thymic stromal lymphopoietin (TSLP) 1008–1010
 - TKIs. *See* tyrosine kinase inhibitors (TKIs)
 - TNFR-associated factor (TRAF) 1418–1419
 - tocilizumab (TCZ)
 - Castleman’s disease 2032
 - CRP 2032–2033
 - IL-6. *See* Interleukin 6 (IL-6)
 - monotherapy 2025, 2026
 - rheumatoid arthritis. *See* rheumatoid arthritis
 - sJIA. *See* systemic-onset juvenile idiopathic arthritis
 - TOL-101 (Tolera Therapeutics) 1080–1081
 - toll-like receptors (TLRs)
 - anti-TLR2 1146–1147
 - anti-TLR3 1147–1149
 - anti-TLR4 1149–1151
 - description 1145–1146
 - inhibitors 1146–1151
 - TLR2 1146
 - TLR3 1147–1149
 - TLR4 1149–1150
 - tositumomab
 - CD20 2116–2117
 - nonhematologic side effects 2117
 - production 2116
 - response rate 2117
 - risks 2117
 - therapeutic regimen 2117–2118
 - tralokinumab 1003, 1004
 - transactions, patents
 - commercial success 726
 - description 726
 - licensing 727–728
 - sale 728–729
 - university/small biotechnology company 727
 - transcription activator-like effector nucleases (TALENs) 451, 576, 577–578, 608

- transgenic animals 318–319
- transgenic rodents
 - BAC integration 81
 - construction, human Ig transloci. *See* human Ig transloci construction
 - designer zinc finger endonucleases, endogenous Ig loci. *See* zinc finger (endo)nucleases (ZFNs)
 - DNA rearrangement 77
 - embryonic stem (ES) cells 77
 - expression comparison, human and chimeric IgH loci. *See* human and chimeric IgH loci
 - FDA-approved therapeutic monoclonal antibodies 77, 78
- transmissible spongiform encephalopathies
 - active immunotherapy 1225
 - disease and target 1224–1225
 - passive immunotherapy 1225
- transmissible spongiform encephalopathy (TSE) 1244–1245
- trastuzumab emtansine 763–764, 1878–1879
- trastuzumab monotherapy
 - chemotherapy regimens 2043
 - median survival 2043
 - response rates 2044
- trastuzumab resistance
 - alternative ErbB ligands 1873
 - description 1871, 1872
 - HER2 interaction 1873
 - membrane-associated glycoprotein MUC4 1871
 - p95HER2 expression 1872
 - PI3K-AKT-mTOR signaling pathway 1872–1873
- tregalizumab 1084–1085
- trifunctional antibodies (trAb)
 - affinity and ion-exchange chromatography 1467
 - anti-drug antibodies (ADAs) 1466
 - biomarkers treatment 1490–1491
 - bispecific CrossMab antibodies 1466–1467
 - H/H chain assembly 1467–1468
 - human IgG-like bsAb formats 1466–1467
 - immunogenicity 1466–1467
 - low target antigen expression 1473–1474
 - mAb chimerization 1466
 - mouse/rat hybrid-hybridomas 1467
 - phase II trial (SECIMAS) 1466
 - quadroma technology 1467
 - triomab antibody concept 1466
 - triomab[®] trAb family. *See* triomab[®] trAb family
 - in tumor treatment. *See* tumor treatment
 - triomab[®] trAb family
 - anti-CD20 × anti-CD3 lymphomun 1484–1488
 - anti-EpCAM × anti-CD3 catumaxomab 1474–1481
 - anti-GD2 × anti-CD3 ektomab 1488–1490
 - anti-HER2/neu × anti-CD3 ertumaxomab 1482–1484
 - CASIMAS trial 1476
 - malignant ascites treatment 1474–1481
 - pharmacokinetic analysis 1477
 - SECIMAS study 1476
 - time-to-next therapeutic puncture (TTP) 1475
- tumor-associated macrophages (TAMs) 828
- tumor control ratio (TCR) 1709
- tumor growth inhibition (TGI) 1710
- tumor therapy
 - antibody engineering 17
 - bispecific antibodies 35
 - CDC and ADCC 35
 - enzyme prodrug activation 441
 - epithelial differentiation antigens 33–34
 - human monoclonal antibodies 35–36
 - leukocyte differentiation antigens 33
 - therapeutic effects 34–35
- tumor treatment
 - anti-EpCAM antibody titers 1472
 - autologous human *ex vivo* systems 1468
 - catumaxomab-mediated concerted attack 1469
 - CLL patients 1472
 - cytokine secretion and tumor cell elimination 1469
 - ELISPOT analysis 1472, 1473
 - EpCAM and HER2/neu expression profile 1471
 - Fc region, role 1470
 - gastric and ovarian cancer 1471
 - intraoperative catumaxomab application 1471
 - peritoneal carcinomatosis (PC) 1471
 - polyclonal T cells 1468
 - stem cell transplantation (SCT) 1472
 - T cell activation markers 1468
 - TAA-specific binding 1468
 - TAA-specific MHC class I-restricted CD8⁺ T cells 1471
 - therapy and autoimmune diseases 288
 - trAb-stimulated T lymphocytes 1471
 - trastuzumab with chemotherapy 1470–1471
 - tri-cell complex 1468

- tumor treatment (*contd.*)
- tumor-reactive antibodies 1471
 - vaccination-like effects 1470–1472
 - tumstatin 829–830
 - tyrosine kinase inhibitors (TKIs) 2048
- u**
- UF/DF. *See* ultra/diafiltration (UF/DF)
- ulcerative colitis 1573–1574, 1608–1609
- ultra/diafiltration (UF/DF) 622
- upstream processing. *See also* commercial manufacturing processes
- cell culture. *See* cell culture
 - description 604
 - expression systems. *See* expression systems
 - holistic model 604–605
 - MCB and WCB 604
 - urticaria/angioedema 1803, 1812, 1813
 - US biosimilars 684
 - USAN Council (USANC) 1283
 - ustekinumab
 - ACCEPT (NCT00454584) 2073
 - action mode 2070
 - Crohn’s disease. *See* Crohn’s disease
 - DLQI scores 2074
 - meta analyses, long-term use 2078
 - multiple sclerosis 2077–2078
 - NCT00747344 (Pearl) 2074
 - ongoing observational studies 2083
 - PHOENIX-1 (NCT00267969) 2072–2073
 - PHOENIX-2 (NCT00307437) 2073
 - psoriasis. *See* psoriasis
 - studies with no results 2079–2082
 - uveitis
 - adalimumab (Humira®) 1314–1316
 - autoimmune 943
 - description 943
 - immunosuppressive drugs 943
 - TNF-blocking therapy 943–944
- v**
- vascular addressin protein-1 (VAP-1) 1134–1135
- vascular endothelial growth factor (VEGF)
- antibodies 835
 - biological effects 830
 - cancer therapy 830
 - chemotherapeutic agents 831
 - fusion constructs 835–836
 - intracrine VEGFR1/VEGF signaling 831
 - ligand 833–835
 - resistance mechanisms 836
 - RTK 830
 - tumor vasculature 831
 - VEGF-A 2089
- vastatin 829
- vatelizumab 1134
- VAY736 1119
- vectors, phage display
- in alphabetical order 48, 49–56
 - amber stop (TAG) codon 48, 57
 - *Erwinia caratovor*a 48
 - Fab fragments 48
 - Hyperphage/Ex-phage 57
 - lacZ and gIII promoter (gIII) 48
 - pSEX81/pHAL14 48
 - vedolizumab 900–901, 1129
- VEGF. *See* vascular endothelial growth factor (VEGF)
- veltuzumab 1120–1121
- venom immunotherapy (VIT) 1813–1814
- VH and VL 494
- V_HH 492, 493
- viral diseases and anti-infectious monoclonal antibodies
- CCR5 1203
 - CMV 1203–1204
 - HCV 1204
 - HIV infection 1202–1203
 - immunoassays 1206
 - influenza 1204–1205
 - mAbs 1201–1202
 - Pfizer® 1203
 - RSV 1202
 - SARS 1206
- VIT. *See* venom immunotherapy (VIT)
- VNAR 492, 493
- VX-15 1086
- w**
- Waldenström’s Macroglobulinemia (WM) 1936–1937
- web resources
- antibody V domain humanization 246–247
 - IGHG CH amino acid positions. *See* IGHG CH amino acid positions
 - IMGT data 212
 - Kabat data 211–212
 - only-heavy-chain antibodies 247–249
- WM. *See* Waldenström’s Macroglobulinemia (WM)
- x**
- xenograft models
- of AML 1550
 - F(ab) 2 fragments conjugated to CPG2 479
 - human cancer 347

- multiple human cancer cell lines 839
- obinutuzumab 1709–1712
- in SCID mice 1121

Y

- yeast
 - and bacterial display 319–320
 - endogenous AOX promoter 566
 - eukaryotic folding and secretion apparatus 565
 - Fc-receptor binding, antibodies 568
 - fermentation process 565
 - GlcNAc and galactose residues 567
 - immunoglobulin binding protein (BiP) chaperone 568
 - Kex2 protease 567
 - ManII and GnTII 567
 - O-glycosylation 568
 - *P. pastoris* 566
 - pharmaceutical production 566
 - proteolytic degradation 567
 - recombinant antibody expression 566
 - *Y. lipolytica* and *K. lactis* 566
 - yeast-expressed scFv-Fc fusion proteins 568–569
- yttrium-90 ibritumomab tiuxetan (Zevalin®)
 - absolute neutrophils count (ANC) 1586
 - adverse events 1586–1587
 - aggressive (DLBCL) NHL 1588
 - chelators 1583
 - clinical therapeutic efficacy 1585–1586

- dosing 1584
- First-Line Indolent Trial (FIT) investigators 1587
- frontline chemotherapy 1589–1590
- indications 1588
- in lymphoma, therapeutic advantages 1582
- in mantle cell lymphoma 1588–1589
- NHL 1579, 1580
- preclinical results 1585
- preparation 1582–1584
- radioimmunotherapy 1581
- stem cell transplantation 1590–1592
- uses 1587–1588

Z

- zalutumumab 762
- zalutuzumab 832
- zanolimumab 758–759, 1083–1084
- ZFNs. *See* zinc finger (endo)nucleases (ZFNs)
- zinc finger (endo) nucleases (ZFNs)
 - detrimental deletions 83
 - DNA repair pathways 577
 - double-strand breaks, target sites 82, 83
 - homolog recombination, nucleases 576
 - knockout lines, fully silenced Ig loci 82
 - mutations/knockout animals 82
 - sequence-recognition and cleavage function, *FokI* 82
 - and TALENs 577

