

# Development Pipeline as at 30 June 2012

## Line Extensions

| Compound   | Mechanism                                    | Area Under Investigation  | Phase | Date Commenced Phase | Estimated Filing |          |          |          |
|--|--|---|-------|----------------------|------------------|----------|----------|----------|
|  |  |   |       |                      | US               | EU       | Japan    | Emerging |
| <b>Cardiovascular</b>  |  |   |       |                      |                  |          |          |          |
| Axanum   | proton pump inhibitor + low dose aspirin FDC | low dose aspirin associated peptic ulcer in high risk CV patients         | III   |                      | Withdrawn        | Launched | 1H 2013* | Approved |
| Brilinta/<br>Briliq<br>EUCLID  | ADP receptor antagonist                      | outcomes study in patients with PAD                                       | III   | 3Q 2012              | 2016             | 2016     | 2016     | 2016     |
| Brilinta/<br>Briliq<br>PEGASUS-TIMI 54   | ADP receptor antagonist                      | outcomes study in patients with ACS                                       | III   | 4Q 2010              | 2015             | 2015     | 2015     | 2015     |
| Crestor <sup>#</sup>   | statin                                       | outcomes in subjects with elevated CRP                                    | III   |                      | Launched         | Launched |          | Launched |
| Forxiga <sup>TM</sup><br>(dapagliflozin)/<br>metformin<br>FDC <sup>#</sup>         | SGLT2 inhibitor + metformin FDC              | diabetes  | III   | 3Q 2007              |                  | 3Q 2012  |          |          |
| Forxiga <sup>TM</sup><br>(dapagliflozin) <sup>#</sup>                              | SGLT2 inhibitor                              | diabetes – add on to DPP-4  | III   | 1Q 2010              |                  | 3Q 2012  |          |          |
| Forxiga <sup>TM</sup><br>(dapagliflozin) <sup>#</sup>                              | SGLT2 inhibitor                              | diabetes – add on to insulin and add-on to metformin long-term data       | III   | 2Q 2008              |                  | 3Q 2012  |          |          |
| Forxiga <sup>TM</sup><br>(dapagliflozin) <sup>#</sup>                              | SGLT2 inhibitor                              | diabetes – in patients with high CV risk - Study 18 and 19 long-term data | III   | 1Q 2010              |                  | 2H 2013  |          |          |
| Forxiga <sup>TM</sup><br>(dapagliflozin) <sup>#</sup>                              | SGLT2 inhibitor                              | diabetes – triple therapy (dapa+met+SU)                                   | III   | 1Q 2011              |                  | 2H 2013  |          |          |
| Kombiglyze<br>XR <sup>TM</sup> /<br>Komboglyze <sup>TM</sup><br>FDC <sup>#**</sup> | DPP-4 inhibitor + metformin FDC              | diabetes  | III   |                      | Launched         | Approved |          | Approved |
| Onglyza <sup>TM</sup><br>SAVOR-TIMI<br>54 <sup>#</sup>                             | DPP-4 inhibitor                              | outcomes study  | III   | 2Q 2010              | 2016             | 2016     |          | 2016     |

| Compound                              | Mechanism  | Area Under Investigation                    | Phase | Date Commenced Phase | Estimated Filing |          |          |          |
|---------------------------------------|--|---|-------|----------------------|------------------|----------|----------|----------|
|                                       |  |   |       |                      | US               | EU       | Japan    | Emerging |
| <b>Gastrointestinal</b>               |  |   |       |                      |                  |          |          |          |
| <i>Entocort</i>                       | glucocorticoid steroid                               | Crohn's disease / ulcerative colitis        | III   |                      | Launched         | Launched | 2014     | Launched |
| <i>Nexium</i>                         | proton pump inhibitor                                | peptic ulcer bleeding                       | III   |                      | Filed***         | Launched |          | Launched |
| <b>Infection</b>                      |  |   |       |                      |                  |          |          |          |
| <i>FluMist/Fluenz</i>                 | live, attenuated, intranasal influenza virus vaccine | influenza                                   | III   |                      | Launched         | Approved |          | Launched |
| <b>Neuroscience</b>                   |  |   |       |                      |                  |          |          |          |
| <i>Diprivan</i> #                     | sedative and anaesthetic                             | conscious sedation                          | III   |                      |                  | Launched | 2H 2013  | Launched |
| <i>EMLA</i> #                         | local anaesthetic                                    | topical anaesthesia                         | III   |                      |                  | Launched | Launched | Launched |
| <b>Oncology</b>                       |  |   |       |                      |                  |          |          |          |
| <i>Faslodex</i>                       | oestrogen receptor antagonist                        | 1 <sup>st</sup> line advanced breast cancer | III   |                      | 2016             | 2016     | 2016     | 2016     |
| <i>Iressa</i>                         | EGFR tyrosine kinase inhibitor                       | treatment beyond progression                | III   | 1Q 2012              |                  | 2015     | 2015     | 2015     |
| <b>Respiratory &amp; Inflammation</b> |  |   |       |                      |                  |          |          |          |
| <i>Oxis</i>                           | long-acting β <sub>2</sub> agonist                   | COPD  | III   |                      |                  | Launched | Approved |          |
| <i>Symbicort</i>                      | inhaled steroid/ long-acting β <sub>2</sub> agonist  | asthma / COPD                               | III   | 4Q 2011              | 2014             |          |          |          |
| <i>Symbicort</i>                      | inhaled steroid/ long-acting β <sub>2</sub> agonist  | COPD  | III   |                      | Launched         | Launched | Filed    | Launched |
| <i>Symbicort</i>                      | inhaled steroid/ long-acting β <sub>2</sub> agonist  | SMART                                       | III   |                      |                  | Launched | Launched | Launched |

#Partnered product

\* Nexium low-dose aspirin indications approved in 1H 2012

\*\*Kombiglyze XR™ US; Komboglyze™ FDC EU

\*\*\*2<sup>nd</sup> CRL received in June 2011

## NCEs

## Phase III/Registration

| Compound  | Mechanism  | Area Under Investigation                                   | Phase | Date Commenced Phase | Estimated Filing |          |          |          |
|---|--|--|-------|----------------------|------------------|----------|----------|----------|
|   |  |  |       |                      | US               | EU       | Japan    | Emerging |
| <b>Cardiovascular</b>                                 |  |  |       |                      |                  |          |          |          |
| Brilinta/Briliq                                       | ADP receptor antagonist  | arterial thrombosis  | III   |                      | Launched         | Launched | 1H 2013  | Launched |
| Forxiga <sup>TM</sup><br>(dapagliflozin) <sup>#</sup> | SGLT2 inhibitor  | diabetes   | III   | 3Q 2007              | Filed*           | Filed**  | 1H 2013  | Filed    |
| <b>Infection</b>                                      |  |  |       |                      |                  |          |          |          |
| CAZ AVI <sup>#</sup><br>(CAZ104)                      | beta lactamase inhibitor/ cephalosporin                                      | serious infections   | III   | 1Q 2012              | N/A              | 2014     | 2014     | 2014     |
| Q-LAIV<br>Flu Vac***                                  | live, attenuated, intranasal influenza virus vaccine (quadrivalent)          | seasonal influenza   | III   |                      | Approved         | 4Q 2012  |          |          |
| Zinfo <sup>#</sup><br>(ceftaroline)                   | extended spectrum cephalosporin with affinity to penicillin-binding proteins | pneumonia / skin infections                                | III   | 1Q 2007              | N/A              | Filed**  |          | Filed    |
| <b>Neuroscience</b>                                   |  |  |       |                      |                  |          |          |          |
| naloxegol<br>(NKTR-118) <sup>#</sup>                  | oral peripherally-acting opioid antagonist                                   | opioid-induced constipation                                | III   | 2Q 2011              | 2H 2013          | 2H 2013  |          |          |
| <b>Oncology</b>                                       |  |  |       |                      |                  |          |          |          |
| Caprelsa  | VEGFR / EGFR tyrosine kinase inhibitor with RET kinase activity              | medullary thyroid cancer                                   | III   |                      | Launched         | Launched | 2014     | Filed    |
| Ranmark <sup>#</sup><br>(denosumab)                   | anti-RANKL MAb   | bone disorders stemming from bone metastasis               | III   |                      | N/A              | N/A      | Launched | N/A      |
| <b>Respiratory &amp; Inflammation</b>                 |  |  |       |                      |                  |          |          |          |
| fostamatinib <sup>#</sup>                             | spleen tyrosine kinase (SYK) inhibitor                                       | rheumatoid arthritis                                       | III   | 3Q 2010              | 2H 2013          | 2H 2013  |          | 2H 2013  |
| lesinurad   | selective inhibitor of URAT1   | chronic management of hyperuricaemia in patients with gout | III   | 4Q 2011              | 2014             | 2014     | 2016     | 2014     |

<sup>#</sup>Partnered product<sup>\*</sup>CRL received in January 2012<sup>\*\*</sup>Positive opinion received from CHMP in 1H 2012<sup>\*\*\*</sup>sBLA in US, MAA in EU

## NCEs

Phases I and II

| Compound                | Mechanism   | Area Under Investigation                             | Phase | Date Commenced Phase | Estimated Filing |    |       |          |
|-------------------------|---|--|-------|----------------------|------------------|----|-------|----------|
|                         |   |  |       |                      | US               | EU | Japan | Emerging |
| <b>Cardiovascular</b>   |   |  |       |                      |                  |    |       |          |
| AZD4017                 | 11BHSD  | glaucoma   | II    | 1Q 2011              |                  |    |       |          |
| AZD2820 <sup>#</sup>    | melanocortin receptor type 4 (MC4r) partial agonist peptide | obesity  | I     | 2Q 2011              |                  |    |       |          |
| <b>Gastrointestinal</b> |   |  |       |                      |                  |    |       |          |
| tralokinumab            | anti-IL-13 MAb  | ulcerative colitis                                   | II    | 2Q 2012              |                  |    |       |          |
| <b>Infection</b>        |   |  |       |                      |                  |    |       |          |
| AZD9773 <sup>#</sup>    | anti-TNF-alpha polyclonal antibody                          | severe sepsis  | II    | 1Q 2008              |                  |    |       |          |
| CXL <sup>#</sup>        | beta lactamase inhibitor/cephalosporin                      | MRSA   | II    | 4Q 2010              |                  |    |       |          |
| AZD5847                 | oxazolidinone antibacterial inhibitor                       | tuberculosis   | I     | 4Q 2009              |                  |    |       |          |
| MEDI-550                | pandemic influenza virus vaccine                            | pandemic influenza prophylaxis                       | I     | 2Q 2006              |                  |    |       |          |
| MEDI-557                | anti-RSV MAb – extended half-life                           | RSV prevention in high-risk adults (COPD/CHF/ Other) | I     | 3Q 2007              |                  |    |       |          |
| MEDI-559                | paediatric RSV vaccine                                      | RSV prophylaxis                                      | I     | 4Q 2008              |                  |    |       |          |
| <b>Neuroscience</b>     |   |  |       |                      |                  |    |       |          |
| AZD3241                 | myeloper-oxidase (MPO) inhibitor                            | Parkinson's disease                                  | II    | 2Q 2012              |                  |    |       |          |
| AZD3480 <sup>#</sup>    | alpha4/beta2 neuronal nicotinic receptor agonist            | Alzheimer's disease                                  | II    | 3Q 2007              |                  |    |       |          |
| AZD5213                 | histamine-3 receptor antagonist                             | Alzheimer's disease / ADHD                           | II    | 2Q 2012              |                  |    |       |          |
| AZD6765                 | NMDA receptor antagonist                                    | major depressive disorder                            | II    | 3Q 2007              |                  |    |       |          |
| AZD1446 <sup>#</sup>    | alpha4/beta2 neuronal nicotinic receptor agonist            | Alzheimer's disease                                  | I     | 4Q 2008              |                  |    |       |          |
| MEDI-5117               | anti-IL-6 MAb   | OA Pain  | I     | 2Q 2012              |                  |    |       |          |

#Partnered product

## NCEs

Phases I and II (continued)

| Compound  | Mechanism                              | Area Under Investigation                  | Phase | Date Commenced Phase | Estimated Filing |    |       |          |
|---|--|---|-------|----------------------|------------------|----|-------|----------|
|   |  |   |       |                      | US               | EU | Japan | Emerging |
| <b>Oncology</b>   |  |   |       |                      |                  |    |       |          |
| AZD4547   | FGFR tyrosine kinase inhibitor         | solid tumours                             | II    | 4Q 2011              |                  |    |       |          |
| AZD8931   | erbB kinase inhibitor                  | breast cancer chemo. combi./solid tumours | II    | 2Q 2010              |                  |    |       |          |
| fostamatinib <sup>#</sup>   | spleen tyrosine kinase (SYK) inhibitor | haematological malignancies               | II    | 1Q 2012              |                  |    |       |          |
| MEDI-551 <sup>#</sup>   | anti-CD19 MAb                          | haematological malignancies               | II    | 1Q 2012              |                  |    |       |          |
| MEDI-573 <sup>#</sup>   | anti-IGF MAb                           | solid tumours                             | II    | 2Q 2012              |                  |    |       |          |
| MEDI-575 <sup>#</sup>   | anti-PDGFR-alpha MAb                   | NSCLC / glioblastoma                      | II    | 4Q 2010              |                  |    |       |          |
| olaparib  | PARP inhibitor                         | gBRCA ovarian cancer                      | II    | 1Q 2012              |                  |    |       |          |
| selumetinib <sup>#</sup><br>(AZD6244)<br>(ARRY-142886)            | MEK inhibitor                          | solid tumours                             | II    | 4Q 2006              |                  |    |       |          |
| tremelimumab  | anti-CTLA4 MAb                         | solid tumours                             | II    | 3Q 2004              |                  |    |       |          |
| AZD1208   | PIM kinase inhibitor                   | haematological malignancies               | I     | 1Q 2012              |                  |    |       |          |
| AZD1480   | JAK1, 2 inhibitor                      | solid tumours                             | I     | 2Q 2009              |                  |    |       |          |
| AZD2014   | TOR kinase inhibitor                   | solid tumours                             | I     | 1Q 2010              |                  |    |       |          |
| AZD3514   | androgen receptor down-regulator       | prostate cancer                           | I     | 3Q 2010              |                  |    |       |          |
| AZD5363 <sup>#</sup>  | AKT inhibitor                          | solid tumours                             | I     | 4Q 2010              |                  |    |       |          |
| AZD8330 <sup>#</sup><br>(ARRY 424704)                             | MEK inhibitor                          | solid tumours                             | I     | 1Q 2007              |                  |    |       |          |
| MEDI-0639   | anti-DLL-4 MAb                         | solid tumours                             | I     | 2Q 2012              |                  |    |       |          |
| MEDI-3617 <sup>#</sup>  | anti-ANG-2 MAb                         | solid tumours                             | I     | 4Q 2010              |                  |    |       |          |
| MEDI-565 <sup>#</sup>   | anti-CEA BiTE                          | solid tumours                             | I     | 1Q 2011              |                  |    |       |          |
| MEDI-6469 <sup>#</sup>  | murine anti-OX40 MAb                   | solid tumours                             | I     | 1Q 2006              |                  |    |       |          |
| moxetumomab pasudotox <sup>#</sup>                                | anti-CD22 recombinant immunotoxin      | haematological malignancies               | I     | 2Q 2007              |                  |    |       |          |
| selumetinib<br>(AZD6244)<br>(ARRY-142886)<br>/MK2206 <sup>#</sup> | MEK/AKT inhibitor                      | solid tumours                             | I     | 4Q 2009              |                  |    |       |          |
| volitinib <sup>#</sup>  | MET inhibitor                          | solid tumours                             | I     | 1Q 2012              |                  |    |       |          |

#Partnered product

## NCEs

Phases I and II (continued)

| Compound                              | Mechanism                    | Area Under Investigation                                   | Phase | Date Commenced Phase | Estimated Filing |    |       |          |
|---------------------------------------|------------------------------|--|-------|----------------------|------------------|----|-------|----------|
|                                       |                              |  |       |                      | US               | EU | Japan | Emerging |
| <b>Respiratory &amp; Inflammation</b> |                              |  |       |                      |                  |    |       |          |
| AZD2115#                              | MABA                         | COPD   | II    | 2Q 2012              |                  |    |       |          |
| AZD5069                               | CXCR2                        | asthma   | II    | 4Q 2010              |                  |    |       |          |
| AZD5423#                              | inhaled SGRM                 | COPD   | II    | 4Q 2010              |                  |    |       |          |
| AZD8683#                              | muscarinic antagonist        | COPD   | II    | 4Q 2010              |                  |    |       |          |
| benralizumab#                         | anti-IL-5R MAb               | asthma / COPD  | II    | 4Q 2008              |                  |    |       |          |
| brodalumab#                           | anti-IL-17R MAb              | psoriasis / psoriatic arthritis / asthma                   | II    | 4Q 2009              |                  |    |       |          |
| mavrilimumab#                         | anti-GM-CSFR MAb             | rheumatoid arthritis                                       | II    | 1Q 2010              |                  |    |       |          |
| MEDI-546#                             | anti-IFN-alphaR MAb          | SLE  | II    | 1Q 2012              |                  |    |       |          |
| MEDI-8968#                            | anti-IL-1R MAb               | COPD   | II    | 4Q 2011              |                  |    |       |          |
| sifalimumab#                          | anti-IFN-alpha MAb           | SLE  | II    | 3Q 2008              |                  |    |       |          |
| tralokinumab                          | anti-IL-13 MAb               | asthma   | II    | 1Q 2008              |                  |    |       |          |
| AZD8848#                              | inhaled TLR7                 | asthma   | I     | 2Q 2012              |                  |    |       |          |
| MEDI-2070#                            | anti-IL-23 MAb               | Crohn's disease  | I     | 2Q 2010              |                  |    |       |          |
| MEDI-4212                             | anti-IgE MAb                 | asthma   | I     | 1Q 2012              |                  |    |       |          |
| MEDI-551#                             | anti-CD19 MAb                | scleroderma  | I     | 2Q 2010              |                  |    |       |          |
| MEDI-570#                             | anti-ICOS MAb                | SLE  | I     | 2Q 2010              |                  |    |       |          |
| MEDI-5872#                            | anti-B7RP1 MAb               | SLE  | I     | 4Q 2008              |                  |    |       |          |
| MEDI-7183#                            | anti-A4b7 MAb                | Crohn's disease / ulcerative colitis                       | I     | 3Q 2010              |                  |    |       |          |
| MEDI-7814                             | anti-C5/C5a MAb              | COPD   | I     | 1Q 2012              |                  |    |       |          |
| MEDI-9929#                            | anti-TSLP MAb                | asthma   | I     | 4Q 2008              |                  |    |       |          |
| RDEA3170                              | selective inhibitor of URAT1 | chronic management of hyperuricaemia in patients with gout | I     | 3Q 2011              |                  |    |       |          |

#Partnered product

## Development Pipeline - Discontinued Projects between 31 December 2011 and 30 June 2012

### **Cardiovascular**

| <b>NCE/Line Extension</b> | <b>Compound</b> | <b>Reason for Discontinuation</b> | <b>Area Under Investigation</b> |
|---------------------------|-----------------|-----------------------------------|---------------------------------|
| NCE                       | AZD2927         | Safety/Efficacy                   | atrial fibrillation             |

### **Neuroscience**

| <b>NCE/Line Extension</b> | <b>Compound</b> | <b>Reason for Discontinuation</b> | <b>Area Under Investigation</b>         |
|---------------------------|-----------------|-----------------------------------|---|
| NCE                       | AZD2423         | Safety/Efficacy                   | chronic neuropathic pain                |
| NCE                       | AZD3839         | Safety/Efficacy                   | Alzheimer's disease                     |
| NCE                       | MEDI-578        | Regulatory                        | OA pain                                 |
| NCE                       | TC-5214         | Safety/Efficacy                   | major depressive disorder (monotherapy) |
| NCE                       | TC-5214         | Safety/Efficacy                   | major depressive disorder (adjunct)     |

### **Infection**

| <b>NCE/Line Extension</b> | <b>Compound</b> | <b>Reason for Discontinuation</b> | <b>Area Under Investigation</b> |
|---------------------------|-----------------|-----------------------------------|---------------------------------|
| NCE                       | AZD5099         | Safety/Efficacy                   | serious infections              |
| NCE                       | MEDI-534        | Safety/Efficacy                   | RSV/PIV prophylaxis             |

### **Respiratory & Inflammation**

| <b>NCE/Line Extension</b> | <b>Compound</b> | <b>Reason for Discontinuation</b> | <b>Area Under Investigation</b> |
|---------------------------|-----------------|-----------------------------------|---------------------------------|
| NCE                       | AZD1981         | Safety/Efficacy                   | asthma/COPD                     |
| NCE                       | AZD2423         | Safety/Efficacy                   | COPD                            |

### **Comments**

As disclosure of compound information is balanced by the business need to maintain confidentiality, information in relation to some compounds listed here has not been disclosed at this time.

Submission dates shown for assets in Phase III and beyond.