European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

London, 18 December 2008
Doc. Ref. EMEA/617936/2008

Report from SME Office on its 3rd Year of Operation

On 15 December 2005, the EMEA launched an "SME Office" to provide financial and administrative assistance to micro, small and medium-sized enterprises (SMEs), pursuant to Commission Regulation (EC) No 2049/2005[1] (hereafter referred to as the SME Regulation). On the third anniversary of the SME initiative, an update on SME related activities is provided here, with emphasis this year on the type of assistance that has been offered to companies thus far.

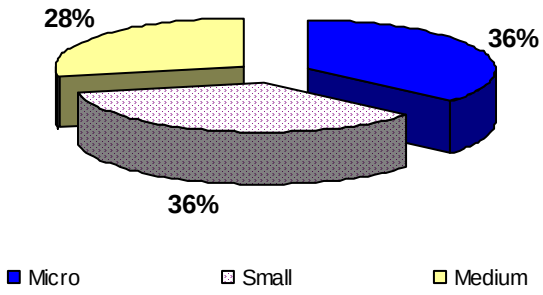
SME companies registered with EMEA

Currently, 372 companies have SME status actively assigned by the EMEA (for updated list of companies see Annex). A further 40 companies have declarations under review, 32 have been withdrawn and 44 have expired[2]. The large majority of companies are developing medicinal products for human use, 14 are veterinary companies, 15 companies are developing products for both human and veterinary use and 35 are regulatory consultants[3].

In 2008, the number of companies assigned SME status by the agency increased by 50% compared to the previous year. The number of renewal requests increased by 91% compared to 2007. Companies from 21 countries across the EEA have contacted the SME office to date. The geographic distribution of companies is similar to that reported last year, with the majority of companies assigned SME status, to date, being based in the UK, Germany, France, Sweden, and the Netherlands.

Information on the size of companies that are requesting assistance from the agency is presented in figure 1. The relative proportion of micro-enterprises (36%), with less than 10 employees and not more than € 2 million in turnover or balance sheet total, remained relatively high in 2008. An analysis of companies assigned status in 2007-2008, showed that a high proportion of the companies are newly created, 35% being established in the last 3 years.

Figure 1: Size of companies assigned SME status by EMEA – Dec. 2008



[1] *Official Journal L 329, 16/12/2005 pp. 4-7*
[2] A company's SME status will expire two years after the date of closure of the accounts on which the declaration has been based. SME status may be maintained by submitting the latest annual accounts to the EMEA.
[3] Regulatory consultancies, which fulfil the definition of an SME and are established in the Community, may benefit from the provisions of the SME Regulation on behalf of SME clients. It is necessary for the regulatory consultancy to obtain SME status, and the client to fulfil the definition of an SME within the meaning of Recommendation 2003/361/EC.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

Financial and Administrative Assistance offered to SMEs

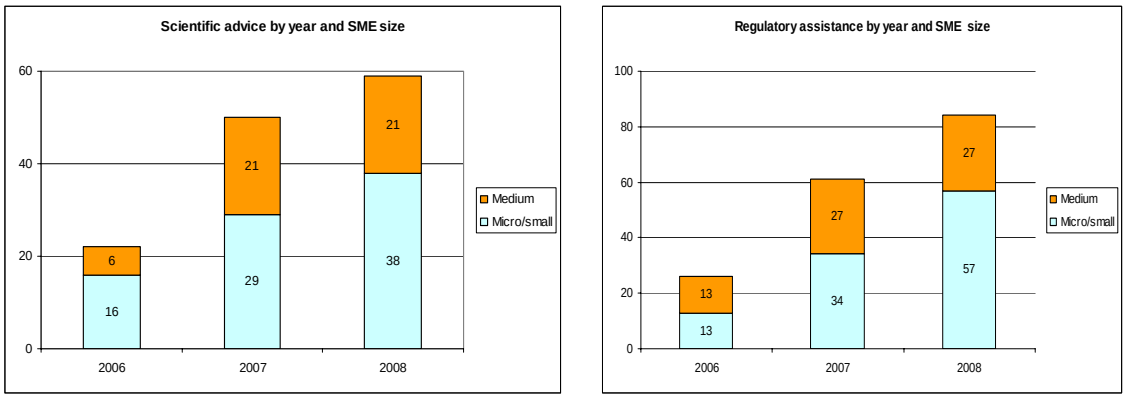
Scientific Advice

More than 130 SME companies have requested scientific advice from the EMEA since the SME initiative started in December 2005. A breakdown of the numbers of SMEs seeking scientific advice by year and company size is presented in figure 2 below.

In 2008 requests for scientific advice from SMEs increased slightly over 2007. The majority of companies in 2008 requested advice on more than one area of development. Clinical advice was sought in the majority of cases (47%), with preclinical and quality requests featuring in 30% and 23% of cases respectively. It was particularly encouraging to see that the number of companies seeking follow-up advice as development proceeds, was up 50% on the previous year.

Financial assistance offered to SMEs for scientific advice in 2008 (€ 2.9 million) was at a similar level to 2007. To date, fee reductions totalling of € 6.9 million have been processed for scientific advice.

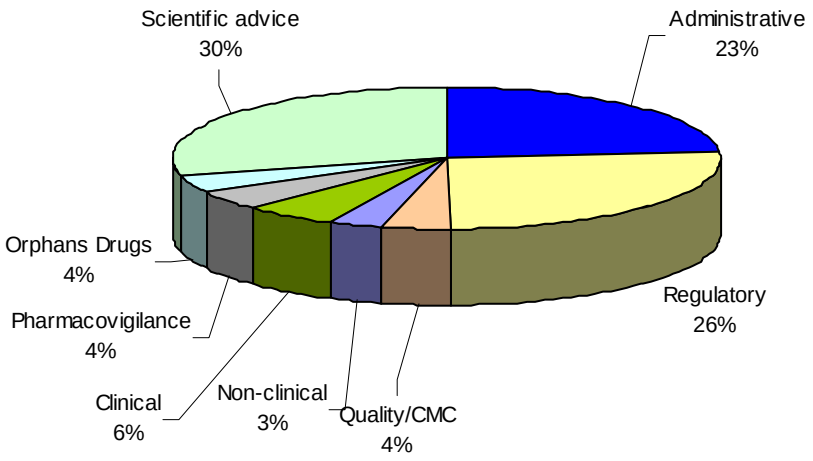
Figure 2: Scientific advice and regulatory assistance by year and company size



Regulatory Assistance

The provision of regulatory assistance through the SME office to micro and small enterprises increased significantly compared to 2007 (see figure 2 above). To date, more than 170 requests for assistance have been processed by the SME office. An overview of the scope of regulatory assistance is provided in figure 3 below. Requests for regulatory and administrative assistance related mainly to the marketing authorisation application (MAA) filing strategy (e.g. eligibility to centralised procedure, accelerated review, and conditional approval/exceptional circumstances), MAA pre-submission issues (e.g. CTD, and invented name review), and general queries about SME incentives.

Figure 3: Scope of regulatory assistance provided to SMEs



Applications for marketing authorisation (MAAs)

Since December 2005, thirty-eight SME companies have submitted MAAs, 33 for human medicinal products and 5 for veterinary medicinal products. Payment of fees totalling € 5 million, for MAAs and inspections, have been deferred by SMEs to date.

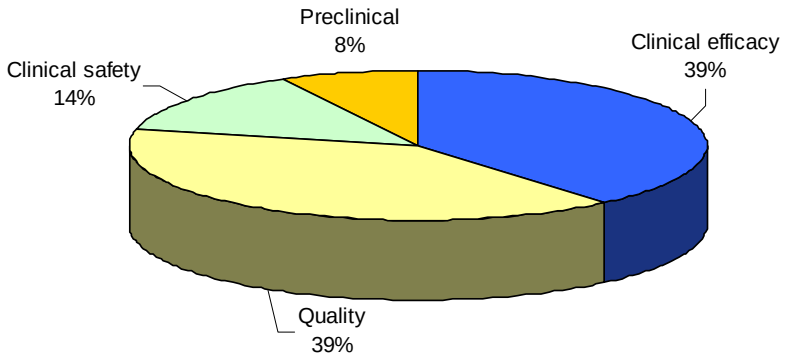
Of the veterinary medicinal products that have been subject of MAAs, three have received positive outcomes and 2 are ongoing.

For human medicinal products, the trend to date is unfortunately less positive. Of the human medicinal products that have been subject of MAAs, 6 have received positive outcomes (4 have been granted Community marketing authorisations and 2 are currently in the decision-making process) and 12 have resulted in negative outcomes (3 negative opinions and 9 withdrawals). Fifteen applications are currently ongoing.

A preliminary analysis into the impact of scientific advice at the stage of the marketing application has shown that many small companies in particular do not take the advice fully into account. The following observations can be made on the 18 applications from SMEs for medicinal products for human use that have received an outcome to date:

- Overall 55 % (10/18) had previously sought scientific advice. Of those companies with a positive outcome 83% (5/6) had received EMEA advice. Of those with a negative outcome, 42% (5/12) had previously sought advice but only one company (8%) had taken the advice into account and as such qualified for a conditional fee exemption.
- Seventy-two percent (13/18) of the applications were for designated orphan medicinal products, 83% of those with a positive outcome and 66% of those with a negative outcome.
- One application, for the orphan medicinal product Soliris, was reviewed to an accelerated time-table and received a positive opinion from the CHMP in 147 days.
- The average active time for the 18 applications from SMEs was 181 days. The majority of companies requested additional time to respond to questions raised by the CHMP during the procedure. The average response (so-called “clock-stop”) time for SME companies was 7 months.
- On average 9 major objections per application were raised by CHMP at day 120 of the procedure. A breakdown of the areas where major objections arose is provided in figure 4. The agency has noted that major objections ran particularly high in the area of quality. This year’s SME workshop, which focussed on quality, aimed to increase awareness of this important aspect of development.
- A number of applicants have indicated their intention to seek scientific advice and re-submit applications once further data has been generated suggesting that some of the applications were filed prematurely.

Figure 4: Major objections in Day 120 List of Questions for SMEs (18 MAAs)



Although the SME initiative is still at an early stage, it is apparent from the experience gained with MAAs to date that it is important for companies to open up an early dialogue with the EMEA. Scientific advice should be sought proactively and comprehensively on key issues in development (quality, non-clinical, clinical) at the planning stage and follow-up advice should be sought as development proceeds. This is important, particularly, if the company deviates from the advice given on key aspects of the pivotal clinical trial such as the primary endpoint, the choice of the comparator and the statistical analysis plan. Experience over the years has shown that deviation in these aspects of the scientific advice is likely to result in major objections during the evaluation and eventually to a negative MAA outcome.

It is important to note that in the area of advanced therapy medicinal products, the assistance available to SMEs will be reinforced, with the introduction of the certification process next year. This will provide SMEs with a unique opportunity to have quality and non-clinical documentation evaluated by the EMEA which should facilitate the evaluation of any future MAA based on the same data.

Translation assistance

The SME office's experience in providing translations for SME companies has been built on in 2007, with a total of 8 companies having now benefited from this service. In 2009, the SME office will focus on the refining the translation process and publishing a formal procedure. Applicant enterprises remain responsible for the Norwegian and Icelandic translations and may opt to take over responsibility for some EU languages where particular competences lie.

Training/Workshop for SMEs:

More than 140 representatives of SME companies and their stakeholders participated in the 2nd SME Workshop, titled 'Focus on Quality', on 8 February 2008.

The next SME Workshop will take place on 2 February 2009 and will focus on non-clinical aspects of development, with an overview of data requirements for new chemical entities and biologicals from an EU assessor's perspective. Registration in the workshop, has once again been limited to company's assigned SME status by the EMEA and representatives of stakeholder organisations. Further information is available on the EMEA web-site.

Future Updates from the SME Office

The SME office News Bulletin, launched in May 2007, will be published quarterly in 2009.

Contacts for further information

E-mail queries: smeoffice@emea.europa.eu
Ms. Melanie Carr/ Dr. Constantinos Ziogas : Tel (44 20) 7418 8575 /8463

List of companies that currently have SME status assigned by the EMEA
(status on 18 December 2008)

Company Name	Country
AB Science	France
Abigo Medical AB	Sweden
Acacia Pharma Limited	United Kingdom
Action Pharma A/S	Denmark
Active Biotech AB	Sweden
ActoGeniX N.V.	Belgium
Acure Pharma AB	Sweden
AcureOmics AB	Sweden
Addex Pharmaceuticals France	France
Addmedica	France
ADIENNE S.r.l.	Italy
Adventrx (Europe) Ltd	United Kingdom
Advicenne Pharma	France
Aeterna Zentaris GmbH	Germany
Affimed Therapeutics AG	Germany
Agennix Limited	United Kingdom
AGIRx (Active Gene Interventions) Ltd.	United Kingdom
AGT Sciences Limited	United Kingdom
AKELA Pharma Oy (Ltd.)	Finland
Alan Boyd Consultants Ltd.	United Kingdom
Algeta ASA	Norway
Alienor Farma	France

Alimentary Health Limited	Ireland
Alizyme Therapeutics Limited	United Kingdom
Alliance Pharmaceuticals Limited	United Kingdom
Alloksys Life Sciences BV	The Netherlands
Altonabiotec AG	Germany
Amarin Corporation plc	United Kingdom
Amarin Neuroscience Limited	United Kingdom
Amsterdam Molecular Therapeutics BV	The Netherlands
Anaconda Pharma	France
Antisense Pharma GmbH	Germany
AplaGen GmbH	Germany
Apocare Pharma GmbH	Germany
Applied Regulatory Consulting Ltd	United Kingdom
Archivel Farm, S.L.	Spain
Ardana Bioscience Ltd	United Kingdom
Ark Therapeutics Ltd	United Kingdom
Arpida A/S	Denmark
AS Biotech GmbH	Austria
ASB Associates Limited	United Kingdom
A-Skin Nederland B.V.	The Netherlands
Astex Therapeutics Ltd	United Kingdom
Atlantic Healthcare Limited	United Kingdom
Auralis	United Kingdom
Avir Green Hill Biotechnology Research Development Trade AG	Austria
Avontec GmbH	Germany

Axxonis Pharma AG	Germany
Barrier Therapeutics	Belgium
Bavarian Nordic A/S	Denmark
Bioalliance Pharma SA	France
Bioalvo - Serviços, Investigacão e Desenvolvimento em Biotecnologia, S.A.	Portugal
Biocontrol Limited	United Kingdom
BioInvent International AB (publ.)	Sweden
Biolek Sp. z.o.o.	Poland
Biolipox AB	Sweden
Biomay AG	Austria
Biomedica Life Sciences S.A	Greece
BioMedisinsk Innovasjon AS	Norway
Biomedizinische Forschungsgesellschaft m.b.H.	Austria
BioMonde GmbH	Germany
Bio-Products & Bio-Engineering AG	Austria
Bioprojet Pharma	France
BioSynthema Global Operations B.V.	The Netherlands
Biotec Pharmacon ASA	Norway
BioTech Tools	Belgium
Biotectid GmbH	Germany
Biotie Therapies Corp.	Finland
BioVex Ltd.	United Kingdom
Bioxell S.p.A.	Italy
Bone Therapeutics SA	Belgium

BruCell SA	Belgium
Canary Wharf Life Science Ltd.	United Kingdom
Cardinal Systems	France
Cardio3 BioSciences	Belgium
Cardiome (UK) Limited	United Kingdom
Cardiopep Pharma GmbH	Germany
Cellartis AB	Sweden
Cellectis S.A.	France
Cellerix, S. L.	Spain
CellGenix Technologie Transfer GmbH	Germany
CellMed AG	Germany
CellSeed Europe	France
Celogos	France
Celon Pharma Sp. z o.o.	Poland
Chanelle Pharmaceuticals Manufacturing Ltd	Ireland
Chevita Tierarzneimittel GmbH	Germany
Clavis Pharma ASA	Norway
CLL Pharma	France
CMC Contrast AB	Sweden
Co.don AG	Germany
Colithin GmbH	Germany
Combino Pharm, S.L.	Spain
Coretherapix S.L.U.	Spain
corLife GbR	Germany
Corline Systems AB	Sweden

Crusade Laboratories Limited	United Kingdom
Curacyte AG	Germany
Curalogic A/S	Denmark
Cyathus Exquirere PharmaforschungsGmbH	Austria
Cyclacel Limited	United Kingdom
Cytheris S A	France
CZ Veterinaria, S.A.	Spain
D.R.N. srl	Italy
DanDrit Biotech A/S	Denmark
DBV Technologies	France
DCprime B.V.	The Netherlands
Dermatech R&D Ltd.	United Kingdom
DermMatrix AB	Sweden
Develco Pharma GmbH	Germany
Diamond BioPharm Limited	United Kingdom
Diamyd Medical AB	Sweden
Dianne Lee Regulatory Consultancy Ltd	United Kingdom
Diapharm Regulatory Services GmbH	Germany
Diatos SA	France
DNA Therapeutics SA	France
Dopharma Research BV	The Netherlands
DOR BioPharma UK Ltd.	United Kingdom
Dorian Regulatory Affairs BV	The Netherlands
Dr Meng Pharma GmbH	Austria
DREHM Pharma GmbH	Austria

DuoCort AB	Sweden
DuoCort Pharma AB	Sweden
ECBio	Portugal
EleosInc Limited	United Kingdom
Envestia Limited	United Kingdom
EpiCept GmbH	Germany
EPMC Pharma (European Paediatric Medicine Company)	Belgium
Erytech Pharma	France
euroderm GmbH	Germany
European Medical Advisory Services Limited	United Kingdom
EUSA Pharma	France
Exalenz Bioscience BV	The Netherlands
ExperGen Drug Development GmbH	Austria
Faron Pharmaceuticals Ltd.	Finland
Fibrex Medical Research and Development GmbH	Austria
FORMAC Pharmaceuticals NV	Belgium
Fulcrum Pharma (Europe) Limited	United Kingdom
Gendux Molecular Limited	Ireland
Genetic Immunity KFT	Hungary
Genetic Research S.r.l.	Italy
Genfit SA	France
Genitrix Ltd	United Kingdom
Genmab A/S	Denmark
Genmedica Therapeutics SL	Spain

Genta Development Limited	United Kingdom
GLNP (Generic Life quality enhancing Niche Products) Life Sciences B.V.	The Netherlands
GlucoMetrix PVS GmbH	Germany
GPC Biotech AG	Germany
Graftys	France
Gregory Fryer Associates Ltd	United Kingdom
GW Pharma Ltd.	United Kingdom
Haemopep Pharma GmbH	Germany
Henogen SA	Belgium
Hepa Wash GmbH	Germany
Herbert J. Passauer GmbH & Co. KG	Germany
Histocell, S.L.	Spain
Horizon Therapeutics (UK) Limited	United Kingdom
Hormos Medical Ltd	Finland
Hungarotrial Ltd	Hungary
Hyperion Therapeutics Ltd.	United Kingdom
I.Q.A. a.s.	Czech Republic
IDEA AG	Germany
IDM Pharma S.A.	France
Immatics Biotechnologies GmbH	Germany
Immune Targeting Systems (ITS) Limited	United Kingdom
ImmunoBiology Ltd	United Kingdom
Immunomedics GmbH	Germany
Immunservice GmbH	Germany

Immunsystem IMS AB	Sweden
ImmuPharma France SA	France
Immutep S.A.	France
IMTM GmbH	Germany
Incyte Corporation Ltd	United Kingdom
INFAI Institut für biomedizinische Analytik und NMR- Imaging GmbH	Germany
Innate Pharma	France
Innate Pharmaceuticals AB (publ)	Sweden
Innocoll Technologies Limited	Ireland
Innovacell Biotechnologie GmbH	Austria
Innovata Biomed Limited	United Kingdom
Inspiration Biopharmaceuticals EU Limited	Ireland
Institut Clinident SAS	France
Intercytex Limited	United Kingdom
Interface International Consultancy Ltd.	United Kingdom
Intervacc AB	Sweden
IPMB GmbH Institute for Regulatory Affairs & Pharmaceutical Services	Germany
ISA Pharmaceuticals B.V.	The Netherlands
Isotechnika Ltd	United Kingdom
Istituto Biochimico Italiano, Giovanni Lorenzini S.p.A.	Italy
Italchimici S.p.A.	Italy
ITH Immune Therapy Holdings AB	Sweden
Jerini AG	Germany
JJGConsultancy Ltd	United Kingdom

Karo Bio AB	Sweden
Kiadis Pharma Netherlands B.V.	The Netherlands
Kohne Pharma GmbH	Germany
Kuros Biosurgery International AG	Liechtenstein
Lab. CTRS (Cell Therapies Research & Services)	France
Laboratoire HRA Pharma	France
Laboratoire IPRAD	France
Laboratoire Philippe Davioud	France
Laboratoires SERB	France
Laboratories SMB S.A.	Belgium
Laboratorios Ovejero S.A.	Spain
Labtec Gesellschaft für technologische Forschung und Entwicklung mbH	Germany
Lamellar Biomedical Ltd.	United Kingdom
Le Vet. BV	The Netherlands
LIDDS AB	Sweden
Life Research Technologies GmbH	Austria
Lionex Diagnostics &Therapeutics GmbH	Germany
Lipomed GmbH	Germany
LipoNova AG	Germany
Löns Pharma AG	Germany
Lux Biosciences GmbH	Germany
MacroGenics UK Limited	United Kingdom
Magle AB	Sweden
Mapreg	France

Marvel Life Sciences Limited	United Kingdom
MedCell Biosciences Limited	United Kingdom
Medeon Pharmaceuticals GmbH	Germany
MediGene AG	Germany
Medikalla Oy	Finland
Medivir AB	Sweden
Merus Biopharmeceuticals BV	The Netherlands
Micromet AG	Germany
Mithra Pharmaceuticals s.a.	Belgium
Morningside Healthcare Ltd	United Kingdom
Movetis NV	Belgium
Mpex London Limited	United Kingdom
Mucosis BV	The Netherlands
Nabriva Therapeutics AG	Austria
Natepharm SAS	France
Navamedic ASA	Norway
NDA Group AB	Sweden
Neuraxo Biopharmaceuticals GmbH	Germany
Neurochem Luxco II Sarl	Luxembourg
NeurogesX UK Limited	United Kingdom
Neurokey A/S	Denmark
NeuroProgen GmbH	Germany
NeuroSearch A/S	Denmark
Newport Pharmaceuticals Limited	Ireland
Newron Pharmaceuticals SPA	Italy

Nexatio Limited	United Kingdom
Nitec Pharma GmbH	Germany
Nordvacc Läkemedel AB	Sweden
Nova Laboratories Ltd.	United Kingdom
NovaBiotics Ltd	United Kingdom
Novacea Europe Limited	United Kingdom
Novagali Pharma SA	France
NovaThera Ltd	United Kingdom
Novosom AG	Germany
Noxxon Pharma AG	Germany
NsGene A/S	Denmark
Nutri Science Ltd.	Ireland
Oasmia Pharmaceuticals AB	Sweden
Octagon Research Solutions Limited	United Kingdom
OctoPlus N.V.	The Netherlands
Okairòs srl	Italy
Oligovax	France
OMRIX biopharmaceuticals S.A.	Belgium
Oncoscience AG	Germany
Only for children pharmaceuticals	France
Opsona Therapeutics Ltd	Ireland
Orexo AB	Sweden
Orphan Europe SARL	France
Orphix Consulting GmbH	Germany
Oxbridge Pharma Ltd	United Kingdom

OxThera AB	Sweden
Oy Fennopharma Ltd	Finland
Oy Verman AB	Finland
PAION Deutschland GmbH	Germany
Panacos Limited	United Kingdom
PanGenetics BV	The Netherlands
Pantarhei Bioscience BV	The Netherlands
Parabolic Biologicals S.P.R.L.	Belgium
PDC GmbH	Germany
Pepscan Holding N.V.	The Netherlands
PharmacoGenomic Innovative Solutions Ltd	United Kingdom
Pharmafar S.r.l.	Italy
PharmaKodex Limited	United Kingdom
Pharmalink Consulting Limited	United Kingdom
PHARMAQ AS	Norway
Pharmathen S.A.	Greece
Pharmaxis Pharmaceuticals Limited	United Kingdom
Pharmexa A/S	Denmark
Pharming Group N.V.	The Netherlands
Pharmsure Limited	United Kingdom
PharOS - Pharmaceutical Oriented Services Ltd	Greece
Photocure ASA	Norway
Phytopharm Plc	United Kingdom
PINT Pharma GmbH	Austria
PKB Consulting Sas	Italy

Planton GmbH	Germany
Polymun Scientific Immunbiologische Forschung GmbH	Austria
Prana Biotechnology UK Limited	United Kingdom
Praxis Pharmaceutical SA	Spain
PregLem SA	France
Professional Regulatory Services Limited	United Kingdom
ProFibrix BV	The Netherlands
Promefarm S.r.l.	Italy
Prosensa B. V.	The Netherlands
Prospero Therapeutics Ltd	United Kingdom
ProtAffin Biotechnologie AG	Austria
Proteome Therapeutics GmbH	Germany
Protherics PLC	United Kingdom
QuadraMed Limited	United Kingdom
QuoNova Europe GmbH	Germany
Rada-Pharma Uk Ltd.	United Kingdom
Redermis Limited	United Kingdom
Regulatory Pharma Net srl	Italy
Renovo Ltd	United Kingdom
Renuvia Ltd	United Kingdom
Resistentia Pharmaceuticals AB	Sweden
Rheoscience A/S	Denmark
S.A.R.M. Società Antica Ritrovati Medicinali s.r.l.	Italy
Santaris Pharma A/S	Denmark

Santhera Pharmaceuticals (Deutschland) GmbH	Germany
SantoSolve Pharma AS	Norway
SentoClone AB	Sweden
Seratec SAS	France
SIGA Pharmaceuticals (Europe) Ltd	United Kingdom
SME BioAdvisor Ltd	United Kingdom
Solace Pharma (UK) Ltd	United Kingdom
Sparkle srl	Italy
Special Products Limited	United Kingdom
SRD Stroke Research & Development Ltd.	United Kingdom
Summit Corporation plc	United Kingdom
Sunesis Europe Ltd	United Kingdom
SuppreMol GmbH	Germany
Symphogen A/S	Denmark
Synairgen Research Limited	United Kingdom
Synta Limited (UK)	United Kingdom
Syntaxin Ltd.	United Kingdom
Synvolux Therapeutics B.V.	The Netherlands
Systems Biology Laboratory UK Ltd	United Kingdom
t2cure GmbH	Germany
Targanta Netherlands B.V.	The Netherlands
Targeon S.A.S.	France
TBF – Genie Tissulaire	France
Tecnifar Indústria Técnica Farmacêutica S.A.	Portugal
The Weinberg Group Limited	United Kingdom

Therakind Limited	United Kingdom
TiGenix NV	Belgium
Topaz Pharmaceuticals (UK) Limited	United Kingdom
TopoTarget A/S	Denmark
Treague Limited	United Kingdom
Trimed Biotech GmbH	Austria
Trio Medicines Ltd.	United Kingdom
Triskel EU Services, LTD	United Kingdom
Trophos SA	France
TxCell	France
U3 Pharma AG	Germany
Unigene UK, Ltd.	United Kingdom
UroTec GmbH	Germany
Vaxon Biotech	France
Vectura Group PLC	United Kingdom
Vernalis Plc	United Kingdom
VI.REL Pharma S.a.s	Italy
Virostatics SRL	Italy
Vita (Europe) Ltd	United Kingdom
Vita 34 AG	Germany
Vitrolife Sweden AB	Sweden
VIVAVACS SAS	France
Vivus BV	The Netherlands
Voisin Consulting SARL	France
Warburton Technology Ltd	Ireland

Wilex AG	Germany
XCell-Center GmbH	Germany
Yes Pharmaceutical Development Services GmbH	Germany
Zealand Pharma A/S	Denmark
ZF - screens BV	The Netherlands
ZGene a/s	Denmark