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# Patent Analytics Report: Alzheimer's Disease

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### Enquiries

Patent Analytics Hub  
analytics@ipaustalia.gov.au

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# Contents

1	Introduction.....	4
2	Overview: Alzheimer’s related technologies.....	6
2.1	Scale of patenting activity .....	6
2.2	Top applicants .....	6
2.3	Collaboration .....	9
2.4	Applicant origin .....	12
3	Technology breakdown .....	13
3.1	Overall technology breakdown .....	13
3.2	Pharmaceutical Targets .....	14
4	Target markets .....	16
4.1	Worldwide .....	16
4.2	Top Applicants within Australia.....	17
4.3	Top Australian Applicants.....	18
5	Conclusion .....	19
	Appendix A .....	20
	The Patent System .....	20
	Appendix B.....	21
	Data Extraction and Analysis .....	21
	Technology Breakdown .....	21

# 1 Introduction

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Alzheimer's disease is the most common type of dementia.<sup>1</sup> It is a general term used to classify symptoms of memory loss or other loss of intellectual abilities serious enough to interfere with daily life. Alzheimer's disease is a progressive disease, where dementia symptoms gradually worsen over a number of years. Alzheimer's disease is the second leading cause of death of Australians contributing to 5.4 per cent of all male deaths and 10.6 per cent of all female deaths.<sup>2</sup>

There are a range of medications that are available to lessen the symptoms of Alzheimer's disease, however currently there is no cure or methods to stop or slow the progression of the disease.

Current approved medications fall into two categories:

- Cholinesterase inhibitors which target symptoms of memory loss, confusion and problems with thinking and reasoning; and
- Memantine which blocks the neurotransmitter glutamate to prevent cell damage caused by too much cellular calcium movement in the brain.<sup>3</sup>

Research into the cure and prevention of Alzheimer's disease has been progressing for 30 years, during which time many biological targets have been identified as being associated with Alzheimer's disease. These include beta-amyloid proteins, beta-secretases (BACE) and Tau-protein kinases. Beta-amyloid is the chief component of plaques, one hallmark of Alzheimer's brain abnormality. Beta-secretase is one of the enzymes that cause the formation of amyloid plaques. Tau-protein kinase is the chief component that creates tangles in the brain, another hallmark of Alzheimer's disease.<sup>4</sup>

The report aims to capture the current patent landscape of treatments and diagnosis of Alzheimer's disease since 2000. This is achieved through the analysis of data from patent families associated with Alzheimer's disease in general.

A patent is a right that is granted for any device, substance, method or process that is new, inventive, and useful. Patent rights are legally enforceable and give the owner exclusive rights to commercially exploit the invention for a limited period of time. There are two major filing routes for patent applications: international and direct.

The international route involves filing a Patent Cooperation Treaty (PCT) application, which establishes a filing date in all 148 contracting states.<sup>5</sup> Subsequent prosecution at national patent offices, referred to as national-phase entry (NPE), is made at the discretion of the applicant. A patent can only be enforced once a PCT application has entered the national phase and attained a granted status. The use of PCT applications in this report is a good indicator of patent filings across the globe and therefore allows for a representative cross section of the patenting activity in the technology relating to Alzheimer's treatment and diagnosis.

Another route in which patent applications can be filed is directly with the country of interest, these are classified as direct applications. Both types of applications relating to the same invention but filed in different countries may be grouped together and these are known as patent families. Patent families enable us to analyse inventive activity regardless of the number of countries in which protection is sought.

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<sup>1</sup> Alzheimer's Association – [What is Alzheimer's?](#)

<sup>2</sup> Fight Alzheimer's Save Australia – [Statistics](#)

<sup>3</sup> Alzheimer's Association – [Medication for Memory Loss](#)

<sup>4</sup> Alzheimer's Association – [Treatment Horizon](#)

<sup>5</sup> WIPO, [List of PCT Contracting States](#)

It is a requirement of patent law that patent documents are published and that they fully disclose the inventions and this typically occurs within 18 months of filing. The date on which the earliest disclosure of an invention is filed is known as the earliest priority date. As a result of the disclosure requirement, patent literature reflects developments in science and technology and can be used as indicators of research output. Patent documents include other useful information, such as international patent classifications and information about inventors and applicants.

Through the extraction and analysis of data associated with patent documents, it is possible to measure aspects of inventive activity such as scope, intensity, collaboration and impact. These metrics can be developed across technology sectors and by various units of measurement, such as individuals (inventors), institutions (applicants), regions and countries.

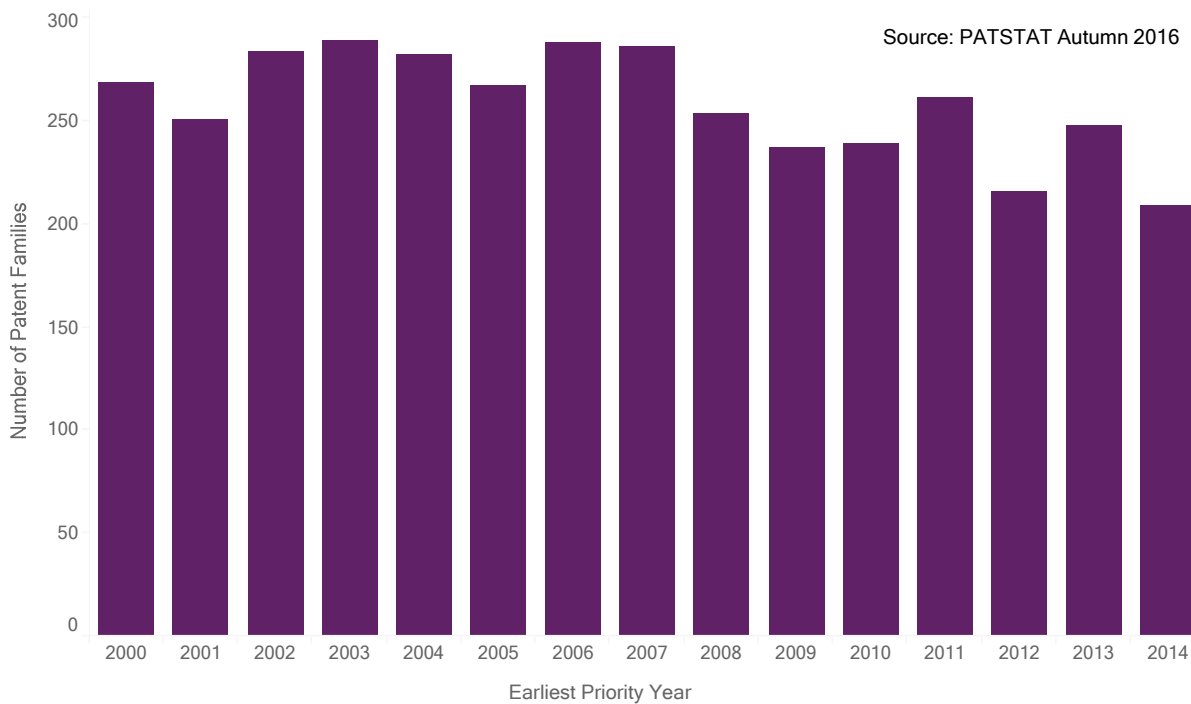
This report analyses data from patents filed through the PCT route in order to focus the study on the most globally relevant patent information relating to the diagnosis and treatment of Alzheimer's disease. It has a particular focus on pharmaceuticals (chemical), biologics, genetic engineering and other medical treatments. It uses the scale and intensity of patent activity to provide an overview of inventions in the area of Alzheimer's disease diagnosis and treatments through the lens of intellectual property (IP).

## 2 Overview: Alzheimer's related technologies

### 2.1 Scale of patenting activity

We identified 3881 unique patent families relating to Alzheimer's disease treatment and diagnostic technologies, from the PATSTAT (Patent Statistical) database Autumn 2016 edition (see Appendix B for a detailed search strategy). The time frame for the analysis in this report is applications with an earliest priority date on or after 1 January 2000 in order to concentrate on the most contemporary technologies in this area. Figure 1 shows these patent families by priority year.

**Figure 1 - Patent families by priority year.**

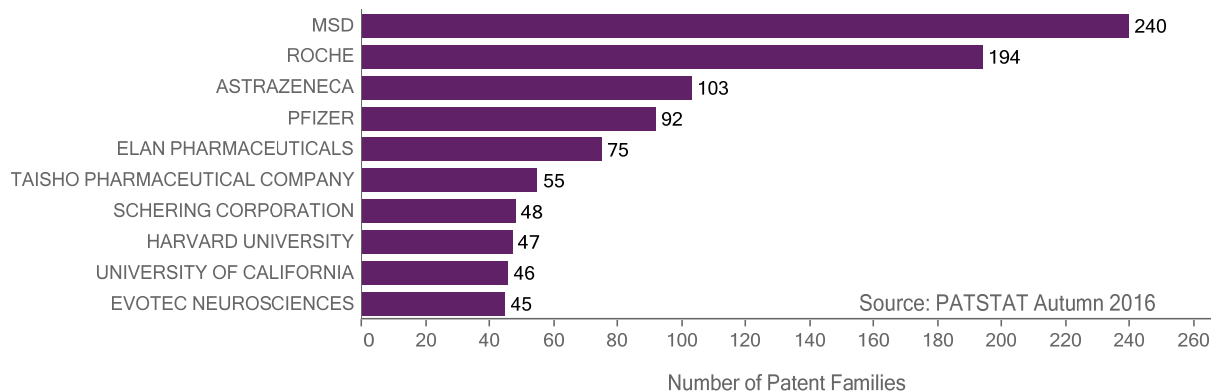


The number of patent family filings has seen a gradual but minor decrease since 2006. Prior to 2006 the patent filings related to the diagnosis and treatment of Alzheimer's disease had been steady. However, there is still significant patent filing activity, for example in 2014 there were 209 patent families filed in relation to the diagnosis or treatment of Alzheimer's disease. There is a lack of filings from 2015 and none in 2016 due to the 18 month international publication lag from the earliest filing year. This publication lag is set out by the PCT guideline which will publish all applications filed as a PCT after 18 months of the earliest priority date (usually the filing date).

### 2.2 Top applicants

Figure 2 shows the top applicants in the patent landscape of Alzheimer's disease related technologies. The top six applicants, Merck Sharp & Dohme (MSD), Roche, AstraZeneca, Pfizer, Elan Pharmaceuticals and Taisho Pharmaceuticals are all world leaders in chemical based pharmaceutical products.

**Figure 2 - Top applicants**



MSD is the largest patent holder identified in this report with 240 patent families. MSD is a United States based company with research focus addressing global health challenges such as Alzheimer’s disease.<sup>6</sup> The company has developed MK-8931, which is an orally administered drug that inhibits beta-amyloid precursor protein cleaving enzyme (BACE) and is currently under phase III clinical trials.<sup>7</sup> The majority of their invention are targeted towards the use of drugs to inhibit beta-secretase enzyme activity ([WO2005113484](#) and [WO2009108550](#)), enhancement of androgen receptors ([WO2006026196](#)), inhibition of kinases ([WO2011037780](#)) and BACE ([WO2016040226](#)). MSD has also been involved in the development of biologic based pharmaceuticals ([WO2006121656](#)) along with the diagnosis and detection of Alzheimer’s disease ([WO2007002482](#) and [WO2013009667](#)).

Roche is a Swedish multinational company and is one of the leading pharmaceutical companies in the world.<sup>8</sup> The company has research dedicated to the treatment of Alzheimer’s disease with advanced trials being conducted for Gantenerumab (anti-amyloid - phase III) ([WO2014056816](#)), Crenezumab (anti-amyloid antibody - phase III) ([WO2008011348](#)) and RG 6100 (a monoamine oxidase-B inhibitor) based therapies.<sup>9,10</sup> Roche holds 194 patent families with pharmaceutical development in the inhibition of beta-secretases ([WO2007110335](#)), Adenosine receptor modulation ([WO0197786](#)) and phosphodiesterase inhibition ([WO2015078836](#)). Roche has also filed patents in biologic based pharmaceuticals using insulin-like growth factors ([WO2008025528](#)) and genetically modifying cells for the production of insulin-like growth factors ([WO2008025527](#)).

AstraZeneca is a British-Swedish multinational and is a global leader in biopharmaceuticals with a strong focus in neuroscience and the treatment of Alzheimer’s disease.<sup>11,12</sup> AstraZeneca has an Alzheimer’s disease product portfolio including Amaranth Daybreak (AZD3293) (beta-secretase inhibitor – phase III) and MEDI1841 (amyloid beta antibody - phase I).<sup>13</sup> Amongst the 103 patent families identified, AstraZeneca has pharmaceuticals that act as beta-amyloid inhibitors ([WO2004031154](#)), kinase inhibitors ([WO2007040436](#) and [WO2010120237](#)), BACE inhibitors ([WO2007149033](#)) and hormonal inhibitors ([WO2006068594](#)). Other areas of interest are medical treatments such as fusion proteins for the degradation of beta-amyloid ([WO2008118093](#)), transmucosal delivery of drugs ([WO2013148966](#)) and administration of drugs targeted towards Alzheimer’s disease ([WO2013009545](#)). They also have patents for the diagnosis of Alzheimer’s

<sup>6</sup> MSD - [Research](#)

<sup>7</sup> MSD - [Pipeline](#)

<sup>8</sup> Roche - [History](#)

<sup>9</sup> Roche - [Alzheimer’s disease](#)

<sup>10</sup> Roche - [Pipeline](#)

<sup>11</sup> AstraZeneca - [About](#)

<sup>12</sup> AstraZeneca - [Neuroscience](#)

<sup>13</sup> AstraZeneca - [Pipeline](#)

disease through the use of heteroaryl substituted benzothiazole derivatives for imaging amyloid deposits in living patients ([WO2007086800](#)).

Pfizer is an American multinational company with a dedicated pipeline of pharmaceuticals targeting neurologic diseases and pain management.<sup>14,15</sup> Pfizer has compounds targeting Alzheimer's disease (PF-05251749, PF-06648671 and PF-06751979) all of which are still in phase I clinical trials.<sup>16</sup> Within the 92 patent families identified in this study, their focus areas include anti-inflammatories ([WO03037351](#)), amyloid inhibitors ([WO2005020991](#)), kinase inhibitors ([WO2008096260](#)), N-methyl-D-aspartic acid receptor antagonists ([WO0247685](#)) and aminotransferase inhibitors ([WO03045384](#)). Pfizer has also developed immunoassay based diagnostic methods for Alzheimer's disease ([WO2011143574](#)).

Elan Pharmaceuticals was an Irish pharmaceutical company which had major interests in the United States. In 2013, the company merged with Perrigo to form Perrigo Company PLC based in the Ireland.<sup>17</sup> Elan Pharmaceuticals had the product Betabloc which was believed to reduce the formation of beta-amyloid plaques.<sup>18</sup> Elan Pharmaceuticals held 75 patent families related to the treatment and diagnosis of Alzheimer's disease. Their main pharmaceutical targets were beta and gamma secretase inhibitors ([WO0202512](#) and [WO03040096](#)) and leukocytes ([EP1940827](#) and [WO0208201](#)). In addition, Elan Pharmaceuticals was also interested in the area of diagnostics with a particular focus on screening markers ([WO2009012237](#)).

Taisho Pharmaceuticals is a Japanese company founded in 1912 specialising in over the counter drugs and other health related products.<sup>19</sup> With regard to the treatment of Alzheimer's disease, Taisho Pharmaceuticals has 55 patent families including those for histamine H3 receptor inhibition ([WO2009063953](#)), arginine vasopressin 1b receptor antagonism ([WO2012043791](#)), glycine-uptake-inhibition ([WO2012115097](#)) and orexin receptor antagonism ([WO2014091876](#)).

Schering Corporation was a German multinational company. In 2006 it was acquired by Bayer to form Bayer Schering Pharma AG.<sup>20</sup> Schering Corporation had 48 patent families with a particular interest in the treatment of Alzheimer's disease using secretase inhibitors ([WO2007084595](#) and [WO2011044184](#)) and Thrombin inhibitors ([WO2005046688](#) and [WO03089428](#)).

Harvard University is an American university, which is a world leader in research and education into medical sciences.<sup>21</sup> It has 47 patent families with research areas being in amyloid inhibitors ([WO2004064869](#) and [WO0214264](#)), apoptosis of cells ([WO2007114948](#)), diagnostic techniques which detect proteins and polypeptides aggregated on a cortical region of an ocular lens ([WO0216951](#)) and use of osteocrin as a method to gauge neuronal activity ([WO2014121083](#)).

University of California is another American-based university that has research interests in Alzheimer's disease.<sup>22</sup> Among the 46 patent families identified in this study is research into the treatment of Alzheimer's disease via neuron growth ([WO2014026164](#)), secretase inhibitors ([WO2016070107](#)) and cyclic peptides as anti-inflammatories ([WO2012167077](#)). They have also developed a range of diagnostic techniques for Alzheimer's disease, such as use of amyloid antibodies ([WO2011072257](#)), modelling of degenerative diseases ([WO0210768](#)) and immunoassays ([WO0241839](#)).

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<sup>14</sup> Pfizer - [Therapeutic Areas](#)

<sup>15</sup> Pfizer - [Pipeline](#)

<sup>16</sup> Pfizer - [Pfizer Pipeline As of February 2, 2016](#)

<sup>17</sup> Perrigo - [Elan Corporation PLC Acquisition](#)

<sup>18</sup> 3B Scientific, [Could This Be the Biggest Breakthrough for Alzheimer's Disease?](#) – 25 September 2015

<sup>19</sup> Taisho Pharmaceuticals - [Corporate Profile](#)

<sup>20</sup> Griffiths, K., [Bayer acquires Schering in €17bn deal](#), 15 June 2006, The Telegraph

<sup>21</sup> Harvard University - [Homepage](#)

<sup>22</sup> UC Newsroom, [UC initiative to spur Alzheimer's disease research](#), 14 January, 2016

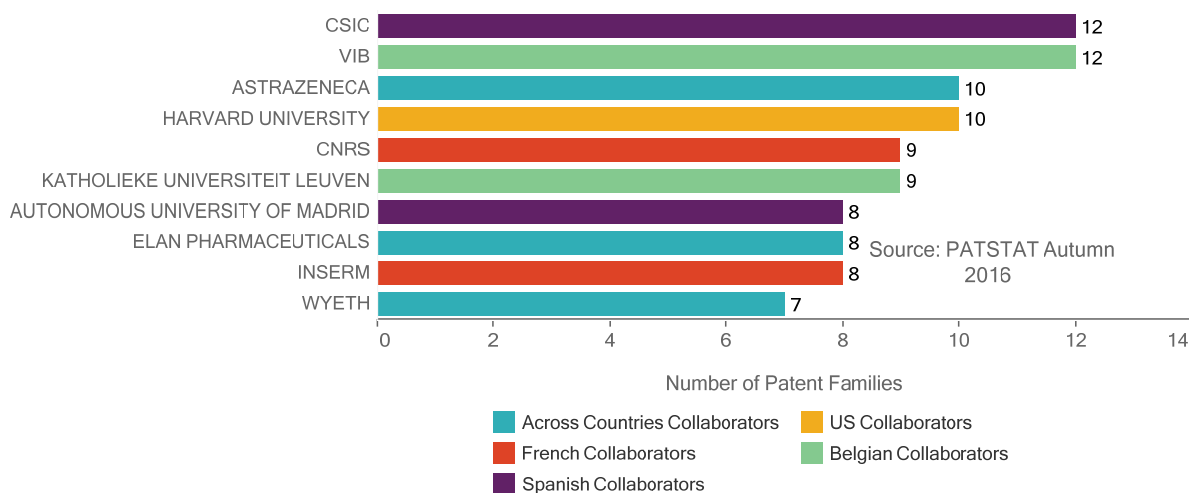


Evotec Neurosciences is a German based biopharmaceutical company founded in 1993 that has a dedicated research and development section for neuroscience.<sup>23</sup> It has 45 patent families relating to the treatment and diagnosis of Alzheimer’s disease. The research ranges from the use of activator proteins for vesicle secretions ([WO03069347](#)), Alzheimer’s disease diagnosis and prognostication using human maguin proteins and nucleic acids ([WO0308661](#)) and steroidogenic acute regulatory proteins (StAR) ([WO03104811](#)), and the regulation of RNA-editing deaminase-2 (ADARB2) proteins for the treatment and diagnosis of Alzheimer’s disease ([WO2006134128](#)).

## 2.3 Collaboration

Figure 3 shows the top ten entities that have collaborated in the development of Alzheimer’s disease diagnostics and treatments. Evidence of collaboration was identified in this study by identifying unique co-applicants present in the application.

**Figure 3 – Collaborations**



In this study three distinct clusters of collaborations were identified within three individual European countries.

### 2.3.1 Collaborations within Spain

The first is in Spain, where Consejo Superior De Investigaciones Cientifica (CSIC) was identified as the highest collaborator in that country with 12 patent families. The CSIC is the Spanish National Research Council and have research interests in the areas of neuroscience.<sup>24</sup>

Some of CSIC’s collaborators include:

- Autonomous University of Madrid on non-human animal models for the study of Alzheimer’s Disease ([WO2007063160](#)) and the use of dicarboxylic amino acid derivatives on the treatment of Alzheimer’s disease ([WO2009074706](#)),
- IMABIS, Universidad de Malaga and Universidad de Sevilla on sulphamide derivatives as neuroprotectors ([WO2012121142](#)), and
- Rockland and PolyAn and the Naranjo research group.<sup>25</sup>

<sup>23</sup> Evotec – [Therapeutic Areas: Neuroscience](#)

<sup>24</sup> CSIC – [Biology and Biomedicine](#)

<sup>25</sup> CSIC – [Naranjo Research group](#)

The second most prolific collaborator located in Spain is Autonomous University of Madrid (UAM) which has 8 patent families that were results of collaborations. Some of the collaborations are with CSIC as mentioned above and with Autonomous University Barcelona on the use of transgenic animal models for development of therapeutics to treat Alzheimer's disease ([WO20056020680](#)).

### 2.3.2 Collaborations within Belgium

The second European country with a collaboration network is Belgium, where Vlaams Interuniversitair Instituut Voor Biotechnologie VZW (VIB) is the top Belgian collaborator with 12 patent families. VIB is a life sciences research institute based in Belgium with research ranging from cancer treatment to neuroscience.<sup>26</sup>

Their collaborators include:

- Katholieke Universiteit Leuven (KU Leuven), the second highest collaborator in Belgium with 9 patent family collaborations all with VIB. The collaboration focuses on screening of compounds that modulate G-protein coupled receptor 3 (GPR3) and beta-arrestin signalling and in particular compounds that reduces the formation of beta-amyloid proteins ([WO2010142603](#)),
- Universiteit Antwerpen on the use of human genetics to diagnose Alzheimer's disease ([WO2015001113](#)),
- Galapagos Genomics for the development and validation of new drugs for Alzheimer's disease,<sup>27</sup>
- VUB (free university of Brussels) on the identification of lipids that might be the culprit in Alzheimer's disease.<sup>28</sup>

Apart from collaborations, KU Leuven has also spun off a company called ADX Neurosciences relating to the development and commercialisation of antibodies for Tau aggregates.<sup>29</sup>

### 2.3.3 Collaborations within France

The third European country with a collaboration network is France. The highest collaborator in that country is the Centre National De La Recherche Scientifique (CNRS), which has 9 patent families that have been a result of collaborations. CNRS is a French government funded research institution with research focus on biological sciences, particularly on brain, cognition and behaviour research.<sup>30</sup>

Some of their collaborations are with:

- Institut National De La Santé et De La Recherche Médicale (INSERM), the second highest collaborator in France. Their collaboration focussed on the inhibition of apoptosis of mammalian nerve cells and applying this to treatment of Alzheimer's disease ([WO0185940](#)),
- Institut Curie and Université Montpellier 2 Sciences et Techniques on indole-derivatives to treat diseases related to pre-messenger RNA splicing ([WO2005023255](#)),
- Université Claude Bernard Lyon and Institut National Des Sciences Appliquées De Lyon on pyrrolidine derivatives for the treatment of Alzheimer's disease ([WO2014006307](#)).

The second highest French collaborator is Institut National De La Santé et De La Recherche Médicale (INSERM) with 8 patent families that arose from collaborations. One particular collaboration involved

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<sup>26</sup> VIB - [Research](#)

<sup>27</sup> Evaluate, [Galapagos Genomics and VIB announce functional genomics collaboration in Alzheimer's disease](#) – 30 August 2001

<sup>28</sup> Flanders – [Flemish scientists discover crucial role of lipids in Alzheimer's](#) – 08 December 2007

<sup>29</sup> KU Leuven – [News\(Tech Transfer Office\)](#)

<sup>30</sup> CNRS – [Biological Sciences](#)

Assistance Publique – Hôpitaux De Paris, CNRS, ICM and Université Pierrre et Marie Curie looking at boosting regulatory T-cells for the treatment of Alzheimer’s disease ([WO2014206899](#)).

### 2.3.4 Collaborations within the United States

Harvard University has 10 patent families that resulted from collaborations. These collaborations include those with MIT and University of Pittsburgh on heterocyclic dyes for *in vivo* imaging and diagnosis of Alzheimer’s Disease ([WO2006020156](#)), with Neurogenetics on the discovery of several single nucleotide polymorphisms and mutations in the Alpha-2-macroglobulin genes (risk factors for Alzheimer’s disease) ([WO03501174](#)) and with the Brigham and Women’s Hospital on drugs that inhibit and modulate the translation of gene associated with amyloid precursor protein production and amyloid secretion ([WO2004112700](#)).

### 2.3.5 Collaborations across countries

Other collaborations outside of Europe are for example AstraZeneca with 10 patent families that resulted from collaborations. These collaborations includes Amylin Pharmaceuticals on polypeptide for reduction of immunogenicity ([WO2013009545](#)) and Astex Therapeutics on pyrrolopyridine derivatives as a BACE inhibitor ([WO2009022961](#) and [WO2007058602](#)). Other non-patent generating collaborations are with Eli Lilly on a phase 3 clinical trial on an antibody selective for beta-amyloid<sup>31</sup> and Astex on a \$40 million dollar deal to develop small-molecule inhibitors to target beta-amyloid.<sup>32</sup>

Elan Pharmaceuticals has 8 patent families that were result of collaborations. Some of Elan’s collaborations included those with Wyeth, a US company, on Pyrimidinyl amide compounds for the inhibition of leukocyte adhesions ([WO2007041270](#)) with Pharmacia & Upjohn on ether amine compounds for inhibitors of beta-secretase enzymes and the formation of beta-amyloid proteins ([WO02094768](#)), and with Pfizer on diaminoalkanes compounds for the inhibition of beta-secretase enzymes ([WO2004024081](#)). The collaboration between Elan Pharmaceuticals and Wyeth includes licensing deals with other parties such as Intellect Neurosciences for patents relating to immunotherapy platforms to prevent the accumulation of aggregated beta amyloid fragments in the brain.<sup>33</sup>

Wyeth has 7 patent families that originated from collaborations. Some of the collaborations are with Elan Pharmaceuticals as stated above and with University of London on polypeptides that have a therapeutic use on the inhibition or regeneration of axons ([WO2008006103](#)).

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<sup>31</sup> PR Newswire, [Lilly and AstraZeneca to develop second potentially disease-modifying treatment for Alzheimer’s disease](#) – 09 December 2016

<sup>32</sup> The Pharma Letter, [Astex in \\$40 million Alzheimer’s Collaboration with AstraZeneca](#) – 10 March 2003

<sup>33</sup> Maza E., [Intellect Neurosciences Grants to Top Tier Global Pharmaceutical Company and Option to License Certain Alzheimer’s Patents and Patent Applicants](#) -10 August 2008, BioSpace

## 2.4 Applicant origin

Figure 4 – Applicant origin

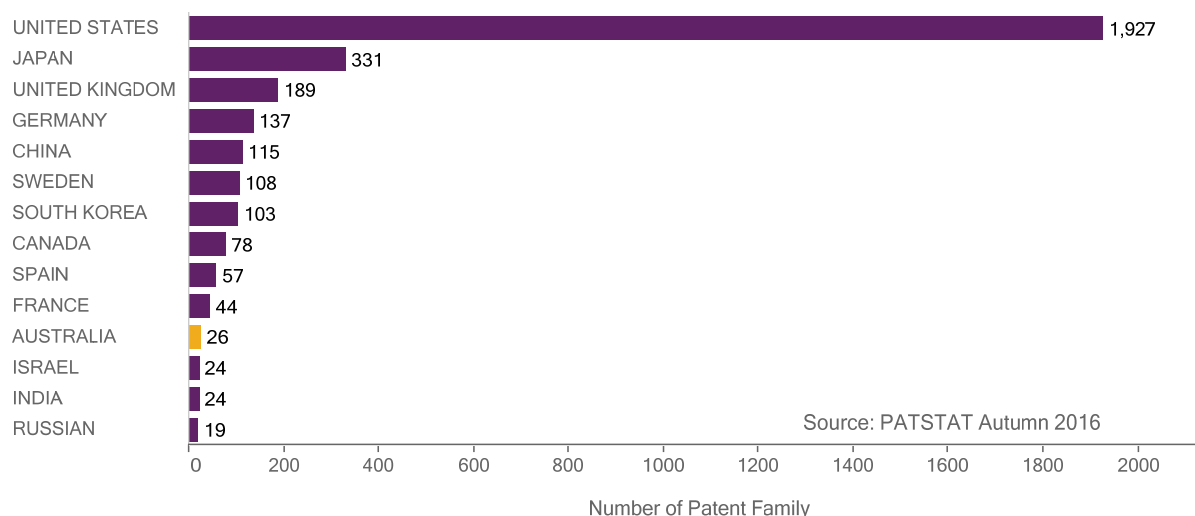


Figure 4 shows the number of patent families originating from each country worldwide this is derived from an applicant's registered address. The most patent families identified in this study have been filed by United States entities (1927 patent families) including MSD, Roche and Elan Pharmaceuticals. The second highest contributor is Japanese entities (331 patent families) such as Taisho Pharmaceuticals. The United Kingdom is in third place with 189 patent families filed. European countries such as Germany (Evotec Neurosciences), Sweden (AstraZeneca), Spain and France are all featured strongly as applicant origins (refer to Section 2.3-Collaboration for more details).

Asian countries such as China (115 patent families) and South Korea (103 patent families) show strong patent family generation. The main Chinese applicants are the Chinese Academic of Sciences (15 patent families), Sunshine Lake Pharma Company (6 patent families) and Shanghai Biowindow Gene Development (4 patent families). The main South Korean applicants are Korean Institute of Science and Technology (KIST – 8 patent families), Seoul National University (5 patent families) and Korean Research Institute of Chemical Technology (5 patent families).

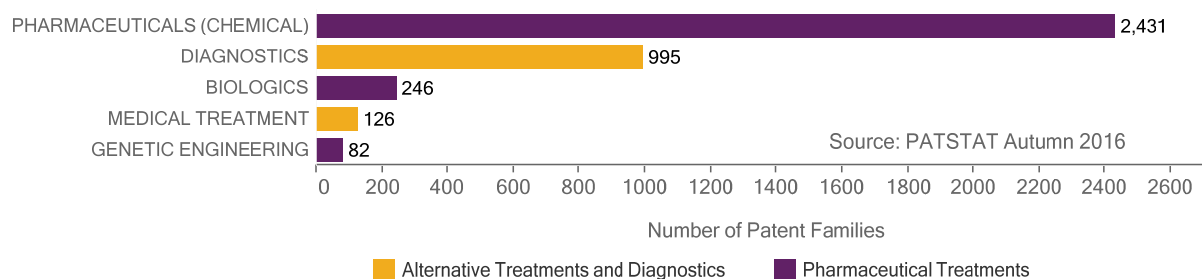
Canada is ranked 8<sup>th</sup> with 78 patent families. The top applicants are McGill University (6 patent families) and University of British Columbia (5 patent families). Australia is ranked 11<sup>th</sup> with 26 patent family members (refer to Section 4.3-Top Australian Applicants for more details).

# 3 Technology breakdown

## 3.1 Overall technology breakdown

Figure 5 shows a breakdown of the technology categories. The patent families were assigned a broad technology category based on their hierarchical International Patent Classification (IPC) and titles (refer to Appendix B for more details).

**Figure 5 – Technology categories**



The major technology categories determined in this study are:

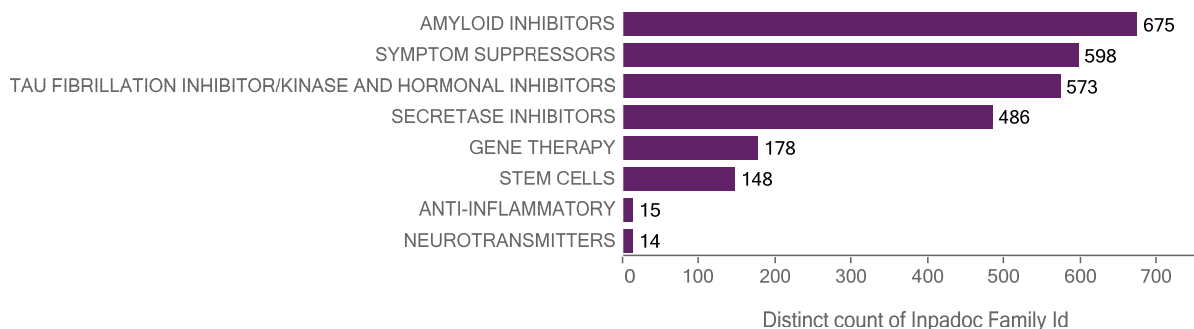
- *Pharmaceuticals (Chemical)* (2431 patent families) relates to the use of small molecule drugs as key active ingredients in the treatment, prevention and minimising symptoms of Alzheimer’s disease. The category captures the production and use of heterocyclic compounds (Benzofuran-[WO2009048274](#), Benzoic acid derivatives-[WO03010143](#), Pyridazine derivatives-[WO03070707](#), Cycloalkane derivatives-[WO2004016616](#) and Steroid derivatives-[WO2005005606](#)) and acyclic compounds (Aminoadamantane derivatives-[WO0162706](#), Diaminediol derivatives-[WO03006013](#) and Statine derivatives-[WO03006021](#)) as an inhibitor or drug that target Alzheimer’s disease.
- *Diagnostics* (996 patent families) are related to the detection and diagnosis of Alzheimer’s disease, either by taking a sample and detecting known biomarkers such as amyloid proteins or secretase enzymes or via non-intrusive imaging. The category captures methods and compounds used in bioassays (biomarkers) (Fibrinogen-[WO2008010660](#), Encephalotoxin-[US2006099598](#), Nucleic acid-[US2003008295](#) and Imidazoline homologs-[WO0216585](#)), antibodies which bind to amyloid, secretase or kinase proteins ([WO2004067038](#) and [WO02082075](#)), imaging with microscopes or nuclear magnetic resonance ([US2003236391](#) and [WO02094191](#)) and models which predict and simulate the progress of Alzheimer’s disease ([WO2004093830](#) and [WO02057496](#)).
- *Biologics* (246 patent families) groups drug treatments utilising biological agents that include antibodies which bind to proteins that cause beta-amyloid plaques ([WO2015017900](#) and [WO2004032868](#)), peptide-based drugs which inhibit certain protein pathways ([WO2009136752](#) and [WO2008057609](#)), plant extracts, that have activity in the treatment of Alzheimer’s disease ([WO20060737265](#) and [WO2007013824](#)) and production, transmutation and implantation of stem cells ([WO2008035908](#) and [WO2010018996](#)).
- *Medical Treatment* (126 patent families) groups other forms of Alzheimer’s disease treatments that do not utilise pharmaceuticals and also includes methods that works to reduce symptoms. It includes within its scope physical treatments such as laser/light therapies ([WO2011116413](#) and [WO2006138659](#)), electrically stimulating nerve cells ([WO03026738](#)), shunts to allow controlled removal of cerebral spinal fluid from the brain ([WO2005051474](#)), devices implantable in the airway ([WO2005102458](#)), training methods to improve memory ([WO2008070790](#)), use of electric fields ([US2016106997](#)) and use of ionising radiation ([US2013323166](#)).
- *Genetic Engineering* (82 patent families) represents transgene implantation (AAV vectors-[WO2006119458](#), VHL gene-[WO0226977](#), Thrombomodulin gene-[WO2004076635](#) and RNA virus

vectors-[WO2010050585](#)), DNA vaccines ([WO2004000877](#) and [WO2006112553](#)) and DNA recombinant technologies ([WO0172802](#)).

## 3.2 Pharmaceutical Targets

A more detailed breakdown of patent families relating to *Pharmaceuticals (Chemical)*, *Biologics* and *Genetic Engineering* and have been grouped as *Pharmaceutical Treatments* (purple) in Figure 5. Figure 6 shows a breakdown of the above mentioned category and includes 2687 patent families and each patent family within *Pharmaceutical Treatments* was hierarchically sorted into one of the following subcategories based on the title and abstract of a representative patent application from the family (see Appendix B for details):

**Figure 6 – Sub-category breakdown**



- **Amyloid inhibitors (675 patent families):** patent families which disclose the utilisation of drugs, antibodies or proteins specifically designed to inhibit or interfere with the production of amyloid proteins. Of particular interest is the delivery of the amyloid protein specific antibodies through the blood brain barrier and into the site in which the plaques are forming. University of Kyoto has disclosed an insoluble carrier for transporting antibodies through the barrier and into the amyloid plaque sites ([WO2016092865](#)). In another aspect, research of the use of antibodies and peptides for inhibition of amyloid formation and deposition are disclosed. For example, Sinai School of Medicine has disclosed a peptide derived from cadherin which inhibit the amyloid deposition in the brain ([WO03087136](#)) and AstraZeneca disclosed a series of ligands, in particular estrogen receptors for their use in the treatment of Alzheimer’s disease ([WO0246164](#)).
- **Symptom suppressors (598 patent families):** patent families which disclose anti-convulsant drugs used to suppress rapid or excessive firing of neurons which occur during seizures and also work to inhibit the seizure spreading throughout the brain. Anti-depressants, enhanced memory and cognitive function drugs are also categorised into this sub-category. Of particular interests are drugs that are disclosed to exhibit multiple effects on symptom suppression. For example MSD disclosed a methylpropanamide derivative that improved an aged-related cognitive decline as well as improving the patients memory function ([WO2004080459](#)). Another drug, quinolinone based, disclosed by Roche has activity on a major modulatory neurotransmitter which has proven to have effects on cognitive memory loss and mood disorders ([WO2006066790](#)). Finally, AstraZeneca has disclosed the use of nicotine based compounds in the reduction of symptoms such as cognitive and memory loss, as well as neuroprotection ([WO2004016616](#)).
- **Tau fibrillation/kinase and hormonal inhibitors (573 patent families):** patent families which disclose drugs that target tau-protein kinases and inhibit their 14 metabolic pathways. These drugs play a major role in cancer treatment as well as Alzheimer’s disease. Tau-protein kinases have been identified as another possible cause of Alzheimer’s disease. One method of inhibition of abnormal tau phosphorylation is through kinase inhibition by pyridine-4-one derivatives ([WO2011049722](#)). Another interesting compound is the use of a more complex molecule (benzimidazole derivatives) in the modulation of neurogenesis via tau or kinase proteins ([WO2014053409](#)). Alternatively, modulations of hormones have also been identified as having an effect on the treatment of

Alzheimer's disease, specifically gamma-aminobutyric acid (GABA) receptors. [WO2007073283](#) disclosed the use of cinnoline compounds for the modulation of GABA receptors.

- Secretase inhibitors (486 patent families): patent families which disclose drugs and antibodies that target and inhibit the activity of beta-secretase (BACE) enzyme, which would in theory prevent the build-up of amyloid proteins. A range of pharmaceutical compounds have been disclosed for their activity in the inhibition of secretase activity. One such class of compounds is phenylcarboxamide derivatives which demonstrated activity in the inhibition of secretase activity ([WO2004043916](#)). Another class of compounds which exhibit similar secretase inhibition activities is heterocyclic aniline derivatives ([WO2010052199](#)). Imidazole compounds have also been identified as a candidate to inhibit the activity of secretase enzymes ([WO2005092864](#)).
- Gene therapy (178 patent families): patent families which disclose genetic treatment of Alzheimer's disease based on transgene implantation, vector insertions and recombinant DNA medicines. The use of mRNA levels as a biomarker for the diagnosis and treatment of Alzheimer's disease allows for a correlation and inhibition of vascular amyloid deposition ([WO2014152869](#)). Also the use of polypeptide and DNA vaccines has been disclosed for the treatment of Alzheimer's disease ([WO2013166473](#)).
- Stem cells (148 patent families): patent families which disclose the use of stem cells towards the treatment of Alzheimer's disease. For example the use of stem cells has been utilized for the production of cholinergic neural cells as well as comprising the step of forming neural cells from stem cells ([WO2016032151](#)).
- Anti-inflammatory (15 patent families): patent families which disclose drugs that are non-steroid-based anti-inflammatories that help to suppress or minimise the inflammatory process. Of particular interest is the use of pyrazole derivatives as a cyclooxygenase inhibitor for the treatment of inflammation and associated diseases ([WO03037352](#)).
- Neurotransmitters (14 patent families): patent families which disclose means of disruption of neurological transmitters and other neurological processes. For example the use of cannabinoids has been demonstrated to mediate cannabinoid-1 receptors and has been disclosed to be beneficial and useful in the treatment, prevention and suppression of symptoms of Alzheimer's disease ([WO2008118414](#)).

# 4 Target markets

## 4.1 Worldwide

In order to look at the target markets of the technologies relating to the treatment of Alzheimer’s disease, we can look at the countries where applicants have elected to enter national phase. The report analysed the number of unique patent families that has been filed into their respective national jurisdictions. The graph below is national phase applications resulting from a PCT application. The PCT applications have been excluded from this figure since they do not represent an enforceable right in any jurisdiction. European patents are enforceable in designated contracting states to the European Patent Convention (EPC) at the date of filing of the application<sup>34</sup>. Alternatively patents can be applied for directly in individual European countries e.g. Germany as per graph below.

**Figure 7 – Worldwide Patent Application Coverage**

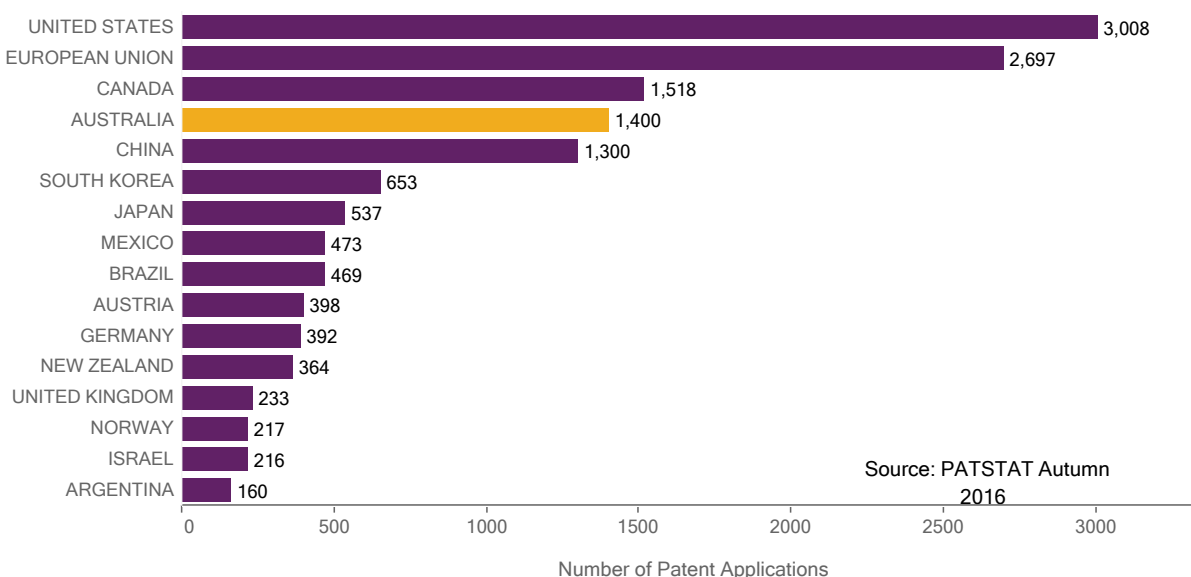


Figure 7 shows the highest number of filings by far is in the United States with 3008 patent applications entering into that market. The European Union is the second largest market with 2697 patent applications but this set represents a collection of designated contracting states. The next largest markets are Canada and Australia, with 1518 and 1400 patent applications filed respectively.

Asian countries such as China, South Korea and Japan are identified in this study as major markets with 1300, 653 and 537 patent applications respectively. Mexico and Brazil are identified as the 7<sup>th</sup> and 8<sup>th</sup> largest patent markets for Alzheimer’s related patents with 473 and 469 patent applications filed respectively.

European markets such as Austria, Germany and Norway have some interest for the applicants as target markets. Other countries like New Zealand, United Kingdom, Israel and Argentina are also identified as significant markets for the diagnosis and treatment of Alzheimer’s disease.

The high number of patent applications entering nationally into Australia (third highest) shows that Australia is considered a significant market for the treatment and diagnosis of Alzheimer’s disease.

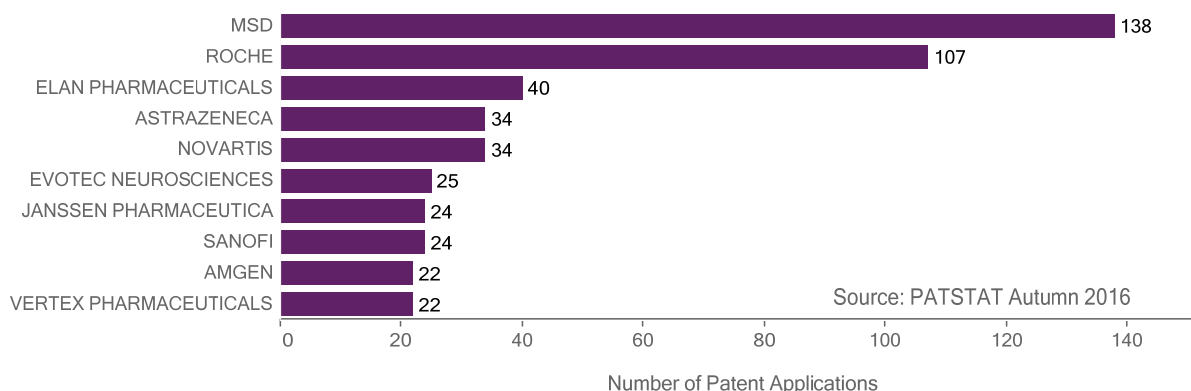
<sup>34</sup> EPO: [Guidelines for Examination - Designation of Contracting States](#)



## 4.2 Top Applicants within Australia

Figure 8 shows the top applicants with applications filed here in Australia. This study has identified the top applicants in Australia to be MSD (138 applications), Roche (107 applications), Elan Pharmaceuticals (40 applications), AstraZeneca (34 applications) and Evotec Neuroscience (25 applications), which is consistent with the top applicants worldwide as discussed in section 2.2. Other applicants such as Novartis (34 applications), Janssen Pharmaceutica Sanofi (both with 24 applications) Amgen and Vertex Pharmaceuticals (both with 22 applications) has also been identified as top applicants in Australia and will be discussed below.

**Figure 8 – Top Applicants within Australia**



Other Top applicants in Australia are:

- Novartis is a global healthcare company based in Switzerland.<sup>35</sup> Some of their patent families disclose the use of monoclonal antibodies for beta-amyloid ([WO2006117131](#)) and drug for secretase activity inhibition ([WO2012095469](#)).
- Janssen Pharmaceutica is a pharmaceutical company that is part of the Johnson & Johnson family of companies located in the United States.<sup>36</sup> Their patent families disclose decan-4-one derivatives as a beta-amyloid inhibition ([WO2004022558](#)) and pryzinone derivatives as a secretase inhibition ([WO2007122173](#)).
- Sanofi is a multinational pharmaceutical life sciences company with headquarters in France.<sup>37</sup> Some of their patent families disclose the use of pyrimidone derivatives as secretase ([WO2008078837](#)) and kinase inhibitors ([WO2009035159](#)).
- Amgen is a multinational biopharmaceutical company based in the United States.<sup>38</sup> They hold patent families that disclose the use of antibodies targeted for beta-amyloid ([WO2005019202](#)) and dihydrothiazine derivatives as secretase inhibitors ([WO2011115928](#)).
- Vertex Pharmaceuticals is a global biotechnology company located in the United States.<sup>39</sup> Some of their patent families disclose the use of heteroaryl compounds as kinase inhibitors ([WO03066629](#) and [WO03049739](#)).

<sup>35</sup> Novartis – [About us](#)

<sup>36</sup> Janssen Pharmaceutica – [Our Credo](#)

<sup>37</sup> Sanofi – [About us](#)

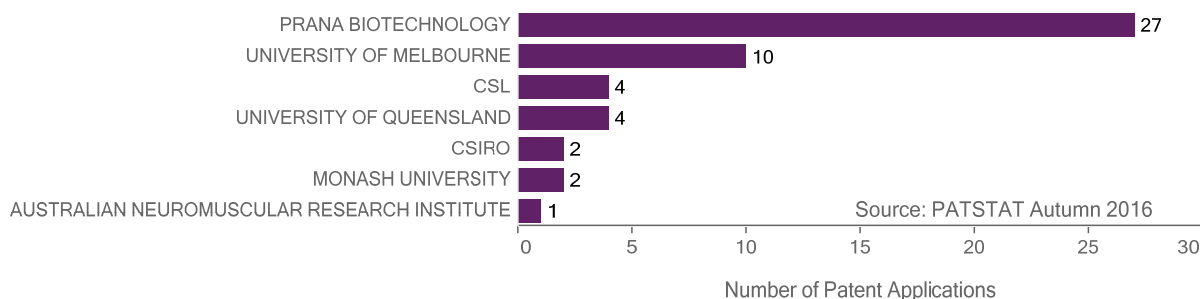
<sup>38</sup> Amgen - [History](#)

<sup>39</sup> Vertex Pharmaceuticals – [We are Vertex](#)

## 4.3 Top Australian Applicants

Figure 9 shows the top applicants originating from Australia.

**Figure 9 – Top Australian Applicants**



Prana Biotechnology, University of Melbourne and CSL are the largest Australian patent holders.

Prana Biotechnology is a Victoria-based biotechnology pharmaceutical and is mainly focused on the development of treatments for neurodegenerative diseases.<sup>40</sup> The company has a lead drug (PBT2) in phase II clinical trial. The drug targets the reduction of beta-amyloid plaques (Alzheimer's disease) and for Huntington's disease ([WO2005095360](#)).<sup>41</sup> Prana Biotechnology is also involved in collaboration with the Michael J. Fox Foundation researching Parkinson's disease (PBT 434).<sup>42</sup>

Other Australian entities identified as being researchers in the area of diagnostic and/or treatment of Alzheimer's disease are University of Melbourne, which filed an application, in collaboration with CSIRO for the use of biomarkers for the screening of Alzheimer's disease ([WO2015179909](#)) and beta-amyloid removal ([WO2011134019](#)).

CSL has evidence of research relating to the production of beta-amyloid antibodies ([WO2009043103](#)) and University of Queensland has research relating to the use of DNA and RNA for the diagnosis and treatment of Alzheimer's disease ([WO2009124341](#)).

CSIRO, the largest publically funded research organisation, has evidence of research relating to method of quantitative and predictive assessment for amyloid biomarkers in biological fluids ([WO2012149607](#)).

Monash University, a Melbourne based research university has disclosed a method of down-regulating the cleavage of beta-amyloid proteins with heparin proteins ([WO2007115372](#)) and in collaboration with University of Tasmania, the use of receptor-associated proteins for the reduction of amyloid proteins ([WO2010088729](#)).

Australian Neuromuscular Research Institute, now known as Perron Institute for neurological and translational science, is Western Australia's longest medical research institute<sup>43</sup>. They have disclosed the control of neurodegeneration by increasing cluster of differentiation 147 (CD147) receptor signaling ([WO2006084333](#)).

<sup>40</sup> Prana Biotechnology – [About](#)

<sup>41</sup> Prana Biotechnology – [pipeline](#)

<sup>42</sup> Prana Biotechnology – [products](#)

<sup>43</sup> Perron Institute – [Home](#)

## 5 Conclusion

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This patent analytics study set out to capture not only Alzheimer's pharmaceutical treatments, but also diagnosis and alternative medical treatments relating to Alzheimer's disease.

3881 patent families were reviewed and the majority of the families still have at least one patent in-force (Figure 1) indicating the commercial relevance of the work that is undertaken in the field. There has been consistent filing of patent families since 2000 to present, which signifies that there is still active research into the diagnosis and treatment of Alzheimer's disease.

Analysis of data relating to patent families regarding different Alzheimer's disease targets gives an indication on which species are considered the most commercially relevant, including beta-amyloid, beta-secretase and Tau-protein kinase. Majority of the patent families are targeting amyloid plaques in the brain and symptom suppressors for Alzheimer's disease. Additionally, there are also significant patent families directed to the diagnosis of Alzheimer's disease with many using antibodies and immunoassays to identify the early on-set of the disease. Other medical methods such as use of electric shock treatments, shunting of cerebral spinal fluid and light and laser therapies were also areas of interest as alternate treatment methods. In summary, the patent landscape of Alzheimer's disease is concentrated around chemical pharmaceuticals in the targeting of beta-amyloid plaques.

The United States has the greatest share of parent families originating. MSD, Roche and AstraZeneca appear consistently as the top applicants across each of the technology classification, and also appear among the holders of the largest patent families. This is consistent with the fact that these companies have active product portfolios in the field of neuroscience research. Also collaborations are a common occurrence between the top applicants and other smaller entities. This suggests that the research into the treatment of Alzheimer's disease is still very active and collaborations are a significant way to progress the research.

In terms of target markets for Alzheimer's treatment, the United States, Canada and Australia were identified as the top 3 target markets. The top applicants identified in this study which filed into Australia were MSD, Roche and Elan Pharmaceuticals. The top Australian applicants identified are Prana biotechnology, University of Melbourne and CSL.

# Appendix A

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## The Patent System

A patent is a right that is granted for any device, substance, method or process that is new, inventive and useful. Australian patent rights are legally enforceable and give the owner, or applicant, exclusive rights to commercially exploit the invention for a period of up to twenty years. In this report, an 'application' refers to a single patent filing. A patent application is published within 18 months of its priority date.

A patent application is considered to be 'in force' when it has not lapsed (due to expiry or non-payment of renewal fees), been revoked or withdrawn. A family has been designated as being in force if it contains at least one in force application.

Patents are classified by initially into a system known as the International Patent Classification (IPC). The International Patent Classification provides for a hierarchical system of language independent symbols for the classification of patents according to the different areas of technology<sup>44</sup>. A further classification system referenced in this report is the CPC refers to the Cooperative Patent Classification which came in force in 2013 is a bilateral system which developed by the EPO and the USPTO which provides more in depth classifications<sup>45</sup>.

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<sup>44</sup> <http://www.wipo.int/classifications/ipc/en/>

<sup>45</sup> <http://www.cooperativepatentclassification.org/>

# Appendix B

## Data Extraction and Analysis

We used four phases of data extraction and analysis.

- Phase 1: Development of an appropriate search strategy based on the aims of the project. The detailed search strategy is shown below.
- Phase 2: Data mining used the EPO's patent statistics database PATSTAT, Autumn 2016 edition, using the following SQL script:

```
select distinct t1.* from patstat.tls201_appln t1  
left join patstat.tls203_appln_abstr t3 on t1.appln_id = t3.appln_id  
where t1.appln_kind = 'W'  
and t1.earliest_filing_year > 1999  
and upper(t3.appln_abstract) like '%ALZHEIMER%'
```

- Phase 3: Data cleaning removed data duplication and ensured the return of the correct records. Data was subsequently categorized according to the technological focus of the patent families as set out in our schema outline at Table #. The technological focus was determined by reviewing the abstracts associated with each of the patent families taking into account the International Patent Classification (IPC) marks for the patent families. In cases where the abstract and IPC marks were insufficient to provide a clear description of the purpose of the invention, the body of the specification was scanned to provide further insight.
- Phase 4: Data analysis used Tableau 10.0 for calculation and visual presentation of patent metrics.

The Autumn 2016 edition of the PATSTAT database was used to identify applications in this study. Later documents may or may not be included in this study depending on the publication date of the with later priority dates of the documents.

## Technology Breakdown

### Top Level Technology Breakdown

We used the following IPC marks and titles to break down the technology in a hierarchical manner:

Classification	IPC Marks
Diagnostics	"G01", "C12Q 1", "A61B 5", "A61B", "G06K 9", "G06Q 50", "H04B 7", "G07C", "H04J" and "H04W"
Pharmaceuticals (Chemical)	"C07C", "C07D" and "A61K 31" Then "A61K 51/04", "A61K 33", "A61K 103", "A61P 25/28", "C08B" and "A61K"
Medical Treatment	"A61M 1", "A61M 27", "A61N 1", "A61K 9", "A01K 67", "A23C 9", "A61F 2", "A61F 7", "A61H", "A61K 47", "A61L 31", "A61K 49", "A61N 5", "A63F 9", "A63F 13", "A63H 33", "B29C 49", "G09F", "G07C", "G09B" and "B01D"
Genetic Engineering	"C12N 15"

Biologics	"C07K 14", "A61K 38", "A61K 39", "A61K 35/12", "C12N 9", "A61K 49/14", "A61K 36", "C12N 5", "C12P 21", "C07K", "A01H", "A01N", "A61K 51/08", "C12R", "C07J", "A61K 35/56", "A23L", "A61K 35/74" and "A23K"
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### Pharmaceutical Targets

For the Pharmaceutical Targets we used the following keywords in the abstract (PCT and DWPI) to hierarchically breakdown the patent families:

<b>Classification</b>	<b>Keywords</b>
Secretase Inhibitors	"secreta", "BACE" and "mema"
Amyloid Inhibitors	"amyloid"
Tau Fibrillation Inhibitor/Kinase and Hormonal Inhibitors	"tau", "fibrill", "kina", "hormo", "GABA", "estro", "PPAR", "steroid", "insulin" and "deacetyl"
Symptom Suppressors	"CONVULSANT", "MAO", "cogn", "tranq", "depress" and "memory"
Stem Cells	"STEM" and "53"
Gene Therapy	"RNA", "gene", "nucl", "recomb", "DNA" and "phosphodiesterase"
Anti-Inflammatory	"inflam"
Reductase Inhibitor	"reducta"
Neurotransmitters	"Acetylch", "cholin", "hydroxytrypt" and "glutamine"
Cellular Death	"death" and "apop"
Other Targets	"a"

