Patent Landscape Report on

Ritonavir

OCTOBER 2011

PATENT LANDSCAPE REPORTS PROJECT

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More information on the project, the ongoing work, and a compilation of reports published also by other institutions is available at: www.wipo.int/patentscope/en/programs/patent_landscapes/pl_about.html

For specific information, requests or proposals, please contact us (patent.information@wipo.int)

Patent Landscape Report on

Ritonavir

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Executive Summary

This report is a patent landscape on Ritonavir. Ritonavir is an antiretroviral drug from the protease inhibitor class used to treat HIV infection and AIDS. Ritonavir is included in the WHO Model List of Essential Medicines (EML)[1]. The originator company is Abbott Laboratories, which markets Ritonavir under the brand name Norvir, or in combination with the protease inhibitor Lopinavir, as Kaletra or Aluvia. The U.S. Food and Drug Administration (FDA) approved the drug in March 1996 for oral solution and in June 1999 for capsules. Abbot later received FDA and European Medicines Agency (EMEA) approval in 2010 for a heat-stable formulation of a 100mg Ritonavir tablet. This has particular importance for developing countries with elevated ambient temperatures.

A major goal of this project is to highlight the technology timeline for Ritonavir from the first filing of this compound in December 1993 by Abbott Laboratories (WO1994014436) to the present filings in which additional patent families attempt to protect subsequent innovations to the compound, variants and derivatives, combinations with other chemicals, methods of production, methods of use, etc. The identification and analysis of these patent documents showed that filings related to Ritonavir have increased dramatically since the initial disclosure and now include over 800 patent families. A patent family is a collection of interrelated patents that often contain the same disclosure and are typically related through dependence on a common priority document or documents. On average, 45% of the patent families identified during this patent landscape include at least one grant of a patent in one jurisdiction and thereby directly protect the various aspects of Ritonavir mentioned above.

This landscape report identified most patent families were initially filed in the United States. The most common assignee was identified as Abbott Laboratories. Nearly all documents are assigned to large pharmaceutical corporations with a minimal number of patents and applications assigned to universities and small pharmaceutical companies.

This report identified a number of innovation tracks that spun-off of the first Ritonavir patent document, WO1994014436. These are related to liquid dosage formulations, solid dosage formulations, synthesis of Ritonavir and its key intermediates, and polymorphs and crystalline Ritonavir. These innovation tracks illustrate important protection related to Ritonavir as subsequent generations continue to narrow the scope of protection in a wide area of technologies while still maintaining protection from the first Ritonavir Patent, a phenomenon that is also sometimes termed “evergreening”.

The single largest area of patenting is related to combination therapies. These documents were not included as an innovation track because of the lack of interrelation between the claims. These documents describe new pharmaceutical agents. The formulations containing new agents also include Ritonavir because it has been shown to be a powerful secondary protease inhibitor. Patenting in the area of combination therapies containing Ritonavir as a secondary protease inhibitor is also expected to increase in the future. There appears to be a large amount of filings for liquid dosage forms and structural information for Ritonavir.

A second notable area of patent filings is in the area of synthesis of Ritonavir and its key intermediates. The synthesis of Ritonavir was first filed for in 1999 (WO2001021603 claiming

[1] http://www.who.int/mediacentre/factsheets/fs325/en/index.html

priority to an earlier Italian patent filed for in September 1999) by Clariant Life Sciences and subsequently assigned to Archimica S.R.L. Since this initial patent, patents have been filed to cover the structure, synthesis and characterization of several key intermediates used in the synthesis of Ritonavir. Because this area has had several patents describing very specific intermediates and methods of preparing the intermediates there are expected to be fewer patents filed related to the synthesis. However, filings related to broader key intermediates and reaction conditions are expected to increase in the future as more efficient synthetic strategies emerge.

A third notable area of patent filings is in the area of solid dosage forms. Because solid dosage forms have had less patenting activity in the past decade, filings are expected to increase in this area to incorporate recent protections on crystalline structure and polymorphs into solid dosage formulations. The combination of the crystalline structure with solid or liquid dosage forms could provide a potential area for future patent filing and protection.

In summary, the patent landscape surrounding Ritonavir is continuing to grow and protect a large number of increasingly narrower technologies related to the synthesis, characterization, and dosage forms. The complex nature of the interrelation of patent families is described in greater detail in the innovation tracks section of this patent landscape report.

Section 1 - Introduction

The following patent landscape report on Ritonavir identifies all patent families that claim inventions involving Ritonavir. The report highlights the technology timeline for Ritonavir from the first filing. The patent families generally relate to the pharmaceutical compound as such, derivatives thereof, combinations, methods of production, uses and pharmaceutical compositions containing Ritonavir. The focus of the search was to identify patent documents covering various aspects of Ritonavir starting with the first key patent application and to confirm what that first key patent application was. It was suspected that WO1994014436 was the first key patent application and during the first part of this landscape project it was confirmed that this is the first patent application on Ritonavir. Additionally, it was a major goal of this landscape to analyze the ways in which the original patent application is still protected by subsequent patents and applications. An objective of the report is to illustrate the complexity of patent protection on a specific chemical compound. A second objective of the report is to describe the search methodology used to perform in-depth analysis of patent literature related to Ritonavir. Statistical analysis was performed on documents related to Ritonavir to visually represent important information related to the patent protection for Ritonavir. Abbott Laboratories is the most assigned company and continues to file in a variety of areas related to Ritonavir including crystal structure and combination therapies comprising Ritonavir. A majority of assignees are large corporations. This finding was anticipated due the large amount of capital needed for drug discovery and to perform research and discovery on pharmaceutical agents.

The report also identifies four innovation tracks. The four areas covered by the innovation tracks are liquid dosage forms, synthesis of Ritonavir and its key intermediates, polymorphs and crystalline Ritonavir, and solid dosage forms. These innovation tracks analyze the interdependencies of relevant patent families claiming improvements that are either specifically adapted to or exclusively related to Ritonavir. The innovation tracks were selected because they represent areas that would be important for developing nations to consider if they are interested in preparing domestic generic pharmaceuticals. The report provides an illustration of the complexity of the patenting activity surrounding Ritonavir. This would be important for countries or organizations involved in policy discussions about patented pharmaceutical compounds. The innovation tracks were also selected because they represent areas that have had a high volume of patenting activity. However, patents and applications claiming combinations of antiretrovirals is a focus of a majority of the patent filings. This is not surprising because of Ritonavir has been shown to be a potent secondary protease inhibitor. These documents typically claim novel compounds with dependent claims describing Ritonavir as a “second pharmaceutical agent”.

A short glossary of definitions for common words and search operators is located at the end of the report.

Section 2 – Search Process

2.1 Introduction

This section describes the search methodology developed in phase 1 of the report. The narrative of this search history shows how the search was performed, specific tools and databases, and challenges encountered and methods of circumventing. This section also discusses the importance of using several chemical identifiers to ensure all relevant documents are retrieved. The complete search history is included in Appendix 4.

2.2 Explanation of Search History and Methodology

The search began with reviewing the published PCT application WO1994014436 identified in the "Terms of Reference" disclosure as a probable key patent and its INPADOC family members. The document was reviewed for relevant keywords and U.S. and European classification codes. A glossary of search operators and other terms can be found in Appendix 2.

The first search approach involved text-based searching using a first search platform, Minesoft Patbase. The search histories for all search engines used are located in Appendix 3. Search query 2 of the Patbase search history was a collection of all INPADOC family members for WO1994014436. In search query 3, backward citation searching[2] was then performed only on WO1994014436 to help identify earlier patent publications describing Ritonavir (RIT). The review of these backward citations did not identify any documents describing RIT. The citations did show a large number of RIT analogs, but none of these documents specifically described RIT. Forward and backward citation searches for the WO19940114436 publication and its family members were performed later and described in more detail below.

Search query 4 was to further review a United States patent, US5142056 also owned by Abbott Laboratories, which is a family member of WO1994014436. US5142056 was granted August, 25, 1992, well before the priority date of WO1994014436. US5142056 claims a Markush structure similar to RIT, but does not specifically disclose RIT. The compound in US5142056 describes the same backbone but uses a pyridinyl group where RIT has a thiazoyl group. Since this compound only differed by a single substitution, search query 5 was performed to identify backward citations of US5142056, in order to check for any prior patents or applications that may have disclosed RIT.

The 77 INPADOC family members of WO1994014436 collected in query 2 were then reviewed in more detail to identify documents disclosing RIT or its analogs as well as to iden-

[2] Backward citation search means identifying all documents that are cited by the document in question. Forward citation search means identifying all documents that cited the document in question.

tify additional keywords and classification codes for later use. Many of these documents described similar analogs but did not specifically discuss RIT. Search queries 6 and 7 were each forward and backward citation searched for relevant family members.

After reviewing all of the relevant families, the Patbase chemical synonym search tool was used to identify commonly used synonyms for RIT. The Patbase chemical synonym search tool provides a fast and easy way to find relevant synonyms and numbers to enhance chemical searching. The tool works by entering a chemical name or number of interest and the corresponding structure is displayed along with a list of names and synonyms including trade names and generic names. The synonyms identified using the Patbase tools were augmented by additional synonyms found using several online resources including ChemSpider, Chemfinder, and Wikipedia. Query 8 shows there are over 14,000 patent families referencing RIT and/or its synonyms. Search query 9 then limited the same list of synonyms to patent families having document only describing the synonyms in the title, abstract or claims (TAC). This limitation on the search parameters reduced the number of families with a relevant document to 2,215. This limited query was important because many of the documents identified in the full text query 8 describe the compound in the background information and are therefore not relevant to the current collection. Search queries 10 and 11 were performed to estimate the total number of families of patents having patent documents that are assigned to Abbott Laboratories since many of the key patents for RIT are assigned to Abbott Laboratories.

Search queries 12 and 13 were performed to find the earliest documents describing RIT which provided an estimate of how many documents might be considered key patents along with WO1994014436.

Search queries 14 and 15 were more forward and backward citation searches on relevant family members of WO1994014436.

Search queries 16-19 were further date limited in short chronologic periods to determine when the first mention of RIT and/or its synonyms occurs. Search query 19 shows 220 documents published prior to December 31, 1980. This large number of results published did not agree with preliminary research. Preliminary searches in the Merck Index, SciFinder Scholar and various online resources do not report RIT before 1994. After reviewing several of these documents, the synonym responsible for returning the documents was “RTV”. “RTV” was found in the claims of all documents and used as an abbreviation for retroviral. Since retroviral or RTV does not specifically refer to RIT, a TAC limited search of the synonyms, excluding RTV, was then re-ran in search query 20, identifying 841 documents. Date restricted search queries 21 and 22 were performed to determine when RIT and/or synonyms first appeared.

The results of search queries 21 and 22 further helped confirm the earliest reference of RIT is WO1994014436. This confirmation was also supported by reviewing the Merck Index, reviewing RIT FDA Orange Book patents, and reviewing file histories of several key family members of WO1994014436.

These steps led to a determination that the first key RIT filing was WO1994014436. A forward citation search was then performed on WO1994014436 in query 23. These families of patent documents citing WO1994014436 were then reviewed to determine how the claims of

these documents differed from WO1994014436 and other earlier key patents. Search queries 24-26 were backward and forward citation searches from the families in query 23 and were performed to find additional relevant documents. The file histories of the relevant documents were also reviewed. File history information contains important correspondence between the patent office and the applicant for patent including the patent examiner search history and cited documents. This also allows for the review of changes in the claim language during prosecution.

After reviewing documents from the citation queries 24-26 a second approach was then performed to find additional relevant documents. The second approach was a structure search using the second search platform, Chemical Abstracts Services (CAS) STN. The Registry file was searched using the CAS registry. The Registry file contains substances identification for more than 56 million organic and inorganic substances. The Registry file identified 889 patent documents containing the substance. The structure search was then performed in the Registry, CAplus and Marpat files. The structure search allows for salts and other limited substitutions. The structure search identified 913 patent documents containing the structure. The results of the registry number search and the structure search were combined and found 916 unique patent families referencing RIT. It is important to perform both registry number search and structure search because the registry number search does not necessarily identify “Markush” structures. Markush structures are only indexed in the Marpat file. Markush structures are defined as generalized formula for a related group of compounds. They describe substituents at several positions, and often thousands of possible compounds can be defined in this way. Using the combination of CAS registry number searching is also important because registry numbers are manually assigned to patent documents by the Chemical Abstracts Services. This step is time consuming and there is potential for newer documents to not have registry numbers assigned. The 916 documents were retrieved and uploaded into Patbase.

Search query 27 contains all the records identified during the STN search. Search query 27 shows only 776 families of documents instead of the precise 916 total documents identified during the STN search. The discrepancy is caused by difference of family groupings between CAS and INPADOC used in Patbase. Search query 28 shows the overlap of documents identified using the RIT and/or synonyms text-based search (query 20) and STN structure search (query 27). There are 119 records unique to STN that were not identified using text searching alone. A majority of these documents were identified in the Marpat file based on Markush structures.

Search query 29 is the combination of all documents identified using text and structure searching. These 968 patent families represent a vast majority of important documents claiming inventions directly related to RIT. All of these families of documents were reviewed and sorted according to claimed invention, including pharmaceutical compositions, combination therapies, preparation methods or synthesis, and methods of treating or detecting HIV/AIDS. These groupings are *the beginning of determining important innovation tracks and creating genealogical patent trees* for RIT.

An additional category to those listed above grouped a large number of documents describing derivatives. Because there are a large number of protease-inhibiting compounds with very similar chemical structures, the collection was primarily limited to documents that claimed RIT or Markush structure representing RIT. However, compounds described as RIT

prodrugs, RIT-containing protecting groups, and pharmaceutically acceptable salts were also included. In addition, documents describing RIT bound to targeted delivery compounds, polypeptide, and carbohydrate groups were also included.

Search query 30 includes all FDA Orange Book patents related to RIT. The Orange Book contains a detailed listing of drugs and drug products approved for use and sale in the United States by the U.S. Food and Drug Administration. These documents are a useful tool for identifying relevant assignees, drug manufacturers, and approved products that appear in the U.S. market.

After reviewing documents referencing RIT and/or synonyms, the search focus shifted to identifying potential key innovation tracks. Search query 31 identifies documents referencing RIT and/or synonyms in titles, abstracts and claims (TAC), and heat or thermal stability in any part of the document. This query illustrates there is a small number of documents describing heat or thermal stability.

In addition to identifying assignees listed in the Orange Book, statistical analysis was performed on all documents identified in query 29. Statistical analysis for the search is defined as determining the most common assignees, inventors, classification codes and their frequency. The most common assignees were identified and searched in queries 32-37. The assignee lists were prepared using a searchable list of all assignees which includes the number of patents associated with an assignee. Many assignees have various spellings and subsidiaries making this analysis tool particularly useful. Search queries 38-43 were combinations of assignees and the list generated in query 29 to determine the number of patents held by each assignee referencing RIT and/or synonyms.

Search queries 44-54 identify documents describing RIT with specific physical forms. These search queries were devised based on the groupings identified from query 29. There are a large number of documents describing specific polymorphs and stabilized compositions. The search queries were used to estimate the number of documents claiming specific methods of preparing or describing physical properties of RIT. Many of the stabilized compositions claim suspensions or dispersions in a variety of liquids and solvents.

Search queries 55-57 identify documents describing solid pharmaceutical compositions. Many of the documents describing solid compositions containing various types of tablets including layered, dispersed or compressed tablets. Many of the solid dose formulations describe improved absorption at various stages of the GI tract. Queries 56 and 57 were performed to determine the specific number of documents describing these effects.

Search queries 58-61 were used to identify documents specifically describing aqueous or liquid phase compositions or delivery methods of RIT.

Specific searches for combinations of RIT and other compounds were not independently searched. Searching for combinations is most effectively done by reviewing documents describing RIT. Since all combination therapies include RIT, it is not efficient to attempt to search for each additional active ingredient. These documents are primarily included in query 29. Once these documents were reviewed they were categorized as combinations. This is the most efficient method of collection because the search captures all documents containing RIT. Combination searches for classification codes and diseases to be treated or

prevented along with compound names are the most effective methods for retrieving relevant documents.

Statistical analysis (performed as previously described) of classification codes (both USPC and IPC) for all documents in query 29 was performed. Relevant classification codes for oral dosage forms were identified and used as a secondary approach to identifying all relevant documents. This is a common technique to ensure complete coverage. Search query 68 illustrates a method of identifying documents related to oral dosage forms that were not identified by text-based searching alone. This is often useful because of the many variations in the language of the claims. Redundancies are also eliminated which improves overall searching efficiency.

Search queries 69-77 employed a similar process as described above to retrieve documents describing emulsions and transdermal deliveries. Search queries 78-80 were performed to identify documents methods or processes to detect or quantify viral diseases.

A third approach was then used to identify documents using text-based searches related to RIT's chemical structure. This is often a useful method for uncovering documents that describe Markush structures. WO1994014436 is an example of a document that would not have been identified using RIT and/or synonyms. Documents describing Markush structures were identified during structure searching in STN, however this ensures that we have collected all relevant documents. These queries were performed using a large number of classifications codes based on the structure (queries 81 and 82). The classification code searches were also combined with text searching to narrow the focus to protease inhibitors and antiretroviral compounds (queries 83-87). To further ensure complete coverage a similar process was continued in search queries 90-93. These queries were prepared to find documents describing antiretroviral compounds containing chemical components of RIT. Search query 91 includes both the broad definition heterocycles and the more specific thiazolyl. Heterocycles were included in the search syntax because patent claims attempt to describe chemical compounds as broadly as possible. The documents identified in query 92 were reviewed finding four documents not originally identified using the previous methods. Search queries 94-97 are citation searches on the four documents identified. These references identified in queries 94-97 were also reviewed.

Thomson Innovation was the third search platform used. Thomson Innovation was valuable to check as part of this process because DWPI has re-written abstracts focused on the novelty of the invention. This is often useful to identify documents that might otherwise be missed without the re-written abstracts. In addition to the re-written abstracts, the DWPI file has coverage extending to 1963 for pharmaceuticals. Documents identified in Thomson Innovation were uploaded into Patbase for further review. The platform used for reviewing documents was Patbase due to its advanced highlighting features. Search queries 98 and 100 are the collection of documents identified in Thomson Innovation. Search queries 99 and 101 were identifying documents unique to the Thomson results and reviewed.

Search queries 102 and 103 were prepared based on similar search queries in Thomson Innovation to ensure complete coverage.

Lexis Nexis Total Patent was the fourth search platform used. Total Patent has several advantages as being used as a peripheral search tool, as its coverage includes all major as

well as many smaller patenting authorities. The search was conducted in the following patenting authorities: US, EP, WO, JP, DE, FR, GB, CA, CN, RU, AT, AU, BE, BR, CH, DD, DK, EA, ES, FI, IE, IN, IT, LU, MC, MX, NL, PT, SE, SU, AP, AR, BA, BG, BN, BO, BY, CL, CO, CR, CS, CU, CY, CZ, DO, DZ, EC, EE, EG, GC, GR, GT, HK, HN, HR, HU, ID, IL, IS, KE, KR, KZ, LB, LT, LV, MA, MD, MN, MT, MW, MY, NI, NO, NZ, OA, PA, PE, PH, PL, PY, RO, SG, SI, SK, SM, SV, TH, TJ, TR, TT, TW, UA, UY, UZ, VE, VN, YU, ZA, ZM, and ZW. A second significant advantage of using Total Patent for chemical searching is because it allows left hand truncation which enables searching for key structural aspects of RIT. For example, RIT contains a four carbon section attached to nitrogen. Searching for butanamido alone will not identify many relevant documents. The description of this key segment of RIT is included in the middle for common chemical nomenclature. Using left hand truncation can help identify documents describing specific chemical structures that may not be found using text-based searching in many search platforms. Documents identified using Total Patent were then uploaded to Patbase for further review (query 104). Search query 105 was used to separate documents already reviewed from new documents identified with Total Patent. These documents were reviewed and search queries 106 and 107 represent citation searches of documents in query 105.

The remaining search queries were based on a similar strategy as previously described. United States Patent Classification (USPC) classification codes were used to identify aspects related to the chemical structure. The classification queries were then narrowed to documents specifically related to treating or prevent viral diseases.

After the collection of all relevant documents the searching portion of the report was completed. The documents were sorted as they were collected into broad categories including pharmaceutical compositions, methods for treating, detecting or screening HIV, synthesis of RIT or its salts or polymorphs, RIT derivatives, screening for drug resistance, coated implant materials or delivery devices, and combinations containing RIT. These broad categories were then further sorted to begin developing key innovation tracks.

This section describes the methodology for retrieving and reviewing all documents related to Ritonavir. This report was prepared using several sophisticated subscription-based databases described above. These databases were useful for efficiently reviewing thousands of documents. Because patent applications and grants are public knowledge this methodology could be performed using any of the publicly-available databases. Several publically-available databases including Patentscope, Espacenet, E.A.S.T. at the U.S. Patent & Trademark Office Public Search Room and Google Patent could have been used to perform the search. The same results as presented in this report could be obtained from the many publically-available databases. The user would need to familiarize themselves with the search command language and allowable operators. For example, when using Google Patent the word “And” does not need to be used because it is automatically placed between adjacent words when the search is performed. A second example for using Google Patent includes using the “~” operator to find synonyms for retroviral. When searching for ~retroviral other synonyms including retrovirus and retroviruses would also be found.

Section 3 - Statistical Analysis

3.1 Introduction

This section provides statistical analysis for all documents identified during the landscape. Documents used in the statistical analysis are located in the corresponding patent database annexed to this report. The statistical analysis includes: total number of families, patents and average family size; patenting and filing activity over time; total families per major classification codes; percentage of families with a PCT family member and percent of families with a PCT family member over time; distribution of families based on priority countries over time; geographic distribution of patent family members; most common assignees and inventors.

3.2 Results

Total number of Ritonavir patent families	**805**
Total INPADOC patents & applications	9,570
Average INPADOC Family Size	11.8 patents or applications/family

In total, 805 INPADOC patent families were identified as claiming Ritonavir. These 805 patent families include 9,570 total granted patents or published applications in those families. The definition for an INPADOC patent family can be found in Appendix 2. An Excel database with all 805 relevant patent families is available separately to this report for download. For a short description of this database see Appendix 3.

Figure 1 below describes patenting activity over time . The graph presents the number of patent families (Y axis) over the earliest filing (priority) year (X axis). This year was chosen rather than the publication year, as this is more indicative of patenting activities since they are less dependent on the varying publication policies and docket backlogs of patent offices. The graph shows a large increase in filings up to 1999, and then a second spike up to 2006. The reduction after 2006 may be attributed to typical lags between a first earliest priority filing, often in the form of a provisional application and the first published application of the patent or application depending from that earliest filing. Additionally, this lag may be due to the maturity of the Ritonavir market and possibly the worldwide economic recession. This reduction was another general trend for patent publications in other areas of technology.

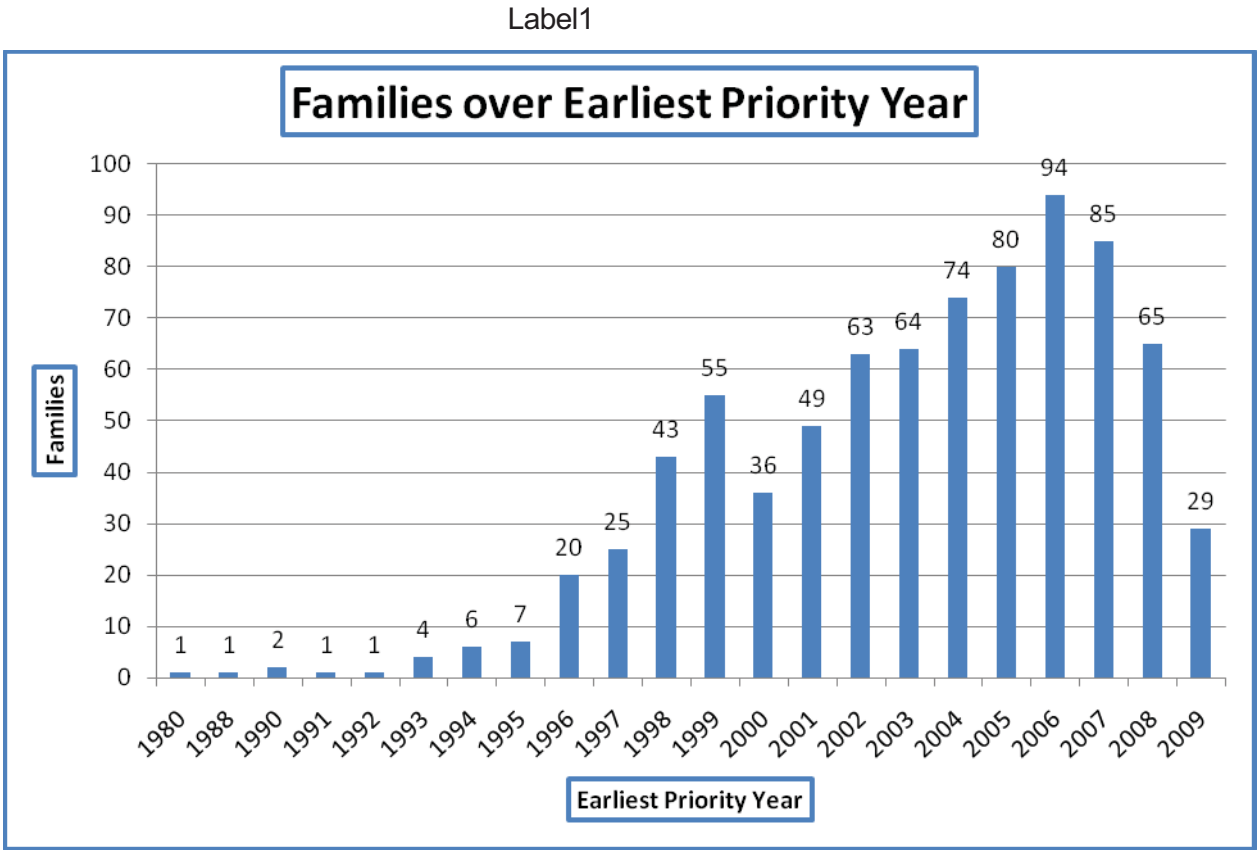


Figure 1: Patenting Activity - Patent Families over Earliest Filing Year (Priority Year)

Figure 2 shows that the overall patent filing trend from the first filing in 1993 has resulted in 45% of patent families receiving at least one granted patent. The breakdown of patent families with grants is shown priority year in Figure 3. Granted patents were identified by reviewing the kind codes for documents in each family manually one by one. For example, publications of the European Patent Office having a "B" kind code are published patents, whereas publications having a "A1, A2, A3" kind code are applications[3]. Each patenting authority has its own kind code system. Families containing granted family members do not necessarily mean that a patent has entered into force at all or is still valid. Granted patents may not be in force for several reasons including that the patent is expired, fees have not been paid, or that it did not survive opposition or revocation procedures.

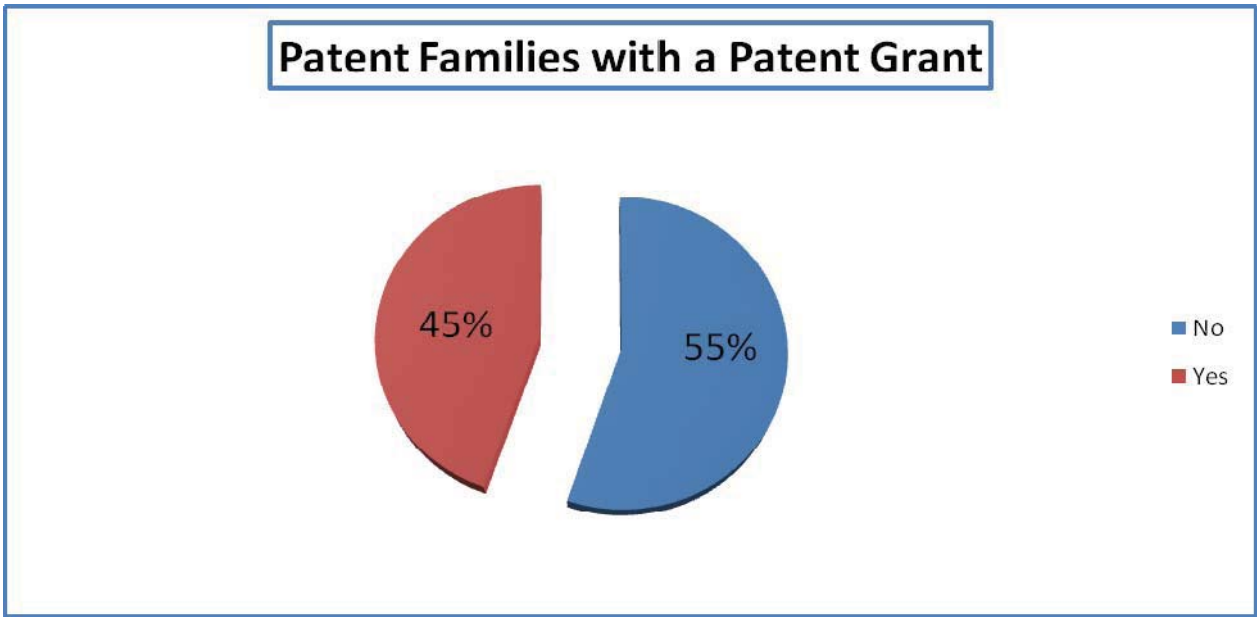


Figure 2: Patent Families with a Patent Grant

[3] See, e.g., the "kind code concordance list" on http://www.epo.org/searching/essentials/data/tables.html; or the respective WIPO Standard ST.16 (http://www.wipo.int/standards/en/pdf/03-16-01.pdf)

Figure 3 further describes patent activity over time similar to Figure 1 but in more detail: The count of families of each publication year is split into two fractions according to whether families included at least one granted patent as family member (at the time the data for the present report were researched (August 1, 2011) through data representing the earliest filing date (in years) for families. The graph presents the number of patent families file per year (Y axis) over earliest priority year (X axis). The yellow bars (bottom bars) represent the fraction of families that do not have a patent granted. The blue bars (top bars) represent the fraction of families that do have at least one patent grant within the family.

The small fraction of grants in younger families reflects the pendency of patent applications, i.e. the time between the filing of an application and the grant of a patent which varies from patent office to patent office and can last for several years. For these families examination may still be pending or may not have been requested yet.

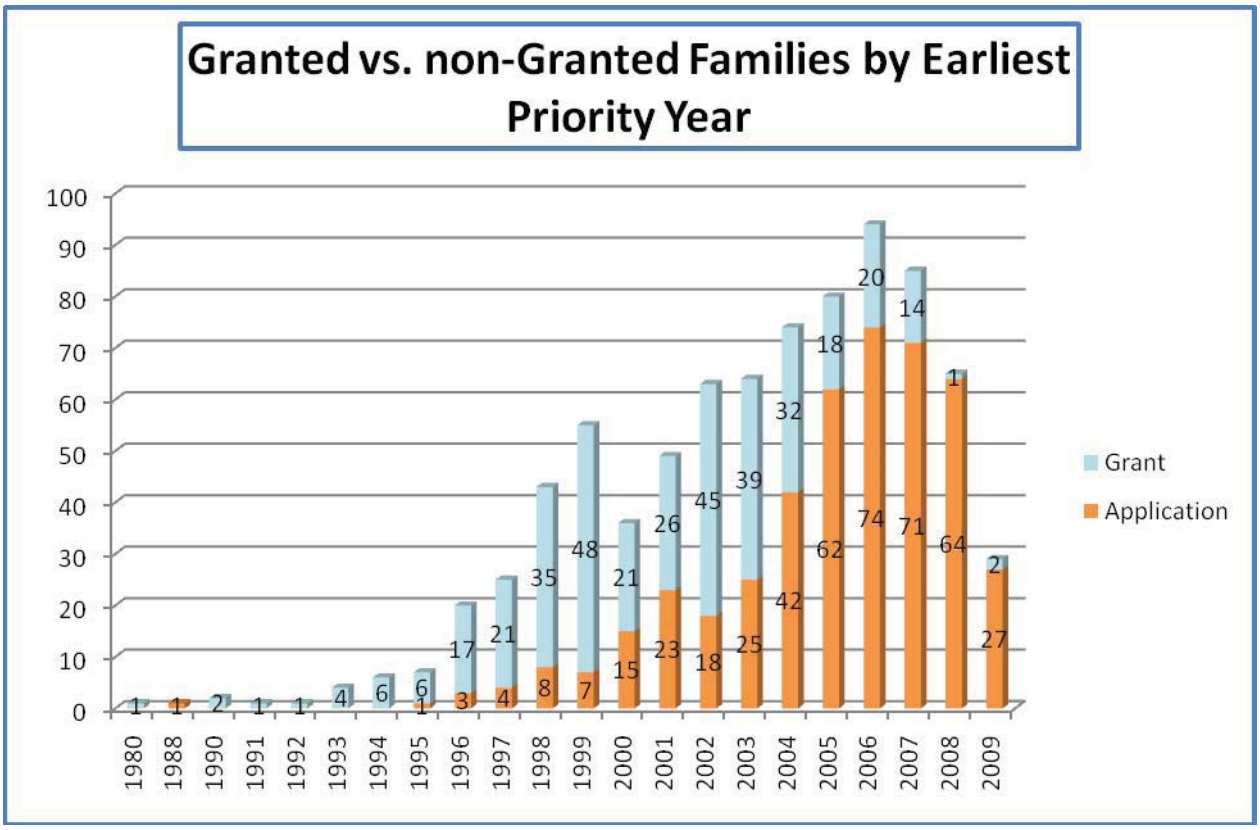


Figure 3: Patent Families per Earliest Filing (Priority) Year with and without Grants

Figures 4 and 5 show the most common ECLA and IPC subclasses for total patent families. At this level of hierarchy ECLA and IPC subclasses are identical; however both of these classifications are indexed in the Minesoft Patbase database and Espacenet. It is interesting to note the different number of documents classified for each ECLA and IPC subclass. All patent documents have to be classified according to the IPC by the publishing patent office while ECLA codes are alloted to documents by the examiners of the European Patent Office (EPO) upon the search of an EPO application or the incorporation of non-EPO publications in the EPO patent database. An ECLA classification may therefore not be available for a given document or it may be different from the IPC classification alloted by the publishing patent office. The statistical analysis tools in Patbase were used to count these major classifications by importing the database into Patbase.

IPC stands for the International Patent Classification and is administered by the World Intellectual Property Organization (WIPO). The scheme was conceived as an indexing system to organize patent documents from around the world based on the technical field of the invention, thereby providing a retrieval system by subject matter, independent of keyword searching. ECLA stands for European Classification, and was designed in-house by the European Patent Office as an enhancement to the IPC classification system. The IPC and ECLA classifications are useful and provide added value because they are assigned by highly skilled personnel. As the body of patent literature expands, the number of documents classified in IPC groups naturally grows. Because a group that still contains thousands of documents hinders the ultimate purpose of a classification scheme, ECLA groups are defined to split these large IPC groups into even smaller divisions, and therefore have narrower group definitions. More information about IPC and ECLA classifications can be found at the following web-based resources:

IPC: http://www.wipo.int/classifications/ipc/en/

ECLA: http://www.epo.org/searching/essentials/classification/ecla.html

Comparative descriptions of the ECLA and IPC as well as other classification systems can be found at

http://www.intellogist.com

The subclasses have been limited to classification codes found on more than 10 families. A majority of documents were classified in two major sections, A- Human Necessities and C- Chemistry. Documents present in the G section (Physics) are representative of documents describing methods of testing, analyzing, and quantifying Ritonavir pharmacological activity and HIV/AIDS patients receiving Ritonavir.

ECLA Subclass	Subclass Title	Count
A61K	Preparations for medical, dental, or toilet purposes	412
C07D	Heterocyclic compounds	226
C07K	Peptides	41
C07C	Acyclic or carbocyclic compounds	25
G01N	Investigating or analysing materials by determining their chemical or physical properties	19
C12Q	Measuring or testing processes involving enzymes or micro-organisms (immunoassay G01N 33/53); compositions or test papers therefore; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes	15

Figures 4: Common ECLA Classification Codes

IPC Sub-class	Subclass Title	Count
A61K	Preparations for medical, dental, or toilet purposes	431
C07D	Heterocyclic compounds	168
A61P	Specific therapeutic activity of chemical compounds or medicinal preparations	36
C07K	Peptides	23
G01N	Investigating or analysing materials by determining their chemical or physical properties	22
C12Q	Measuring or testing processes involving enzymes or micro-organisms (immunoassay G01N 33/53); compositions or test papers therefor; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes	21
A01N	Preservation of bodies of humans or animals or plants or parts thereof	21
C12N	Micro-organisms or enzymes; compositions thereof	17
C07C	Acyclic or carbocyclic compounds	16

Figure 5: Most Common IPC Classification Codes.

Figure 6 illustrates the percentage of patent families with a PCT family member. 90% of all families identified during the data collection contain a PCT family member.

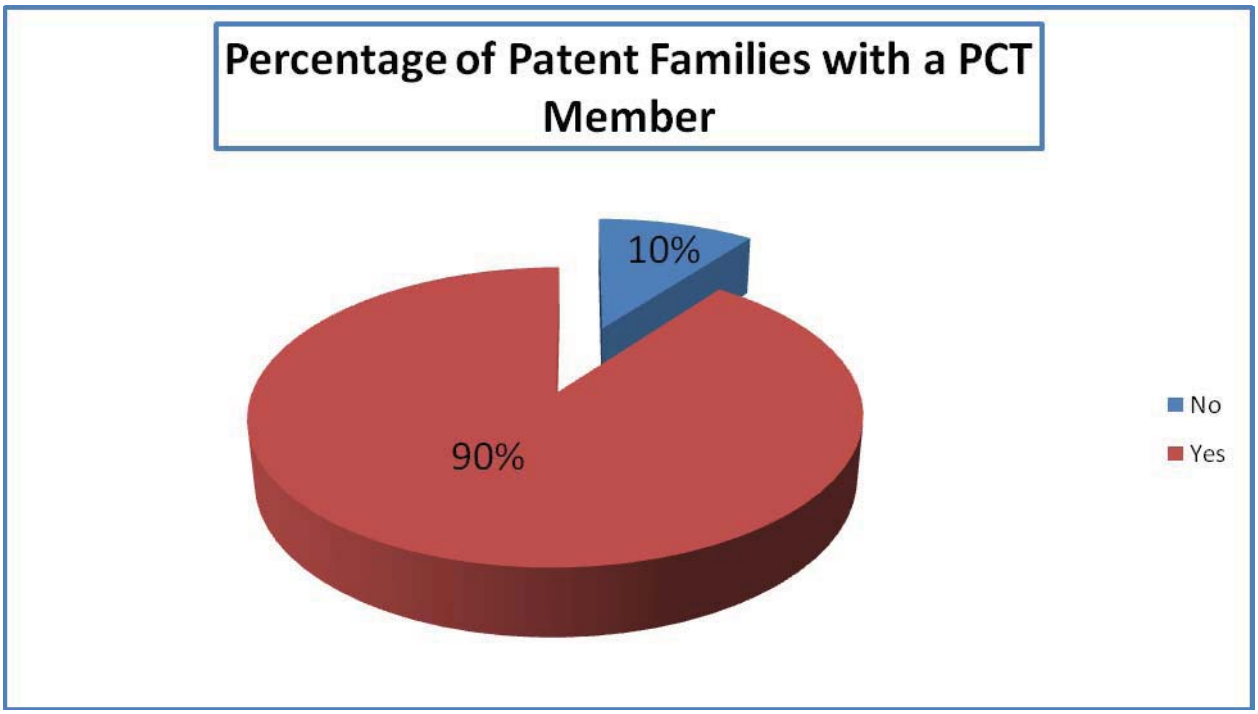


Figure 6: Percent of Families with a PCT Application

Figure 7 shows the percentage of patent families with a PCT family member per earliest priority year of the family. This information is also shown in the second from the right column in Figure 8.

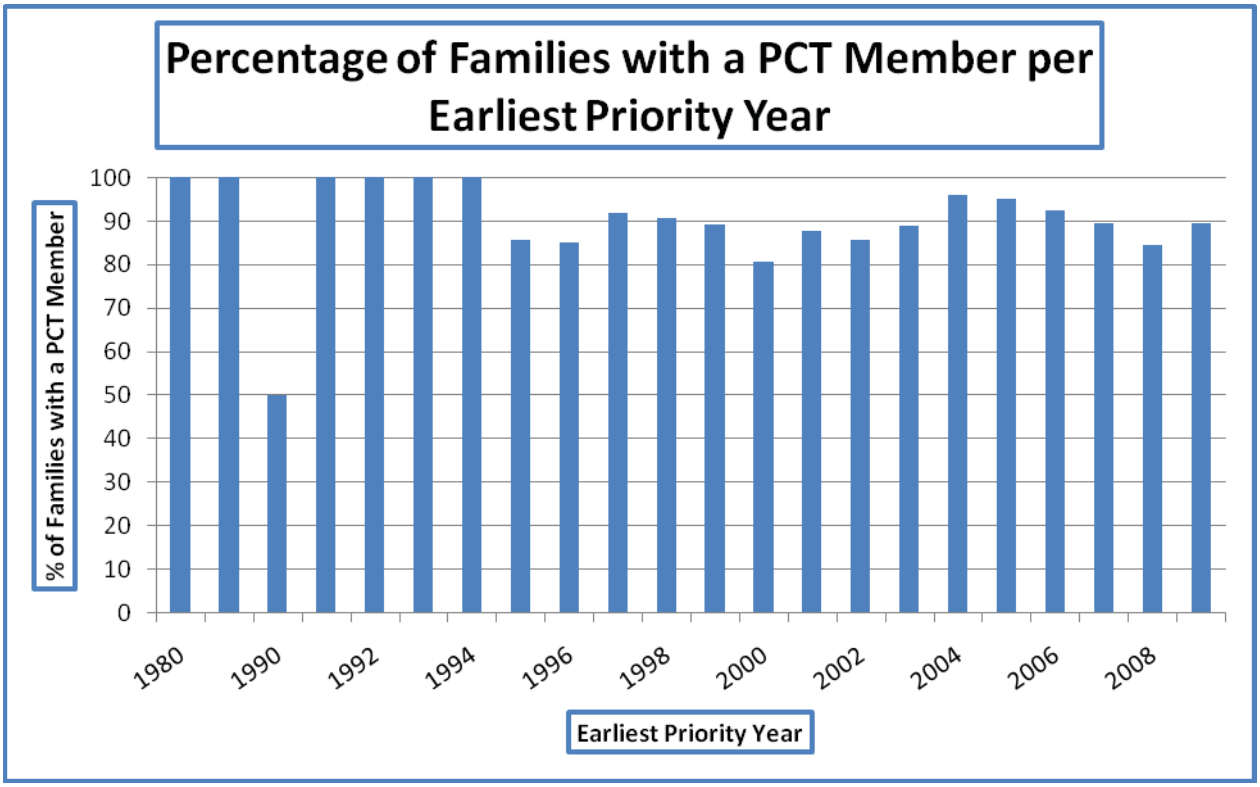


Figure 7: Percentage of total families with a PCT Application per Priority Year

Figure 8 shows the distribution of families over priority countries for each earliest priority year per family. The table was limited to priority countries with three (3) or more documents. The table shows that 611 of the families in the study out of the total 805 families claim priority to United States as the office of first filing (76%) followed by 6% claiming priority to European Patent Office as the office of first filing. This table also shows there are 10 patent families where the office of first filing was WO. The grand total column also indicates countries that are the priority countries but were not included in the chart. These are designated by an asterisk * and listed in parentheses ( ).

Priority Year	AU	BR	CN	DE	DK	EP	FR	GB	IE	IN	IT	JP	SE	US	WO	Families with PCT (%)	Grand To
1980														1		100	1
1988														1		100	1
1990												1		1		50	2
1991														1		100	1
1992														1		100	1
1993														4		100	4
1994												1		5		100	5
1995				1				1						5		86	7
1996						1	1					3		14		85	20*(CH
1997				1				1				1		21		92	25*(HU
1998							2	4			1	1	1	33	1	91	43
1999	1					2					2	6	1	41		89	55* (CA, NL
2000								1	1			2		31		81	36* (IL
2001			1	3		3		2	1		1	3		34		88	49*(KR
2002	1	1		1		3	2			4		1		48		86	63* (KR,
2003	1	1	1	1	2	3	1	1						51		89	64*(CA
2004	1	1	2	1	1	5	2	2		2		1	1	53	1	96	74* (AR)
2005	1			3	2	14			1	7				49	3	95	80*(AU
2006				2		6	2	1	1	5		1	1	72	1	93	94* (KR, RU,
2007		1	1	2	1	2	1			4		1		64	3	89	85*(ES
2008		1	2			2		1		3				52	1	85	65*(ES
2009							1			2				26		90	29
Grand Total	5	5	7	15	6	40	12	14	4	27	4	22	3	611	10	90	**785***

Figure 8: Distribution of Patent Families Priority Country per Earliest Priority Year

Figures 9 and 10 show the geographic distribution of patent family members for offices of first filing. Figure 9 shows the geographic distribution for the office of first filing (OFF) as a pie chart representing offices with more than one family having first priority in that office. Figure 10 shows the raw counts for all families including those only claiming priority once to that authority.

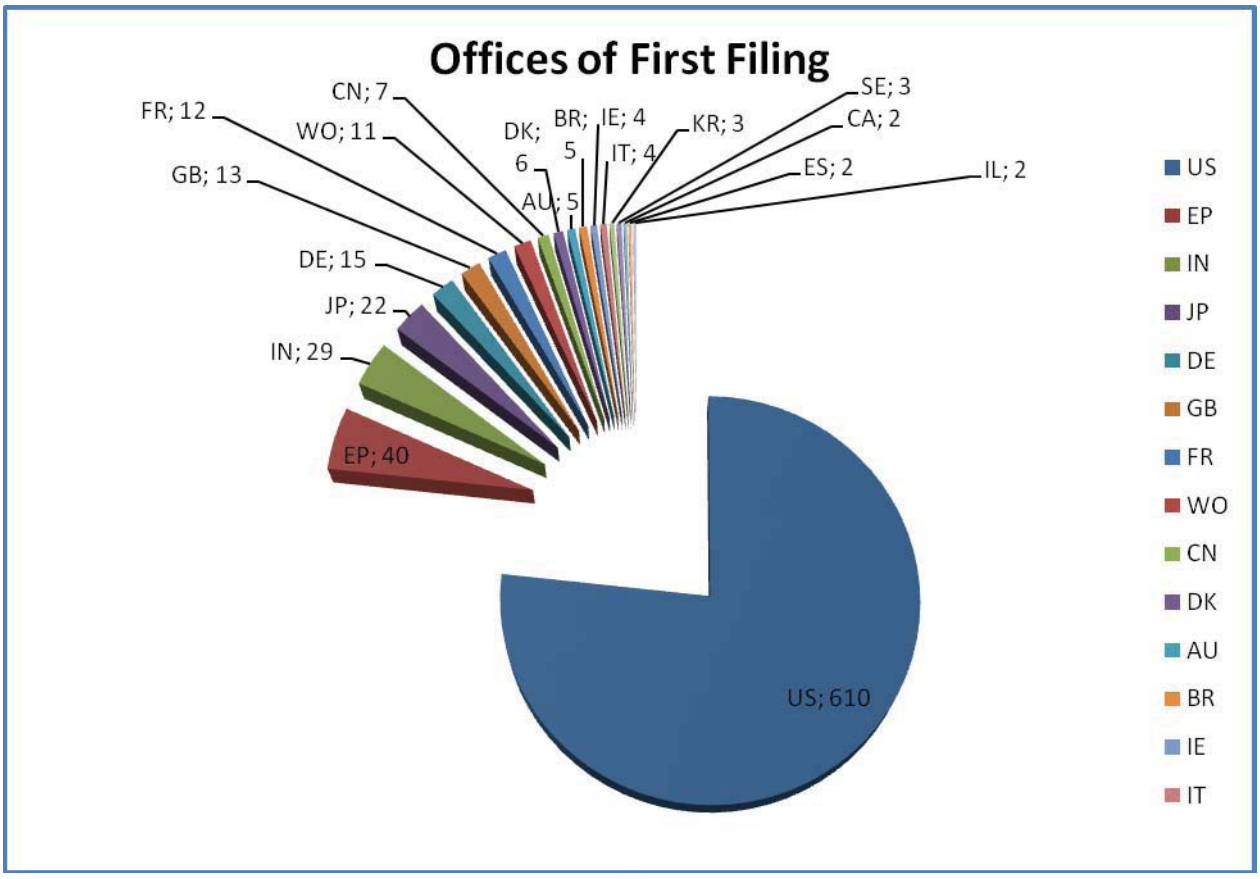


Figure 9: Distribution of Patent Families by Office of First Filing

Patent Authority	Number of Instances of First Priority
US	610
EP	40
IN	29
JP	22
DE	15
GB	13
FR	12
WO	11
CN	7
DK	6
BR	5
AU	5
IT	4
IE	4
KR	3
SE	3
ES	2
IL	2
CA	2
CH	1
AT	1
DK & US	1
AR	1
UK	1
HU	1
ZA	1
NL	1
RU	1
GB & US	1

Figure 10: Total Counts for Offices of First Filing.

Figures 11a and 11b show the geographic distribution of extensions of an application to other jurisdictions, i.e. for each office of second filing (OSF) included in this bar chart, the bar indicates the share of families having at least one family member filed with the respective OSF (in relation to the total of 805 patent families). There were a total of 5,257 instances of second priority claims. Figure 11a shows that WIPO is chosen as the most often OSF by applicants to file subsequent members of the same family. This is not surprising given that WIPO is the authority in which applicants pursue the PCT route. Australia, Canada, the European Patent Office and Japan are also chosen in approximately 50-60% of the families as an OSF. China is the next most often choice as an OSF. This information is useful to gain an understanding about which countries are receiving the most patenting activity. Figure 12 on the next page shows the total instances of second priority. In relation to both Figures 11 and 12, only the first publication of each OSF was counted. Subsequent publications belonging to the same family were ignored for the purposes of counting the times each authority appeared per family.

When interpreting the data, it should be taken into account that there is a certain overlap between counts for a regional office as OSF and the counts of its member offices. For example, some of the counts for Germany (DE) as OSF are related to publications that are derived from applications filed with the EPO (e.g. such with kind code T2). On the other hand, there may be applications that have been filed directly with DE as OSF and not at all with the EPO. Such applications would have to be added to the number of applications filed with the EPO in order to determine the true number of applications with a foreign priority that seek patent protection in Germany. However, the statistics of OSF in Figure 11 of the present report has not undertaken to discriminate further between family members attributable to a particular country as such and the regional office to which it adheres.

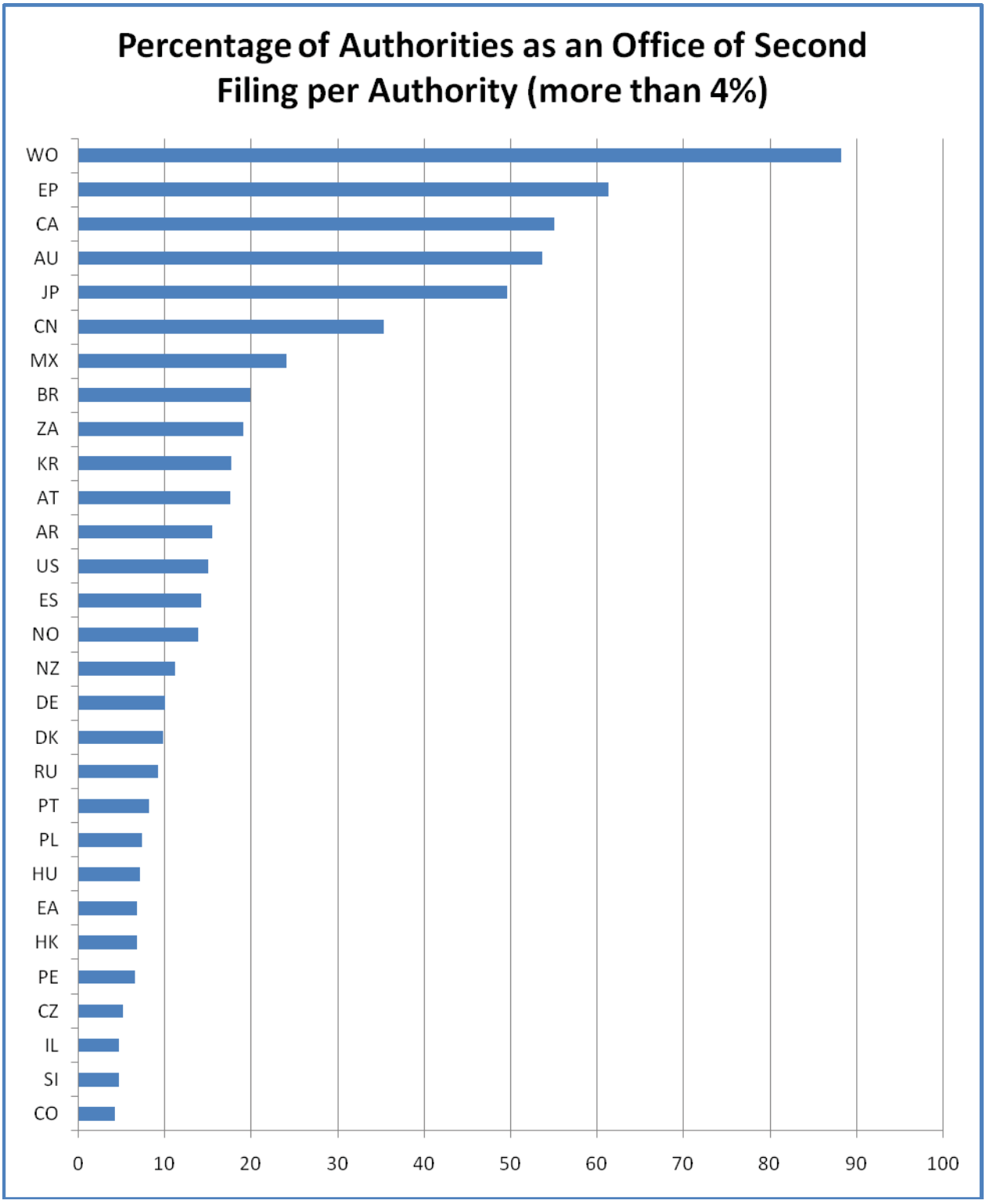


Figure 11a: Geographic distribution of extensions: percentage of families having at least one family member filed with OSF (more than 4%)

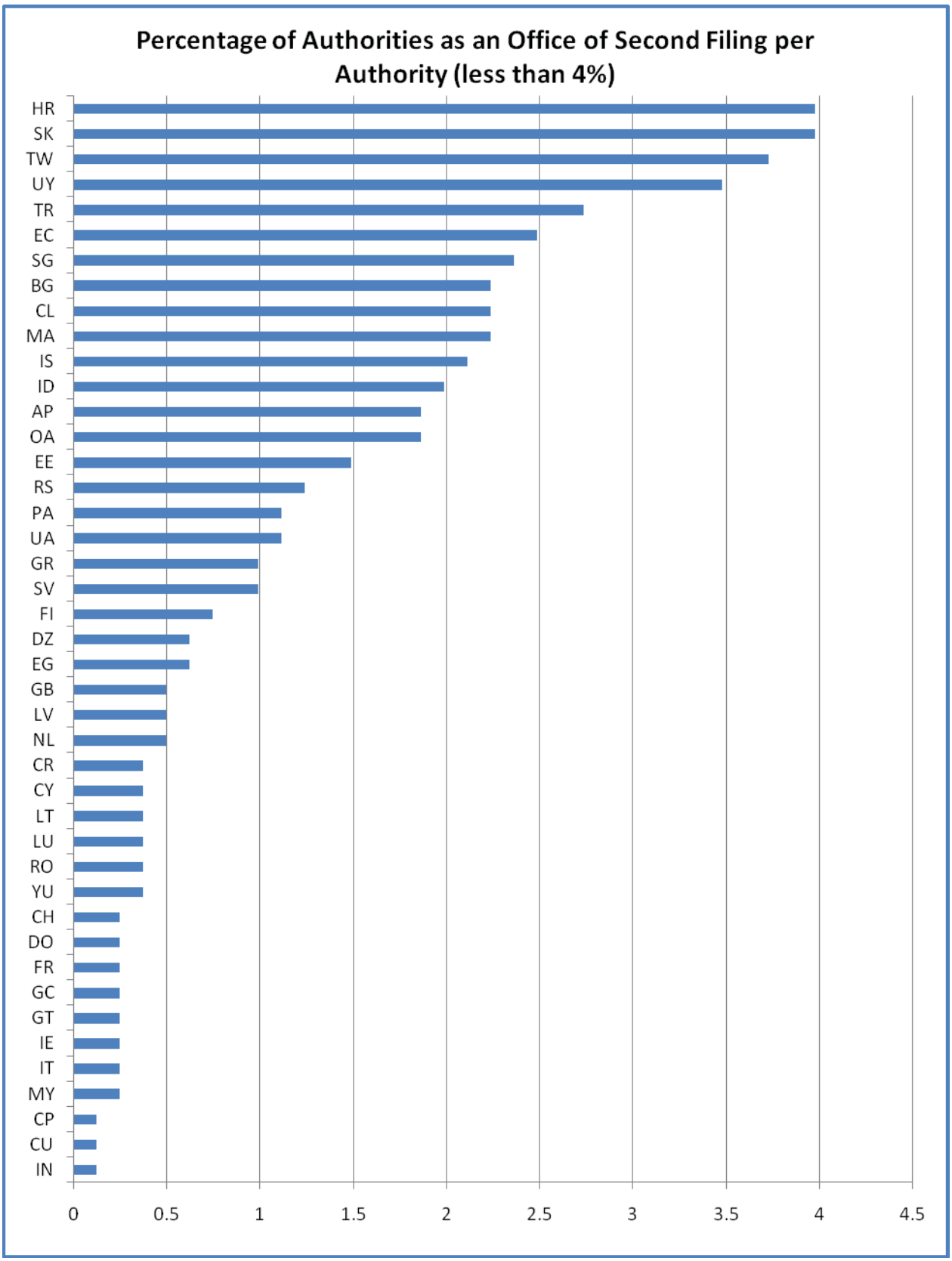


Figure 11b: Geographic distribution of extensions: percentage of families having at least one family member filed with OSF (less than 4%)

Patent Authority	Number of Instances of Second Priority	Patent Authority	Number of Instances of Second Priority
WO	710	BG	18
EP	494	CL	18
CA	443	MA	18
AU	432	IS	17
JP	399	ID	16
CN	284	AP	15
MX	194	OA	15
BR	160	EE	12
ZA	153	RS	10
KR	142	UA	9
AT	141	PA	9
AR	124	SV	8
US	121	GR	8
ES	114	FI	6
NO	111	DZ	5
NZ	90	EG	5
DE	80	NL	4
DK	79	LV	4
RU	74	GB	4
PT	65	CR	3
PL	59	LU	3
HU	57	LT	3
HK	54	CY	3
EA	54	YU	3
PE	52	RO	3
CZ	41	GT	2
SI	37	FR	2
IL	37	CH	2
CO	34	IT	2
SK	32	GC	2
HR	32	MY	2
TW	30	DO	2
UY	28	IE	2
TR	22	IN	1
EC	20	CU	1
SG	19	CP	1

Figure 12: Total Counts for Offices of Second Filing.

Figure 13 shows the most common assignees (those with more than 5 patent families). Abbott Laboratories is assigned the most documents of any assignee. Abbott was the first company to disclose Ritonavir and still continues to actively patent in a variety of areas related to Ritonavir. The focus of most recent filings has been in combinatorial formulations containing Ritonavir as a secondary protease inhibitor. All of these assignees are large chemical or pharmaceutical corporations. These companies actively patent in a wide range of areas related to drug discovery, chemical synthesis, pharmaceutical dosage forms and analytical methods. The most common assignees were counted from a review of the most recent legal status in Espacenet. Some documents with U.S. family members include confirmatory licenses to U.S. government institutions, such as the National Institutes of Health (NIH) via the Secretary for the Department of Health and Human Services. The assignees in this case were counted as the company which granted the confirmatory license. NIH was an assignee on 5 families within the study, showing that governments continue to be a significant presence within the area of HIV anti-retroviral innovation.

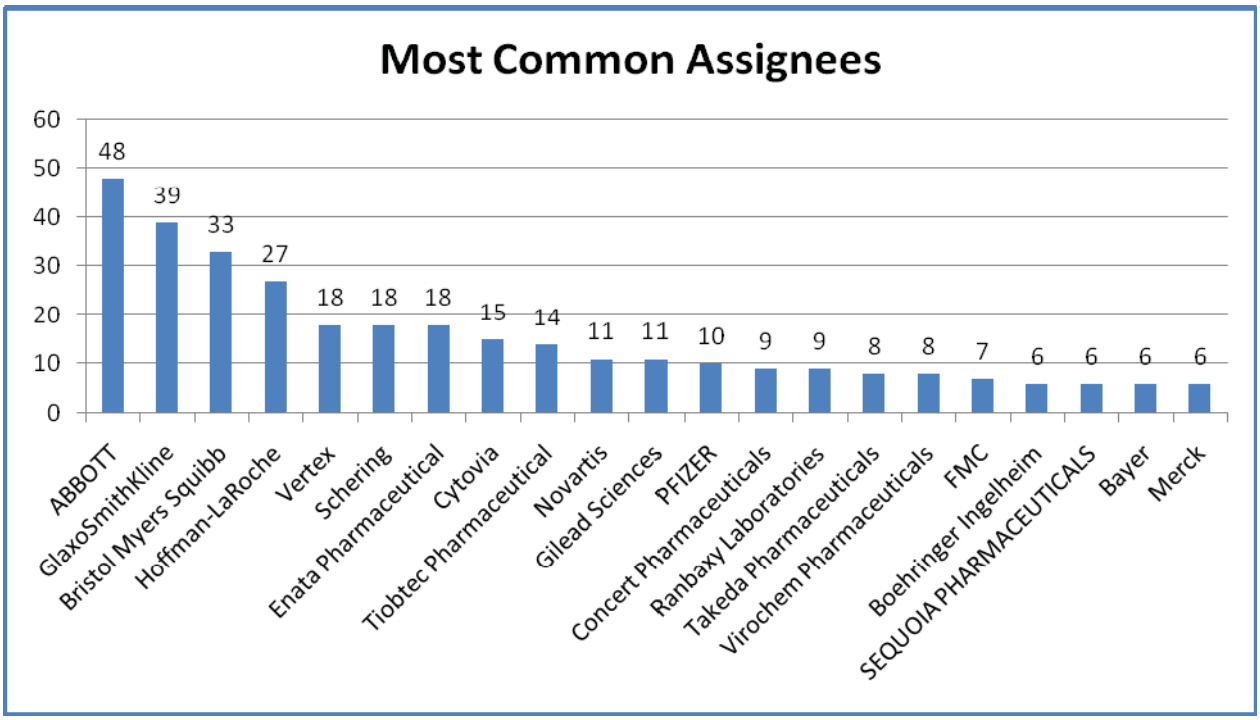


Figure 13: Most Common Assignees

Figure 14 shows the most common inventors and their associated assignee for inventors that appeared on more than 8 patent families. A major reason why Abbott Laboratories doesn't have the most common assignees is because of the large number of inventors often present on their patents and applications. Several of the top inventors listed below are associated with large pharmaceutical companies responsible for patenting formulations containing novel antiviral compounds and Ritonavir as a secondary protease inhibitor.

Common Inventors	Assignee	Count of Inventor
Or, Yat, Sun	Ranbaxy, Enanta	18
Cai, Sui Xiong	Cytovia	13
Kempf, Dale J.	Abbott	13
Zhe, Wang	Enanta	12
De Kock, Herman Augustinus	Tibotec	11
Sirisoma, Nilantha Sudath	Cytovia	10
Gudmundsson, Kristjan	GSK	10
Sweeney, Zachary Kevin	Hoffman-LaRoche	10
Seepersaud, Mohindra	Novartis	9
Aquino, Christopher, Joseph	GSK	9
Simmen, Kenneth Alan	Tibotec	9
Raboisson, Pierre Jean Marie Bernard	Tibotec Pharm	9
Raman, Prakash	Novartis	9
Kazmierski, Wielsaw Mieczyslaw	GSK	9
Grand Total		**138**

Figure 14: Most Common Inventors and Corresponding Assignees

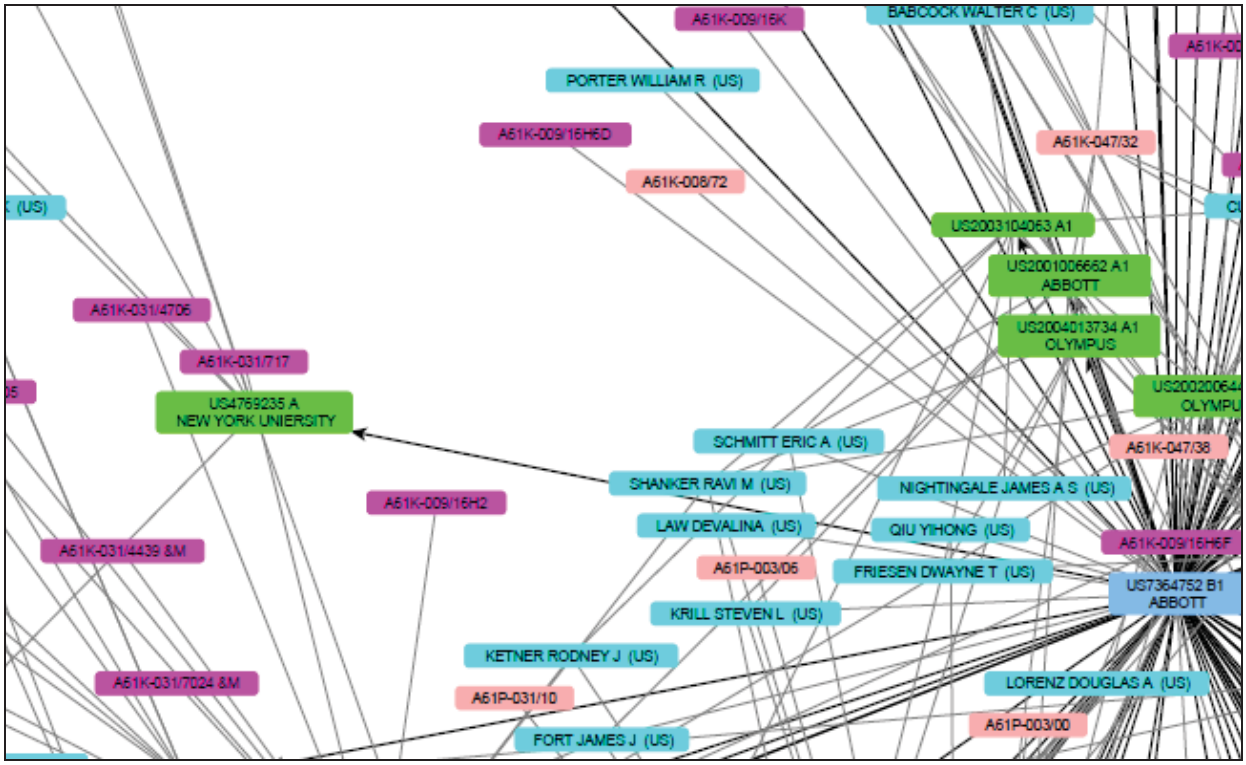
Section 4 - Analysis of Innovation Tracks and Patterns of Continued Protection

4.1 Introduction

4.1.1 Methodology for determining innovation tracks

This section is intended to analyze the interdependencies of different patent families described within each innovation track. Document retrieval aided in elucidating potential innovation tracks. During the document retrieval (phase 1) documents were placed in broad categories based on the claimed invention. These broad categories can be found in the accompanying excel database indicated by columns W, X, Y, Z, AA, and AB. The broad categories relate to the following topics: synthesis and crystalline forms; methods of treating HIV; pharmaceutical formulations; RIT derivatives; combination therapies; and stabilized forms. The broad categories can be reviewed in the attached database. More information about these categories can be found in Appendix 3. Documents contained in each broad category were then analyzed for the most common inventor, assignees, and classification codes and sorted by filing dates. This initial analysis allowed determination of which assignees were actively patenting in a particular technology area. Searches were then performed on these sub-groupings of documents for keywords in the claims related to an envisioned innovation track. The innovation tracks were started by reviewing documents citing the key Abbott patent. Citation analysis was performed using Intellixir in Questels Orbit to visually explore backward and forward citations of one or more INPADOC family member. This snapshot on the following page shows how Intellixir graphically represents citation mapping. The Dictionary section in the Appendices contains a link to an external website with more information about Intellixir.

This figure is a zoom-in view on several of the WO1994014436 citations. The colored lines represent various features including citations, related technical information, primary references, etc. Each reference node also is color coded to include backward citations (green boxes) and forward citations (blue boxes). Each node also contains complete bibliographic information on the INPADOC family. Each node can be selected to show its citations. The citation tool also allows the user to add citations to any node on the graph. When selected, the graph is reoriented to include any citation relationships between the original citation links and newly created citations. This tool was used extensively to investigate inventors and important classification codes related to the cited documents. This feature of Intellixir uses an “exploded” view to arrange the vast amount of information. The color scheme used in the “exploded” view is the same as the previous viewing. The additional information is also color coded so the authors appear as bright blue and ECLA and IPC codes appear magenta and peach, respectively. An example of a zoomed-in portion of the exploded view is shown below.



Intellixir was used in concert with similar citation tools in Minesoft Patbase. The claims of the cited documents were then reviewed to determine which independent claims overlapped with earlier filings and also determine the novel aspect of the invention. The claim analysis was performed manually because there are currently no tools available to compare the inter-relatedness of claims from different INPADOC families.

At this stage the documents identified from the keyword searching were manually reviewed with the results from the citation tools. This comparison helped identify the citation relationship between documents selected during these two steps. Documents that appeared to be particularly interesting, i.e. very broad claim language about liquid oral dosage forms containing Ritonavir, then had their priority data and US file histories reviewed. The US file histories are an important resource because they contain correspondence between the assignee and the examiner reviewing the case. These communications often include non-final rejections which help confirm the novelty of a particular invention. US file histories can be reviewed for any patent application or granted patent at the USPTO website using the following link: http://portal.uspto.gov/external/portal/pair. This website is publically available.

The outcome of these analyses was used to build the following innovation tracks. The innovation tracks are not meant to be static representations. Each innovation track had a select few number of representative documents to illustrate the complex nature of interdependent patent families. The innovation tracks also do not necessarily represent developments in terms of the product being commercialized. As is common in many areas of patenting, including pharmaceuticals, several patents can protect a commercialized product. Determining whether specific patents or innovation tracks have been commercialized is outside the scope of the current report. However, the United States FDA Orange Book listing provides a listing of patents for drugs that have been approved for use by the FDA. These listings also

describe specific formulations and the patents protecting the formulation, for example a 750 mg solid oral tablet or a 500 mg liquid oral gel cap. More information about the FDA Orange Book can be found in the Appendix 2 of this report. A copy of each innovation track is also included in Appendix 1, appended to the document.

4.1.2 Brief description of innovation tracks

Four (4) innovation tracks were explored. The innovation tracks were selected based on their implications to future patent protection of compositions that contain methods of manufacture, and structural characterization of Ritonavir. These characterizations are important considerations, for example, in regard to developing countries with high incidents of HIV/AIDS infections that are interested in domestic generic manufacturing.

The four innovation tracks include:

1) Liquid Oral Dosage Forms

2) Synthesis of Ritonavir and its Key Intermediates

3) Structural Considerations and Polymorphs

4) Solid Dosage Forms.

Each innovation track illustrates sequences of patents filed subsequent to the initial disclosure by Abbott Laboratories in PCT application WO1994014436. Each patent family is represented by a single family member. Each representative family member is located inside a rectangle containing the patent number, assignee, priority date, and a brief description of the novel invention. The representative family member was selected by reviewing the claims of family members. For family members with similar or identical claims, as in the case of an application and a granted patent, the selection was made with the preference to WO, then US, then EP documents.

The innovation tracks contain labels and color coordinated arrows to clearly illustrate the interdependence of different patent families. Definition of each arrow is summarized in the table below.

Colored Arrow	Represents
	Red arrows are used to indicate patent families with the same assignees and/or inventors.
	Green arrows are used to indicate patent families related by backward citations.
	Blue arrows are used to indicate documents with related application or priority data.
	Gold arrows are used to indicate granted patents.

Documents from the same assignee are often cited. For clarity the citation arrows are omitted when two documents share assignee and/or inventors and the relationship is only illustrated by a red arrow. Documents contained within purple boxes are present in more than

one innovation track. Documents included in multiple innovation tracks are considered important because of the broad claim language.

The innovation tracks show generational relationships with the first disclosure of Ritonavir in WO1994014436. Each generation is related to the following generation by means of citations, same inventors/assignees, priority documents, granted patents and/or classification codes. Each generation is easily identified in the graphic representation. The innovation tracks also include secondary references related to a generation and are described in the text and on the graph as “B” references for the purposes of this report. For example, a secondary document considered to be part of a second generation is labeled 2B. These secondary references have similar claimed inventions but do not advance the particular innovation track. These documents could be the part of another innovation track that is not continued. These references could be important in the future to expand into adjacent innovation tracks.

The first innovation track relates to interrelated patent families claiming liquid oral dosage forms and how the subsequent documents still protect the invention claimed in the first disclosure. There are a large number of patent documents describing liquid oral dosage formulations. As will be shown below, the patents and applications describe increasingly narrower formulations through the generations. The narrowed coverage over generations typically claims more specific solvent systems or encapsulation formulations. These documents still encompass the invention claimed in the first disclosure. This is an area that still has a large amount of potential for future filings to attempt to cover more specific solvent systems and methods of preparing the dosage forms. This innovation track is important because of the heat stability issues associated with solid dosage forms of Ritonavir. Liquid oral dosage forms were originally prepared and patented to correct heat stability issues with the solid dosage forms. However, there are very few documents claiming heat stability issues of Ritonavir as the reason for preparing liquid oral dosage forms.

The second innovation track is related to the synthesis of Ritonavir and its key intermediates. This innovation track outlines the interrelated patent families describing various synthetic pathways and key intermediates necessary for preparing Ritonavir. This technical area has limited potential for additional patent protection. The currently protected synthetic routes are well protected by a variety of large pharmaceutical companies and would require a large amount of R&D to devise novel methods of synthesis.

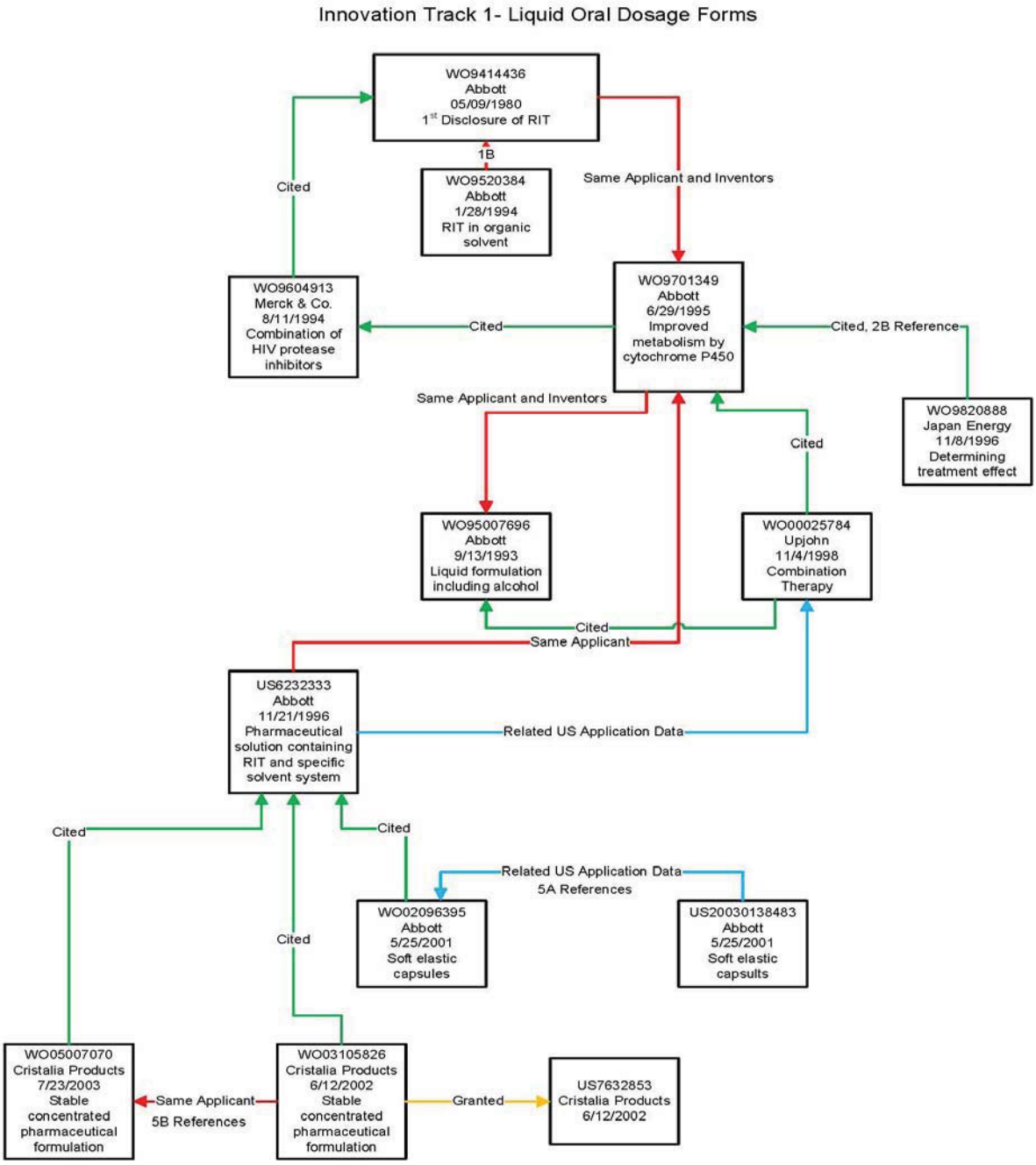
The third innovation track is related to the crystalline structure of Ritonavir. This is a particularly notable innovation track because the crystalline structure of Ritonavir has been found to be important to its therapeutic effectiveness. There has been a large amount of patent activity in the area of characterizing the various Ritonavir crystalline morphologies. The later generations in this innovation track begin to protect formulations with specific forms of Ritonavir. However, the non-active ingredients are still being claimed with very broad language (i.e. crystalline Ritonavir can be dissolved in a pharmaceutically acceptable solvent). Non-active ingredients are ingredients that are commonly present in pharmaceutical dosages that do not have medicinal effects. These non-active ingredients are also commonly referred to as excipients and include such substances as: pill binders, dextrose, pharmaceutically acceptable solvents, taste modifiers and other ingredients that are not intended to treat or prevent a disease or disorder.

The fourth innovation track focuses on solid dosage forms. This area has had the fewest number of filings in the past decade. Problems with producing a stable dosage form was slowed the filing in this area. However, due to the relatively few number of filings related to solid dosage forms, this remains an area that could potentially have increased filing activity in the future.

The innovation track related to the crystal structure is important because it has serious implications to both solid and liquid dosage forms. The combination of ideas of these innovation tracks could provide a potential area for future patent filing and protection.

4.2 Analysis of Innovation Tracks

4.2.1 Innovation track 1: Liquid Oral Dosage Forms*



*Description of colored arrows can be found in table 1 in section 4.1.2.

This innovation track was selected because of the large number of documents describing orally available liquid, gel, or suspension pharmaceuticals. Liquid oral dosage forms are im-

portant because of the thermal instability of Ritonavir. These documents do not claim thermal instability as a reason for preparing liquid oral dosage forms. Liquid dosage forms were determined to decrease the conformational polymorphism exhibited in early solid dosage formulations.

The first generation patent application WO1994014436, assigned to Abbott Laboratories, is the first disclosure of Ritonavir. The '436 document claims a broad Markush structure describing Ritonavir. This initial document only claims a retroviral protease inhibitor and does not describe formulations or intended uses. However, this document claims protection over a large number of potential compounds that are broadly defined by the Markush group. The broad definition of Markush groups is important for the inventor/assignee because compounds with similar chemical structure are very likely to have similar biological activity. The '436 document is heavily cited because it is the first disclosure of Ritonavir. This innovation track includes a document considered 1B reference. WO1995020384 (Abbott) describes a pharmaceutical solution comprising Ritonavir and a pharmaceutically acceptable organic solvent. This is the first disclosure of a liquid formulation including Ritonavir. This reference is important but does not continue in this innovation track and is therefore described as a 1B reference for this report.

Two documents considered second generation are WO1996004913 (Merck) and WO1997001349 (Abbott). WO1996004913 cites the '436 application and describes combinations of compounds including Ritonavir and a novel HIV protease inhibiting compound. This document is important in this innovation track because it broadly claims a formulation that includes a pharmaceutically acceptable carrier. This broad claim does not further limit the scope of the invention since it only includes a general formulation with unspecified dosage form. The second second-generation document is WO1997001349 (Abbott) that cites both the first generation patent and the '913 (Merck) document. The '349 document claims a more narrowly focused invention related to method of improving the pharmacokinetics of a drug, specifically Ritonavir. The independent claims again describe a combination of Ritonavir and another pharmaceutical agent in a composition (claim 21) comprising a pharmaceutical carrier without specifically describing delivery method. WO1998020888 (Japan Energy) is included as a 2B reference. This document describes an AIDS treatment using Ritonavir to elicit an immune system response. This document does not claim a formulation. '888 is considered 2B because it was published in 1998, one year after the '349 document, and because it does not have any subsequent generations of patents.

The third generation patents include WO1995007696 (Abbott) and WO2000025784 (Upjohn). The '696 patent is related to the '349 document by the applicant and describes one of the first liquid oral dosage forms. This document claims a pharmaceutical composition comprising a solution of Ritonavir and a pharmaceutically acceptable alcohol or a mixture of alcohol and a pharmaceutically acceptable organic solvent. In other independent claims Ritonavir is present in an alcoholic solvent system which includes a pharmaceutically acceptable acid. The specific alcohol and acids are not disclosed in any independent claims, but does narrow the scope of the invention considerably. The dependent claims describe additional ingredients and encapsulating the solution in a hard or soft elastic gelatin capsule. This encapsulation plays an important role in the stability of Ritonavir and is described further in subsequent generations. The second third generation patent '784 cites WO1997001349. The '784 document claims a method of increasing human blood levels of tipranavir by administering Ritonavir. This document does not specifically describe a phar-

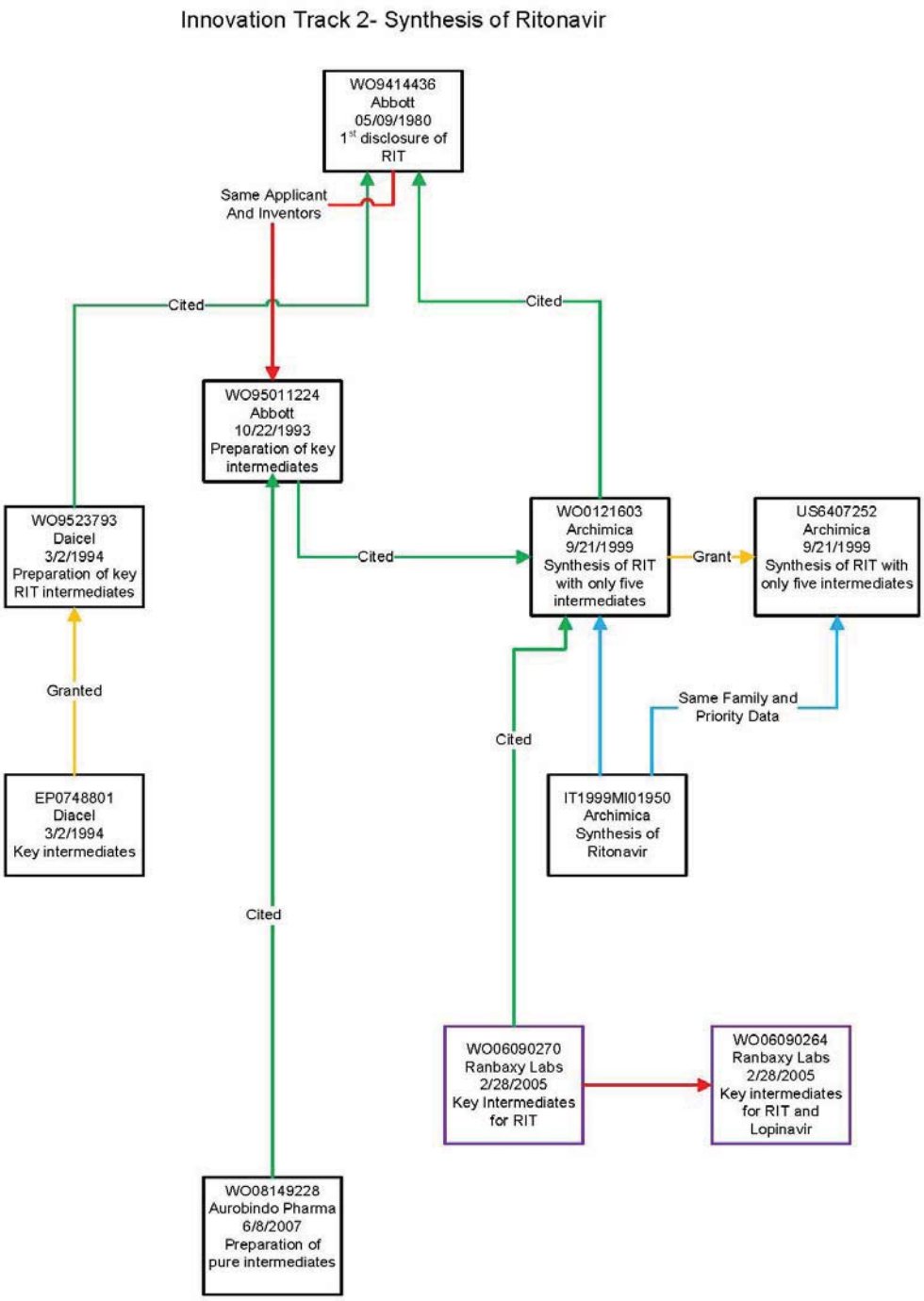
maceutical composition but does illustrate the importance of Ritonavir as a secondary medicament. This document reduces the coverage of the second generation ‘349 document.

The fourth generation patent US6232333 (Abbott) document is related by US application data to the ‘095 document. The ‘333 document claims an orally administrable composition comprising Ritonavir with a more specific solvent system. Ritonavir is dissolved in a pharmaceutically acceptable organic solvent comprising long chain fatty acids and an alcohol. The solvent system is further defined as mono-unsaturated and di-unsaturated C12 to C18 fatty acids. The solvent system is similar to the solvent system described in the third generation ‘696 patent with a narrower focus; thus including broader protection of the third generation document and the more specific definition outlined in the ‘333 patent.

The fifth generation is divided into 5a and 5b. The 5a references cite the ‘333 patent and are assigned to Abbott. Both 5a references WO2002096395 and US2003138483 describe soft elastic capsules having a fill and a shell material. The fill includes generic pharmaceutical agents in combination with alcohol and fatty acids. The shell is comprised of a gelatin and a plasticizing agent. These documents are focused primarily on the delivery device but are important because they further narrow the solvent system and delivery system described in the fourth generation US6232333 (Abbott) document. This type of patent is notable because its claims incorporate a novel elastic capsule, broadly described in earlier documents, and important pharmaceutical agents and solvent systems. A combination of various novel features of previous documents is an interesting workaround to patenting a similar formulation or process.

The fifth generation 5b documents are also related to the ‘333 document by citations. These documents WO2005007070 (Cristalia Products) and WO2003105826 (Cristalia Products) describe another example of a highly specified pharmaceutical composition. These documents claim Ritonavir with surfactants, an antioxidant, mixtures of specific alcoholic solvents, and mixtures of medium chain mono-diglycerides. These documents further define inventions claimed by Abbott Laboratories to attempt to gain patent coverage in the area of liquid oral dosage of HIV drugs. It is not difficult to envision these documents being cited by as yet-published patents further defining the solvent system and specific weight percentages of the active pharmaceutical ingredients.

4.2.2 Innovation track 2: Synthesis of Ritonavir*



*Description of colored arrows can be found in table 1 in section 4.1.2.

This innovation track was selected to illustrate the technical hurdles, which are present for developing nations to synthesize Ritonavir. The innovation track shows how the complexity

of preparing a compound reaches beyond simply licensing for the initial disclosure and synthesis strategies. One of the most important aspects that could easily be overlooked when trying to prepare a compound is access to key synthetic intermediates. Key intermediates are defined as a compound, which is produced in the course of a chemical synthesis, which is not itself the final product, but is used in further reactions to produce the final product. The key intermediates are compounds that are converted to Ritonavir through common chemistry synthetic routes. Often these intermediates that are critical precursor for preparing Ritonavir are under patent protection. The main key ingredient is the central portion of the molecule that is described as 1,6-diphenylhexane. Key intermediates are also important because they can often be used to prepare several Ritonavir analogs that are all described in the initial Abbott Laboratories patent application WO1994014436. This innovation track highlights several key intermediates required to prepare Ritonavir. Using current synthetic strategies Ritonavir could not efficiently be prepared without licensing of these key intermediates.

The first generation patent application WO1994014436, assigned to Abbott Laboratories, is the first disclosure of Ritonavir. The ‘436 document claims a broad Markush structure describing Ritonavir. This initial document only claims a retroviral protease inhibitor and does not describe possible synthetic strategies, methods or intermediates.

The second generation document is WO1995011224 (Abbott) and cites the ‘436 document. This document claims a synthesis of the Markush backbone for Ritonavir in the ‘436 document. While this intermediate is not claimed to be directly converted to Ritonavir it is still an important intermediate worth noting. Claiming synthesis of this backbone would also be important for protecting synthesis of Ritonavir analogs.

The third generation includes two patents WO1995023793 (Daicel) and WO2001021603 (Archimica/Clariant) and a 2B document US6407252 (Clariant). WO1995023793 describes novel synthetic methods to prepare the substituted 1,6-diaminohexane present as the backbone of Ritonavir. This document was published shortly after the key patent (WO1994014436) so this is not the only intermediate but it could be a very important document in the future for new methods of preparing Ritonavir or similar analogs. The ‘793 document and its granted EP0748801 both describe the same preparation of key intermediates. The second third-generation document is WO2001021603, and its granted patent US6407252 (2B). These documents describe a process to prepare Ritonavir using only five intermediate stages. This synthetic route is extremely efficient. The important advantage of this synthesis is that it uses the same starting materials as the first generation ‘436 document, but performs the synthesis with fewer reactants and materials making this a particularly attractive route because it is both environmentally and economically conservative. The claims are more restrictive than expected for a second generation synthesis, but due to the highly efficient method of preparing this severely limits other patents from preparing Ritonavir in a similar manner. IT999MI01950, which is located below the ‘603 and ‘252 documents is the priority document for this family from which the broader family members covering synthesis than the ‘252 document claim priority.

Please note PCT application WO1995023793 (Daicel) is included in the associated database; although the database only contains documents that specifically describe or are related to Ritonavir. However, this document is note-worthy in the context of this report, and

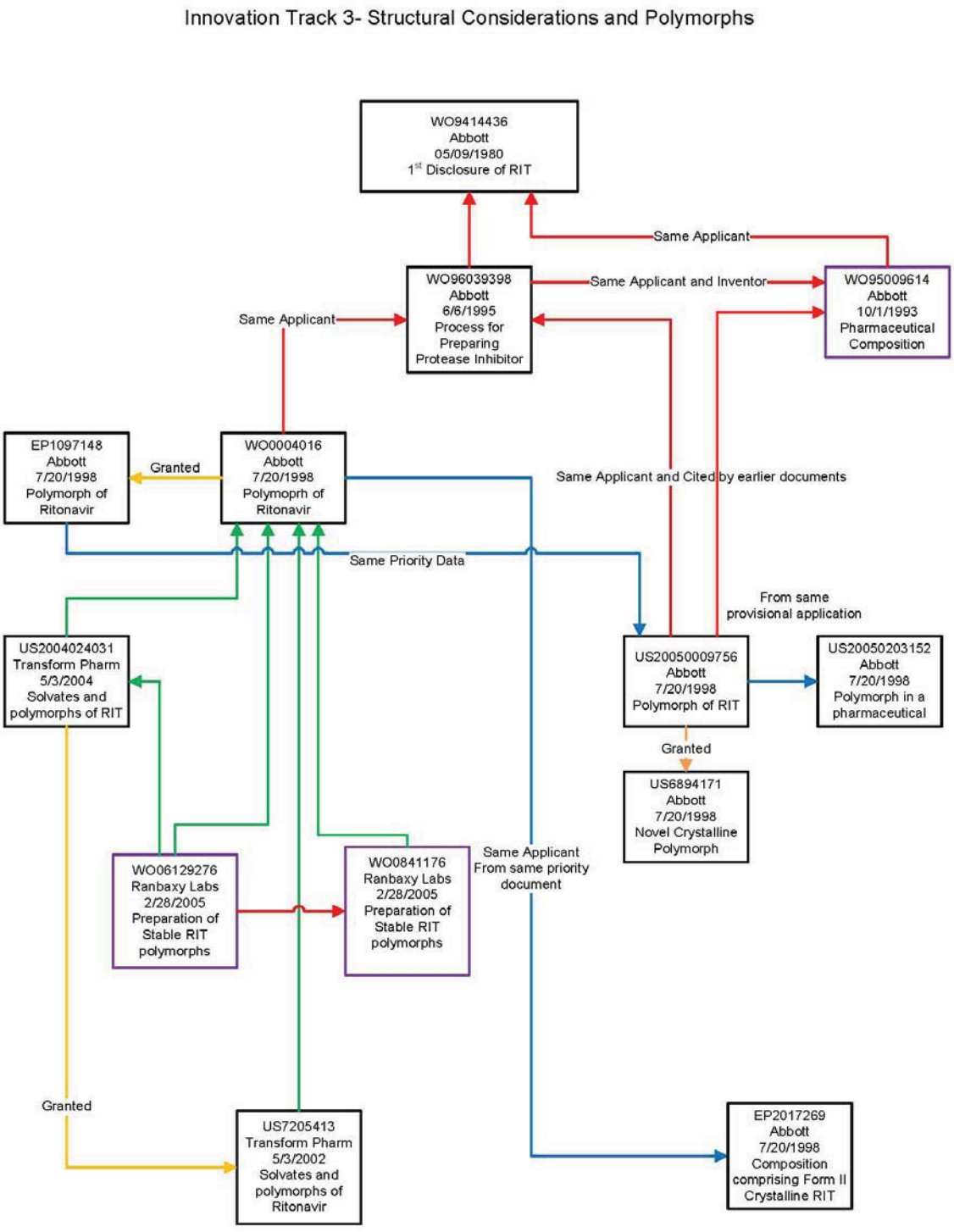
the Synthesis of Ritonavir Innovation track, because it is representative of patent protection related to key intermediates and products that are integral in preparing Ritonavir and its therapeutically analogous compounds. This document describes a substituted 1,6-diaminohexane compound and methods of its preparation which is the backbone of Ritonavir. The inventors do describe this compound as a key intermediate in the synthesis of medicines such as retrovirus protease inhibitors. However, the inventors do not specifically describe this compound being used as a precursor for Ritonavir.

The fourth generation includes two Ranbaxy Laboratories patents, WO2006090270 and WO2006090264. These documents both claim methods of synthesizing key intermediates useful for preparing both Ritonavir and Lopinavir. These intermediates are useful for preparing a wide range of antiviral drugs. The broad claim language describing the final synthetic product could be described as Ritonavir because the variables are broadly defined as acid labile amino protecting groups. The groups present in Ritonavir are essentially the acid-labile portions of the molecule that are removed when contacted with acid in the digestive tract. The synthetic strategy in both incorporates similar intermediates from the third generation '793 (Daicel) documents. However, the '270 and '264 documents provide more specific reaction conditions and describe more specific reactants used in the process. This generation of documents has potential for further growth as alternative methods of preparing Ritonavir as well as a whole class of related antiviral drugs. The claims only describe classes of reagents and not specific reagents or reaction conditions (time, temperature, solvents, etc) which could be further specified in future patents.

The fifth generation is comprised of WO2008149228 (Aurobindo Pharma). This document cites WO1995011224 (Abbott). This document could potentially be considered a third generation document, but because it was published December 11, 2008 this was designated a fifth generation document. This document claims processes for preparing substantially pure dibenzylamino-3-hydroxy-1,6-diphenylhexane, potentially a key intermediate in the synthesis of Ritonavir. The substantially pure compound is one of the intermediates in the synthesis outlined in the fourth generation '270 document.

Many of the intermediates described in the Archimica patent (US6407252) could also be subject to similar patent protection in the future. Patenting of the isolation and characterization of these yet-claimed key intermediates are potentially jumping off point to begin future patent coverage.

4.2.3 Innovation track 3: Structural Considerations and Polymorphs*



*Description of colored arrows can be found in table 1 in section 4.1.2.

This innovation track was selected because of the importance of the crystalline structure of Ritonavir to its therapeutic effectiveness. Each Ritonavir polymorph can be described in

several different ways. This particular area has seen a lot of patenting activity since Abbott discovered the issue of heat instability of crystalline Ritonavir in its solid dosage forms in the late 1990's. The innovation track is particularly note worthy because the documents in later generations can be important in the innovation tracks related to both liquid and solid dosage forms.

The first generation patent application WO1994014436, assigned to Abbott Laboratories, is the first disclosure of Ritonavir. The '436 document claims a broad Markush structure describing Ritonavir. This initial document only claims a retroviral protease inhibitor and does not describe structural considerations or conformational polymorphs of Ritonavir.

The second generation contains two documents, WO1996039398 and WO1995009614, both assigned to Abbott. The '398 document family claims a method of preparing an HIV protease inhibiting compound. This also describes preparing an acid addition salt of the compound. The Markush group prepared broadly covers Ritonavir because the Markush structure is very general. The addition salt allows for this compound to be considered a crystalline solid. This document does not specifically disclose the crystalline conformation. The second second-generation document '614 family, claims a solid pharmaceutical composition comprising Ritonavir. This document does not disclose Ritonavir as crystalline. This document was included because it is one of the first patents to describe a solid pharmaceutical composition comprising Ritonavir. The '614 document is also present in the next innovation track.

The third generation documents claim a version of Ritonavir polymorphs. WO200004016 (Abbott) and its published patent EP1097148 describe a crystalline polymorph of Ritonavir and methods of its use and preparation. These documents claim X-ray diffraction patterns of a polymorph. As will be described in subsequent generations, the actual crystal form is not specifically described because this is the first X-ray characterization. These claims leave potential for patenting around the crystal structure of Ritonavir.

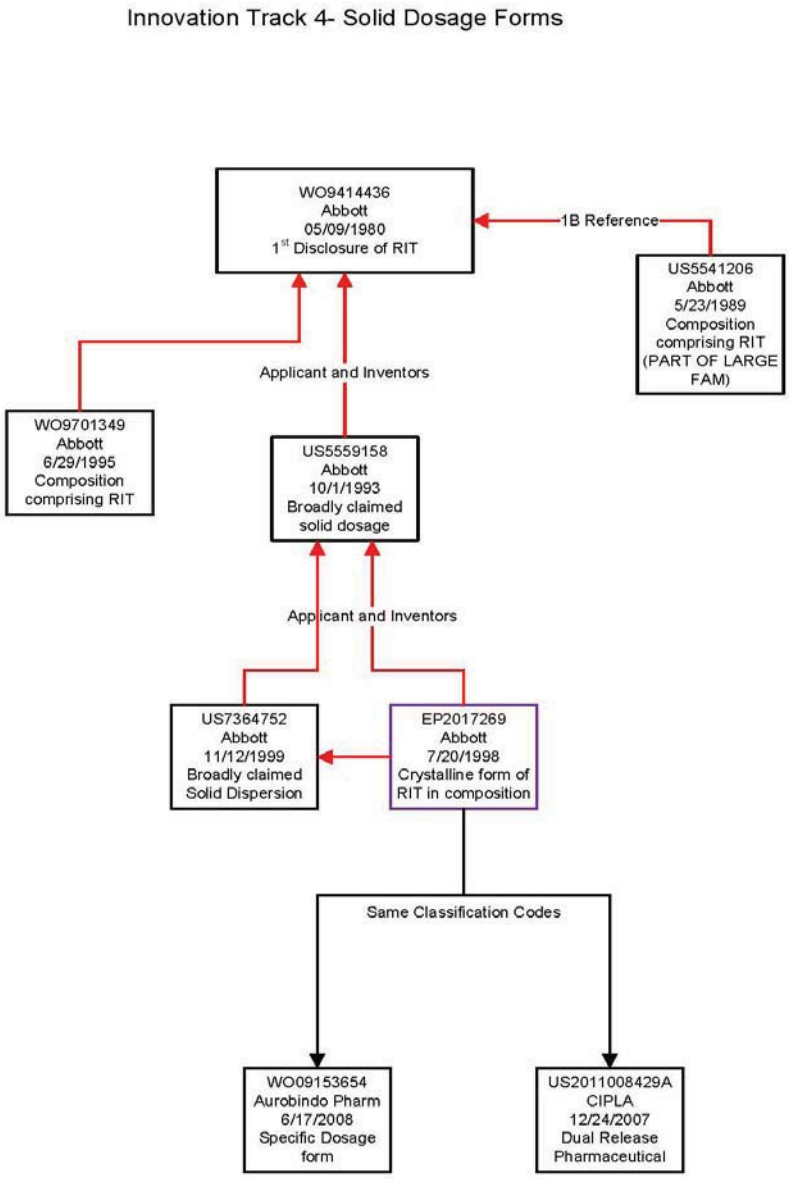
The fourth generation contains three patent families including US2004024031 (Transform Pharm), US20050009756 (Abbott) and US20050203152 (Abbott). US2004024031 cites the Abbott PCT '016 and further describes polymorphs, solvates and compositions. The '031 document claims five specific forms of Ritonavir with unique melting points and X-ray diffraction patterns. The document also claims specific methods for preparing each form of Ritonavir. The preparation methods do not describe reaction conditions, but do generally describe "a solvent system comprised of formamide and an immiscible or partially miscible solvent to provide a mixture, and reducing the solubility of Ritonavir". These reaction conditions are general in their description, but this document contains five lengthy independent claims. This application has since been granted as US7205413. The second document in the fourth generation, US20050203152, claims a pure amorphous form of Ritonavir with a specific glass transition temperature. This document is important because a pure compound with a glass transition temperature below room temperature would need to be stored in refrigeration to prevent conformational polymorphism. The third document in the fourth generation, US20050009756, describes the similar claims and has the same priority data as EP1097148. The '031 document describes the same crystal structure as the EP1097148 document but also includes an independent claim describing substantially pure amorphous Ritonavir.

The fifth generation contains two PCT applications from Ranbaxy Laboratories, WO2006129276 and WO2008041176. These documents were also included in innovation track 1. These documents cite both US2004024031 and WO2000004016. These documents further refine the claims by describing a process for preparing Form I of Ritonavir similar to the cited document US2004024031. The novel limitation compared to the '031 document is that a seed crystal was not used to prepare the Form I crystals. The dependent claims also provide detailed about reaction conditions for the preparation of the crystals.

The sixth generation contains three documents. The first is US7205413, which is the granted patent of the fourth generation document US200402031 and contains the same list of claims describing very specific forms of Ritonavir and methods of making the same. The second in the sixth generation documents is EP2017269 (Abbott). This documents shares priority data and also cites the second generation document US5567823 (Abbott) which describes Ritonavir synthesis. EP2017269 claims a method for preparing a pharmaceutical composition comprising Form II crystalline Ritonavir. The Form II crystals have the same crystalline structure identified in the third generation document WO2000004016 (Abbott). The earlier document did not appear to assign the crystal structure with a "form" because this was one of the first references to crystal structures of Ritonavir.

This is still a very active area of patenting because many of the patents during the last decade have been focused on characterizing crystal structures. Once all stable crystal structures are determined and characterized there is expected to be an increase in patent filings related to specific delivery forms containing the various Ritonavir polymorphs.

4.2.4 Innovation track 4: Solid Dosage Forms*



*Description of colored arrows can be found in table 1 in section 4.1.2.

This innovation track was selected because of the low number of filings related to solid dosage forms in the past decade. Due to problems in production of solid dosage formulations in the late 1990s the focus of pharmaceutical compositions was shifted to liquid or gel dosage

forms. However, with the recent developments in preparing amorphous crystalline Ritonavir, solid dosage forms have great patenting potential in the future.

The first generation patent application WO1994014436, assigned to Abbott Laboratories, is the first disclosure of Ritonavir. The ‘436 document claims a broad Markush structure describing Ritonavir. This initial document only claims a retroviral protease inhibitor and does not describe structural considerations or conformational polymorphs of Ritonavir. A 1B reference is also included in this innovation track. US5541206 claims a less broad Markush structure that defines several antiviral analogs. This document is designated 1B because in addition to claiming a large number of Markush compounds as in ‘436, this document also lists over 50 specific compounds that are defined by standard IUPAC[1] chemical naming.

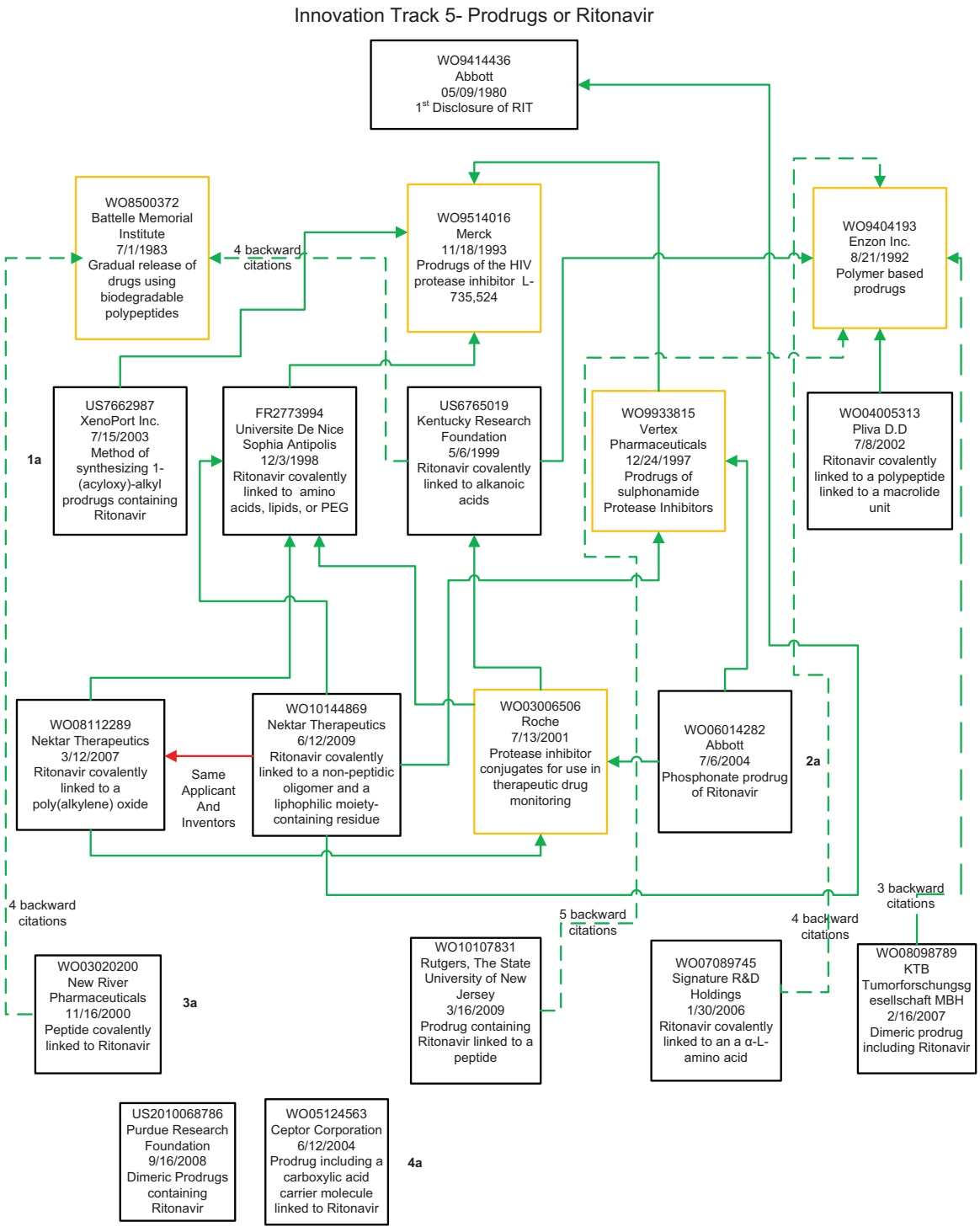
The second generation contains two documents that claim solid dosage forms and methods of preparation. All second generation documents are assigned to Abbott Laboratories and cite the ‘436 document. The broadest independent claim in US5559158 describes a solid pharmaceutical composition comprising a pharmaceutically acceptable adsorbent and Ritonavir. The most specific independent claim describes Ritonavir being present from 10 to 40% by weight and having an adsorbent from about 25-75% by weight. The composition also comprises an unspecified acid. The specific adsorbent material is not described in any independent claim. This document claims very broad coverage for a wide range of solid dosage forms. The second second-generation document is WO1997001349 (Abbott), and cites the first generation patent. The ‘349 document claims a more narrowly focused invention related to method of improving the pharmacokinetics of a drug, specifically Ritonavir. The independent claims again describe a combination of Ritonavir and another pharmaceutical agent in a composition (claim 21) comprising a pharmaceutical carrier without specifically describing delivery method. This document is also important in the first innovation track because it can be broadly interpreted as any dosage form.

The third generation contains two documents assigned to Abbott Laboratories published in 2008 and 2009. These documents could also be important to innovation track 3 because they describe the use of various crystalline forms in pharmaceutical compositions. There is a significant gap in filings related to solid dosage forms from 2000-2006. US7364752 broadly claims a pharmaceutical composition comprising amorphous Ritonavir as a solid dispersion in a water soluble polymer. The broad claim language is used to increase protection for the ‘614 document. The second third-generation document describes a similar invention. The ‘269 document claims methods for preparing compositions employing Form II crystalline Ritonavir. These two documents broadly protect the use of crystalline Ritonavir in solid dosage forms for Abbott.

The fourth generation is related to the third generation patents by IPC and ECLA classification codes. These documents describe solid dosage forms comprising a combination of drugs. US2011008429 (CIPA) describes a solid dosage form comprising two commonly used antiretroviral drugs Ritonavir and darunavir. The second document WO2009153654 (Aurobindo Pharmaceticals) also claims a combination with a water soluble polymer, similar to the claims of the third generation ‘752 patent. The ‘654 document describes the processes to prepare the solid dosage form in greater detail than the ‘752 document, specifically for solublizing Lopinavir and Ritonavir and spray drying the composition to form a solid dispersion.

The broad independent claim language in both fourth generation documents illustrate the increased potential for patenting of combination formulations in the future.

4.2.5 Innovation track 5: Prodrugs of Ritonavir*



***Description of colored arrows can be found in table 1 in section 4.1.2.**

The fifth innovation track shows the wide variety of prodrug forms of Ritonavir. Documents presented in the orange boxes do not have claims directed to prodrug forms of Ritonavir but

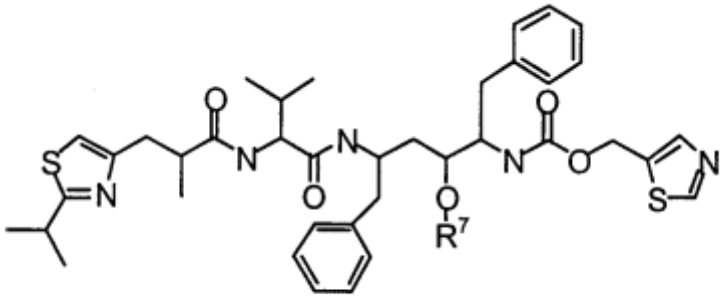
are cited by more than one other document in the innovation track. The documents in the orange boxes help interrelating the documents describing prodrug forms of Ritonavir. Covalently linking Ritonavir to peptides, amino acids, or non-peptidic polymers such as various poly(alkylene) oxides appears to be a recurrent theme throughout the documents in the innovation track.

WO9414436, assigned to Abbott Laboratories, is the first disclosure of Ritonavir. The '436 document claims a broad Markush structure describing Ritonavir. This initial document only claims a retroviral protease inhibitor and does not appear to have claims directed to prodrug forms of Ritonavir. Only one document describing a prodrug form of Ritonavir, WO10144869, cites the '436 document. The other documents may be related to the '436 document by more than 6 backward citations, but do not directly reference the '436 document. WO10144869 is discussed in greater detail below in the paragraph discussing second generation documents.

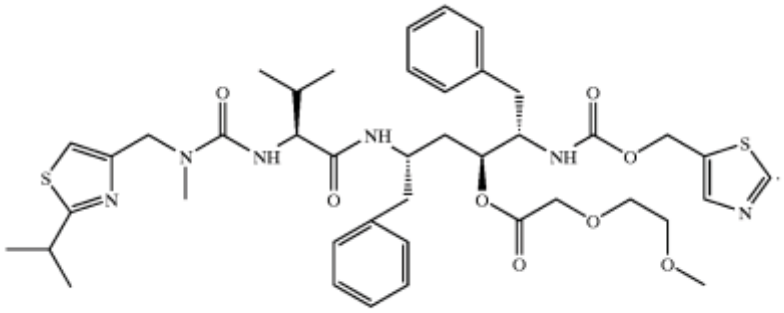
The next documents in the innovation track, WO8500372 (Battelle Memorial Institute), WO9514016 (Merck), WO9404193 (Enzon Inc), do not describe prodrugs of Ritonavir, but are cited either directly or indirectly by more than one document describing prodrugs of Ritonavir. Thus, these documents connect the other documents in the innovation track and appear to be pivotal documents in the progression of Ritonavir prodrug technology. The '372 document describes a biodegradable polypeptide in which drugs may be incorporated. The polypeptide is degraded slowly in the body allowing for the gradual release of drugs. The document claims an esterified cyclic polypeptide including polyaspartate or polyglutamate that may be used as a carrier for drugs. This document is indirectly related by four backward citations to US6765019 and WO03020200, which both describe prodrug forms of Ritonavir and are discussed below. The '372 document is important in the innovation track because many of the documents in the innovation track describe prodrugs of Ritonavir in which Ritonavir is covalently linked to polypeptides or amino acids. Some of the documents in the innovation track also suggest that covalently linking polypeptide or amino acid residues can enhance drug bioavailability. WO9514016 describes ester prodrugs of the HIV protease inhibitor L-735,524, now known as Indinavir. The prodrugs help improve the extended release properties of the protease inhibitor and increase the solubility of the drug in the intestine. Document '016 is directly cited by FR2773994, WO9933815, US7662987, three first generation documents describing prodrug forms of Ritonavir. These documents are discussed in greater detail below. The '016 document is important to the innovation track because it is the earliest document in the innovation track that demonstrates the ability to apply prodrug technology to protease inhibitors. WO9404193 describes polymer based prodrugs comprising drugs covalently linked to polyalkylene oxides. The document suggests that the incorporation of covalently linked polyalkylene oxides is particularly useful for peptide therapeutic agents and functions to prolong the circulating life, improve solubility, and increase the pH stability of the drug. The document has broad independent claims to polypeptide or chemotherapeutic drugs, but does not explicitly claim protease inhibitors or antiviral compounds. WO9404193 is directly cited by US6765019 and WO04005313 (these documents are discussed in greater detail below in the paragraph discussing first generation documents) and indirectly cited by WO10107831, WO07089745, and WO08098789 (these documents are discussed in the paragraph describing third generation documents) by three or more backward citations. The '193 document is important in the innovation track because it presents the concept of covalently linking polyoxyalkylene oxides to therapeutic agents to produce

prodrugs with enhanced properties compared to that of the non-prodrug form. Several of the documents in the innovation track also describe prodrugs comprising Ritonavir covalently linked to polyalkylene oxides or other non-peptidic polymers.

The first generation documents include WO9933815 (Vertex Pharmaceuticals), FR2773994 (Universite De Nice sophia Antipolis), US6765019 (Kentucky Research Foundation), WO04005313 (Pilva D.D), and US7662987 (XenoPort Inc.). WO9933815 appears to describe a prodrug form, in the specification, of Ritonavir having the structure:

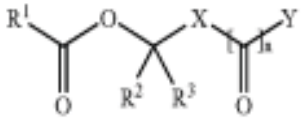


In which R^7 is a variety of moieties. The document however, does not appear to claim said prodrug. The document instead claims prodrugs of sulfonamide protease inhibitors such as VX-478 (Amprenavir) which include phosphonate or ester moieties. '815 cites WO9514016 and is cited by WO10144869 and WO06014282 (both are described below in the paragraph discussing second generation documents). FR2773994 appears to be the earliest document claiming a prodrug form of Ritonavir. The document describes prodrugs of HIV protease inhibitors that improve drug bioavailability and facilitate delivery of the protease inhibitor to the central nervous system. The document has claims describing prodrugs including Ritonavir covalently linked to lipids, amino acids, and or Polyethylene glycols. This document is important to the innovation track because several other documents, having priority dates later than FR2773994, also describe prodrugs in which Ritonavir is covalently linked to amino acid residues or lipids. FR2773994 cites WO9514016 and is cited by three second generation documents: WO08112289A, WO10144869, and WO03006506. US6765019 describes ester and amide prodrugs of chemotherapeutic agents in which a drug is covalently linked to various alkanoic acids such as oxaalkanoic acids, thiaalkanoic acids, oxahydroxyalkanoic acids, oxaalkoxyalkanoic acids, oxadialkanoic acids, and oxaaminoalkanoic acids. The document discusses the enhanced solubility of the prodrug forms and claims a prodrug form of Ritonavir having the following structure (claim 33):



US6765019 cites WO9404193 (described above) and is cited by WO03006506 (discussed below in the paragraph discussing second generation documents). WO04005313 describes compounds in which a therapeutic agent is covalently linked to a peptide that is linked to a macrolide unit. The compounds may act as prodrugs by transporting the compound into the target cell and releasing it inside the target cell in higher concentration than could be achieved by the drug alone. The macrolide unit present in the prodrug allows the prodrug to accumulate in immune system cells and enables the active agent to act predominantly at the infection site. '313 has claims directed to a compound in which Ritonavir is covalently linked to the peptide and macrolide unit. Document '313 cites WO9404193 and also further expands the peptide based prodrug technology, discussed in other documents in the innovation track, by further linking a peptide unit with a macrolide unit. US7662987

has claims directed to a method for synthesizing a 1-(acyloxy)-alkyl compound having the following structure:



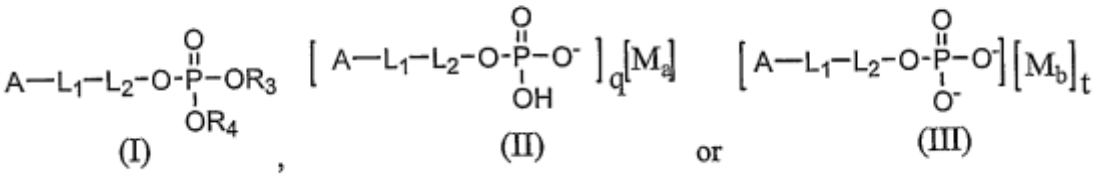
Wherein Y may be Ritonavir. The acyloxyalkyl compounds act as prodrugs and the acyloxyalkyl group helps to improve the bioavailability of poorly absorbed drugs. US7662987 focuses on methods for stereoselective synthesis of acyloxyalkyl prodrugs from l-acylakyl derivatives of pharmaceutically active drugs. US7662987 cites WO9514016 and is not cited by any other documents in the innovation track.

The second generation documents include WO03006506 (Roche), WO06014282 (Abbott), WO08112289 (Nektar Therapeutics), and WO10144869 (Nektar Therapeutics). WO03006506 does not describe a prodrug form of Ritonavir but has claims to compounds comprising Ritonavir, or other protease inhibitors, covalently attached to amide or ester moieties. These compounds function as activated haptens that are useful for generating im-

munogens to HIV protease inhibitors and may be used in assays for therapeutic drug monitoring. The haptens have the following structure:

I-X-(C=Y)m-L-A

wherein I is an HIV protease inhibitor, such as Ritonavir, radical, X is O or NH, Y is O, S or NH, m is 0 or 1, L is a linker consisting of from 0 to 40 carbon atoms arranged in a straight chain or a branched chain, saturated or unsaturated, and containing up to two ring structures and 0-20 heteroatoms, with the proviso that not more than two heteroatoms may be linked in sequence, and A is an activated functionality chosen from the group consisting of active esters, isocyanates, isothiocyanates, thiols, imidoesters, anhydrides, maleimides, thiolactones, diazonium groups and aldehydes. Although WO03006506 does not claim a prodrug form of Ritonavir, it is important in the innovation track becasue it claims a Ritonavir conjugate compound with a similar structure and containing similar moieties to prodrugs of Ritonavir described in other documents of the innovation track. The ‘506 document cites US6765019 and is directly cited by two other second generation documents WO06014282 and WO8112289. WO06014282, assigned to Abbott, has claims directed to phosphonate prodrugs of Ritonavir and other HIV protease inhibitors where the compounds have the general formulas:



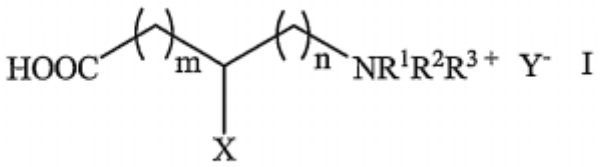
(I) , (II) or (III)

wherein A is Ritonavir or another protease inhibitor. The phosphonate prodrug forms help to increase solubility, bioavailability, and are readily metabolized into the active inhibitors in vivo. The ‘282 document cites WO03006506 and WO9933815, but is not cited by any other documents in the innovation track. The other two documents in the second generation of the innovation track, WO08112289 and WO10144869, have the same applicant (Nektar Therapeutics) and at least one inventor in common. WO08112289 appears to claim a compound comprising Ritonavir covalently attached to a water soluble non-peptidic oligomer that may a poly(alkylene)oxide. The ‘289 document cites the first generation document FR2773994 and another second generation document WO03006506. WO10144869 further expands upon the concept in WO08112289 and claims compounds including a protease inhibitor, such as Ritonavir, covalently attached to both a non-peptidic oligomer and a liphophilic moiety-containing residue via a releasable or stable linkage containing spacer moiety. The non-peptidic oligomer may be a poly(alkylene) oxide and the liphophilic moiety-containing residue may be an organic radical, a naturally occurring amino acid, a non-naturally occurring amino acid, a lipid, a carbohydrate, a phospoholipid, an alkyl carbonate, or a vitamin. The spacer moiety may be a carbamate linkage or other linkages that are enzymatically stable or releasable. The broad claim encompasses may be different groups that may be covalently attached to Ritonavir, or other protease inhibitors, and does not further limit the scope of the invention. The ‘869 document cites the two first generation documents FR2773994 and

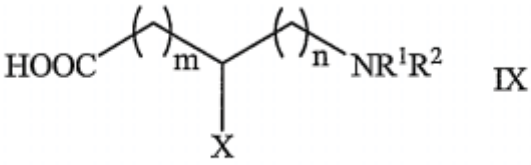
WO9933815. Also, the ‘869 document is the only document in the innovation track to cite the WO9414436 document which contains the original disclosure of Ritonavir.

The third generation documents in the innovation track, WO03020200 (New River Pharmaceuticals), WO07089745 (Signature R&D Holdings), WO08098789 (KTB Tumorforschungsgesellschaft MBH), and WO10107831 (Rutgers, the University of New Jersey), are considered third generation because they are related by three or more backward citations to the documents WO8500372, WO9514016, and WO9404193 (discussed in the third paragraph above). Also, none of the third generation documents are cited by any other documents in the innovation track. WO03020200 has claims directed to a compound in which a peptide is covalently linked to Ritonavir. The peptide moiety helps to stabilize the active agent in the stomach through conformational protection and the delivery of the active agent is controlled by unfolding of the carrier peptide. Upon entry into the upper intestinal track enzymes release the active ingredient by hydrolyzing the peptide bonds of the carrier peptide. The ‘200 document is related to WO8500372 by four backward citations and appears to expand on the polypeptide technology presented in WO8500372. WO07089745 contains claims directed to a compound comprising Ritonavir covalently linked to an α-L-amino acid. The prodrug exhibits enhanced therapeutic qualities such as improved stability, enhanced penetration of blood-brain barrier, improved bioavailability, controlled release properties, increased solubility, etc. The ‘745 document is related by four backward citations to WO9404193. WO08098789 claims prodrugs including two therapeutic or diagnostic agents linked, by way of a cleavable linker, to a protein-binding moiety. The compounds may include Ritonavir as the therapeutic agent. The prodrugs are dual acting and contain two different therapeutic or diagnostic agents. The protein binding moiety of the prodrug helps to deliver the pharmaceutically active compounds to the target site. The ‘789 document is related to WO9404193 by three backward citations. WO10107831 appears to have claims directed to a multimeric nanocarrier for in vivo delivery of a bioactive agent comprising at least two peptide monomers reversibly linked with a bioactive agent that may be Ritonavir. The linkage between the peptides and the bioactive agent is a biodegradable bond such as a disulfide, ester, or carbamate bond. The nanocarrier helps to deliver the bioactive agent to a particular target within the body. The ‘7831 document is related to WO9404193 by five backward citations.

The fourth generation documents in the innovation track, WO05124563 and US2010068786, either do not appear to be related to the other documents in the innovation tract or are related to other documents by more than 5 backward citations. WO05124563 appears to claim a kit including a prodrug compound comprising a carrier molecule and a protease inhibitor that may be Ritonavir. The carrier molecule is represented by the general formulas:



I



IX

wherein each R, R, and R comprises, independently, hydrogen or a branched- or straight chain alkyl group, X comprises OH or NHR, wherein R comprises hydrogen or a branched- or straight-chain alkyl group; Y comprises a pharmaceutically-acceptable anion; and m and n can be an integer from 1 to 10, or the pharmaceutically-acceptable salt or ester thereof. The kit also includes an activator that converts the prodrug to the active form of the compound. The activator may be an acid, an enzyme, a metal, a salt, a polymer, a detergent, or a zeolite. US2010068786 has claims directed to a method for inhibiting therapeutic drug resistances within a cell over-expressing a membrane protein by administering a dimeric prodrug containing a crosslinking agent. The dimeric prodrug may include Ritonavir and co-administration of the monomeric drug and the dimeric prodrug allows for accumulation of the therapeutic drug within the cell. Although US2010068786 has no forward or backward citations, the document appears to expand upon the dual therapeutic prodrug concept presented in WO08098789 (discussed above in the paragraph discussing the third generation documents).

4.3 Summary

These innovation tracks represent how parts of the scope of the WO1994014436 are still under protection in later patents. The key patent only protects the structure of Ritonavir and similar analogs. Subsequent patents, illustrated in the previous innovation tracks, still protect the Ritonavir structure but also extend protection to delivery forms and crystal structures. Liquid/gel formulations receive the most patenting activity of any dosage forms. This type of formulation still has room to protect additional liquid/gel formulations. As illustrated above, there are many companies involved in protecting the use of Ritonavir. However, Abbott Laboratories currently holds a vast majority of patents related to Ritonavir.

These five innovation tracks were selected but do not illustrate the majority of patent fillings. At least 400 patents are related to combination therapies containing Ritonavir as a secondary active ingredient. The use of Ritonavir as a secondary protease inhibitor was not considered an innovation track because of the lack of similarities in claim language. These filings primarily claim novel active pharmaceutical agents and include Ritonavir as a protease inhibitor in dependent claims. This trend is not surprising due to Ritonavir ability to enhance other protease inhibitors.

Section 5 - Report Summary

This report was prepared to illustrate the complex nature of patent protection and statistical trends related to Ritonavir. There have been over 800 patents filed since the initial PCT application WO1994014436 to protect different aspects of Ritonavir and its methods of use. A large number of documents filed subsequent to the initial application still protect the structure of Ritonavir as described in the initial application. As one would suspect, subsequent patent filings continue to narrow the focus of protection of Ritonavir by incorporating novel aspects to the subject of Ritonavir. The implications of patent protection are important for developing countries to consider. Simply licensing the initial key documents will not provide adequate freedom to operate because of the breadth of coverage by subsequent patents. The statistical analysis shows there has been increased filing activity since the initial disclosure, exclude the past two years. These filing trends are expected to continue to increase. Abbott Laboratories is the most assigned company and continues to file in a variety of areas related to Ritonavir including crystal structure and combination therapies comprising Ritonavir. A majority of assignees are large pharmaceutical corporations with universities making a very small minority. The statistical analysis also shows the most common countries for filing applications are the United States followed by the European Patent office. The statistical analysis also shows 88% of patent families file PCT applications. This trend is expected to continue.

Four innovation tracks were also created to illustrate the complexity of the patenting activity surrounding Ritonavir. The five areas covered by the innovation tracks are liquid dosage forms, synthesis of Ritonavir and its key intermediates, polymorphs and crystalline Ritonavir, solid dosage forms, and prodrugs. These innovation tracks analyze the interdependencies of relevant patent families claiming improvements that are either specifically adapted to or exclusively related to Ritonavir. This would be important for countries or organizations involved in policy discussions about patented pharmaceutical compounds. The innovation tracks were also selected because they represent areas that have had a high volume of patenting activity.

The first innovation track relates to interrelated patent families claiming liquid oral dosage forms and how the subsequent documents still protect the invention claimed in the first disclosure. There are a large number of patent documents describing liquid oral dosage formulations. As will be shown below, the patents and applications describe increasingly narrower formulations through the generations. The narrowed coverage over generations typically claims more specific solvent systems or encapsulation formulations. These documents still encompass the invention claimed in the first disclosure. This is an area that still has a large amount of potential for future filings to attempt to cover more specific solvent systems and methods of preparing the dosage forms.

The second innovation track is related to the synthesis of Ritonavir and its key intermediates. This innovation track outlines the interrelated patent families describing various synthetic pathways and key intermediates necessary for preparing Ritonavir. This technical area has limited potential for additional patent protection. The currently protected synthetic routes are well protected by a variety of large pharmaceutical companies and would require a large amount of R&D to devise novel methods of synthesis.

The third innovation track is related to the crystalline structure of Ritonavir. This is a particularly notable innovation track because the crystalline structure of Ritonavir has been found to be important to its therapeutic effectiveness. There has been a large amount of patent activity in the area of characterizing the various Ritonavir crystalline morphologies. The later generations in this innovation track begin to protect formulations with specific forms of Ritonavir. However, the non-active ingredients are still being claimed with very broad language (i.e. crystalline Ritonavir can be dissolved in a pharmaceutically acceptable solvent).

The fourth innovation track focuses on solid dosage forms. This area has had the fewest number of filings in the past decade. Problems with producing a stable dosage form was slowed the filing in this area. However, due to the relatively low number of filings related to solid dosage forms, this remains an area that could potentially have increased filing activity in the future.

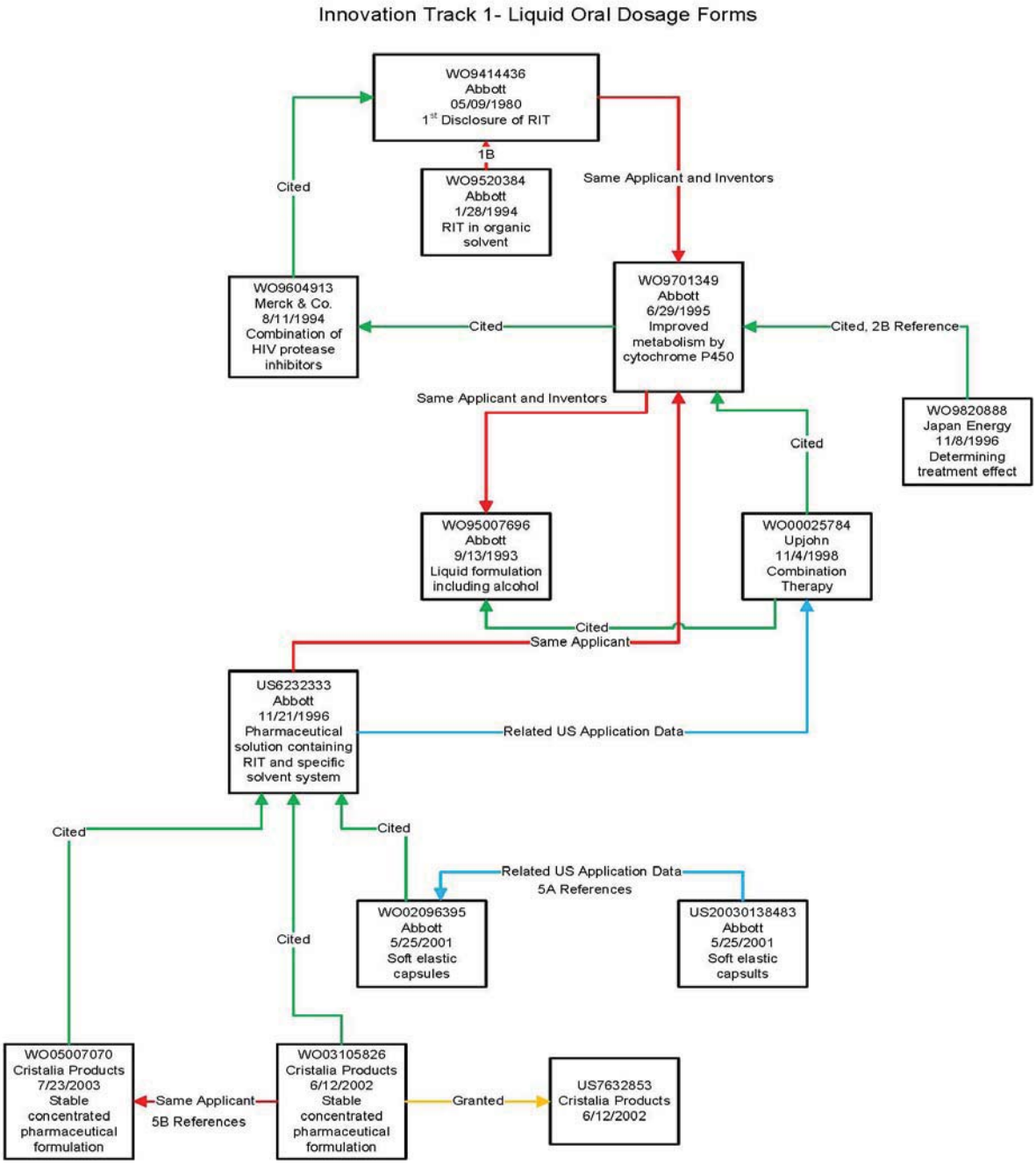
The innovation track related to the crystal structure is important because it has serious implications to both solid and liquid dosage forms. The combination of the concepts protected in each of the dosage form innovation tracks could provide a potential area for future patent filing and protection. The single largest area of patenting is related to combination therapies. These documents were not included as an innovation track because they do not have interrelated claims. These documents describe novel pharmaceutical agents. The formulations for the novel agents also include Ritonavir because it has been shown to be a powerful secondary protease inhibitor. Patenting in the area of combination therapies containing Ritonavir as a secondary protease inhibitor is also expected to increase in the future.

The fifth innovation track is related to prodrugs. This innovation track is important because prodrug forms of Ritonavir enhance solubility, improve bioavailabilty, and improve drug absorption. The prodrug forms of Ritonavir also enhance target specific delivery of Ritonavir and increase the ability of Ritonavir to permeate biological membranes. Also, the prodrug forms of Ritonavir appear to be more easily incorporated into solid dosage forms. Patent activity in the area of prodrugs of Ritonavir appears to be increasing and will continue to increase along with the emerging developments in prodrug technology.

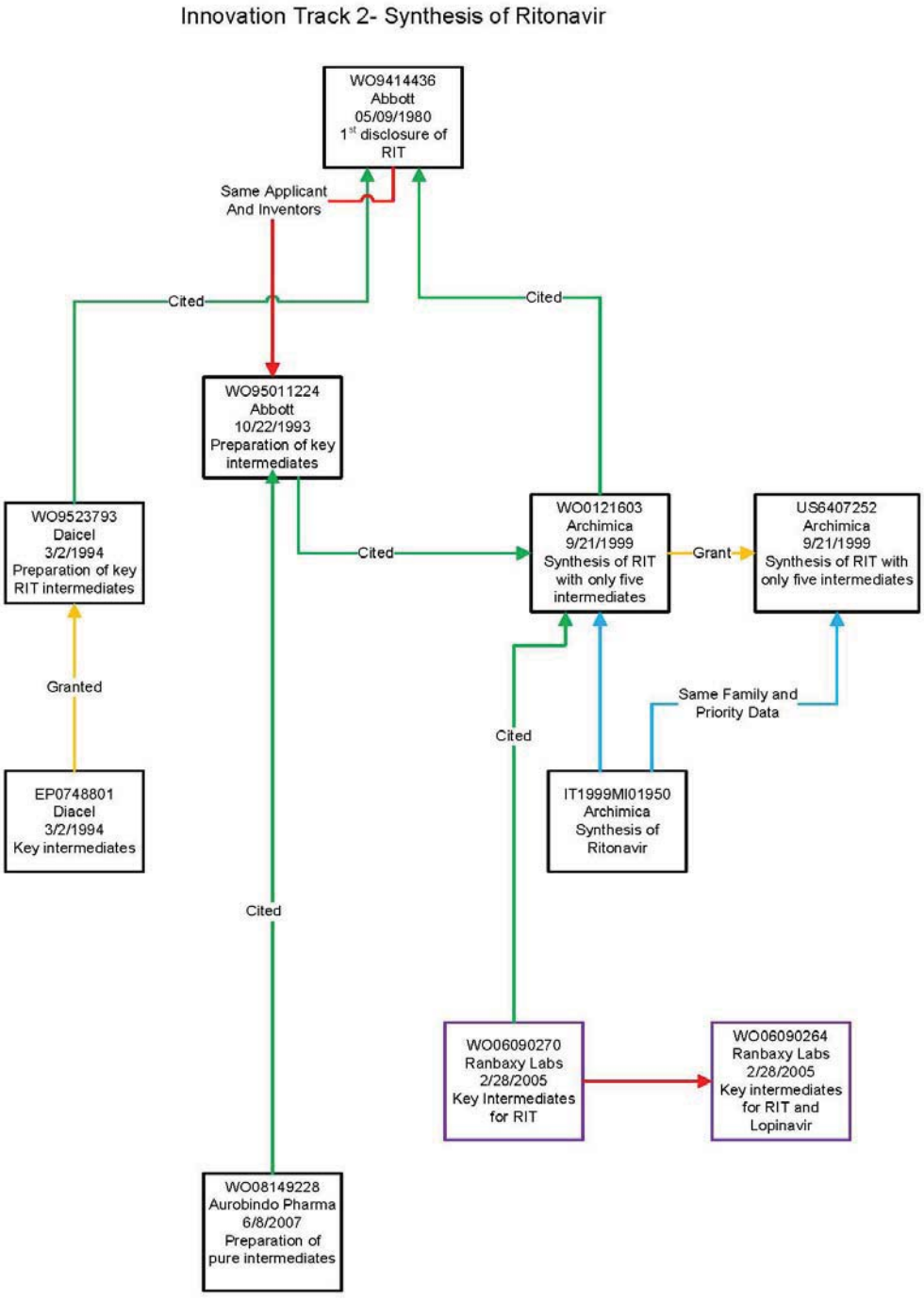
Appendices

Appendix 1 - Innovation Tracks

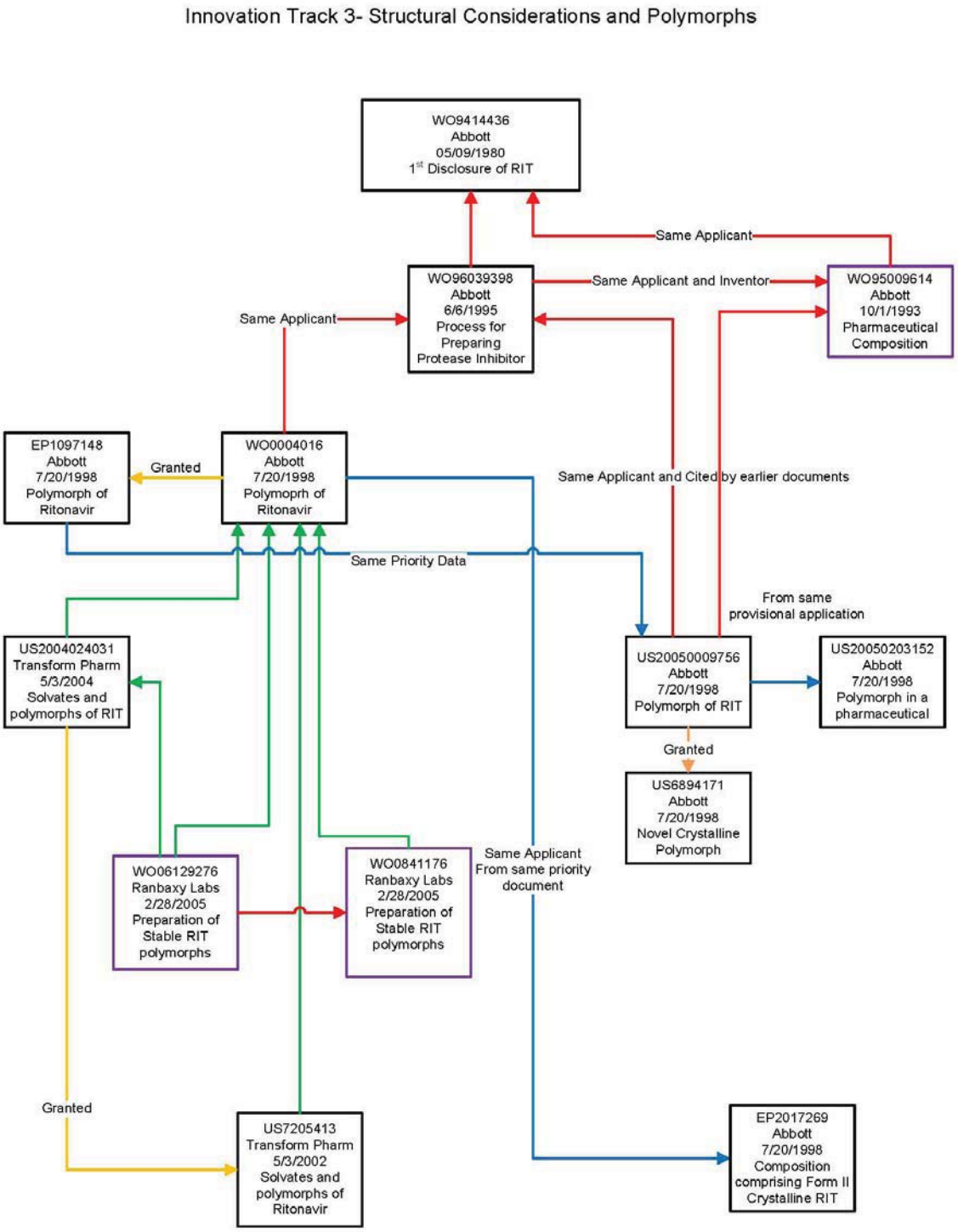
1.1 Liquid Oral Dosage Forms



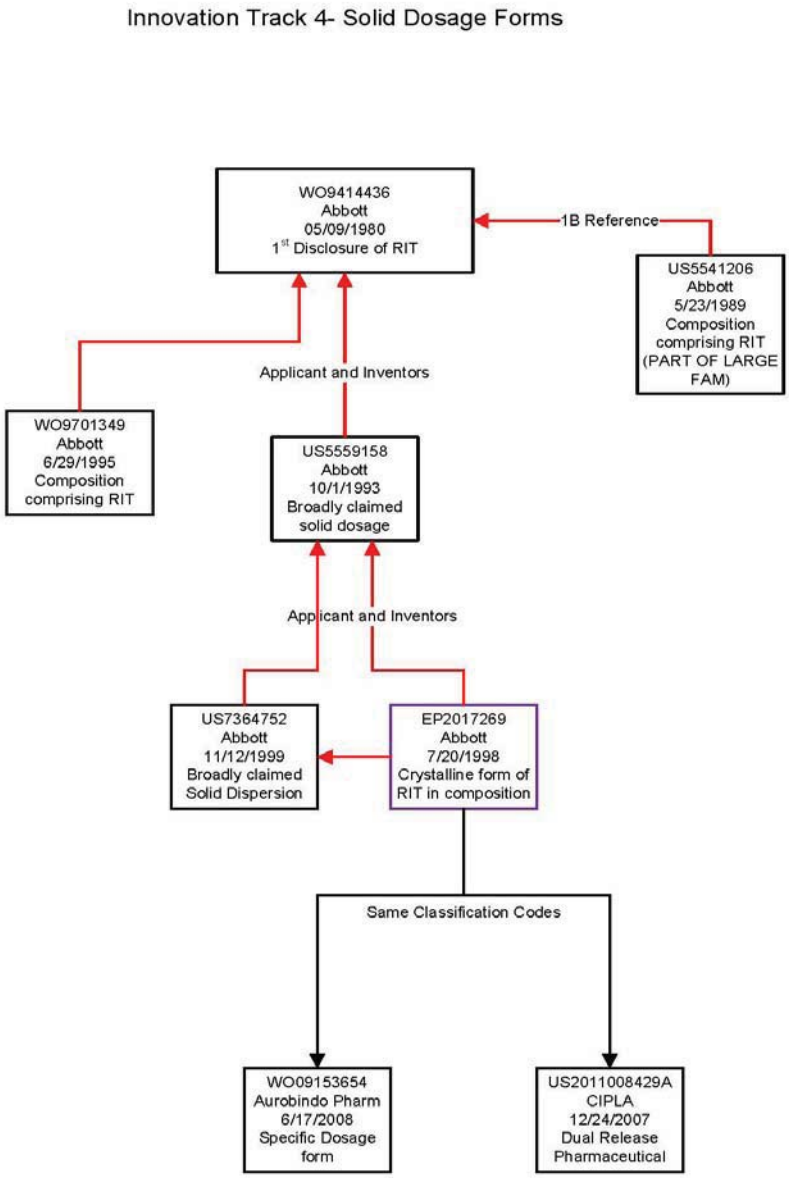
1.2 Synthesis of Ritonavir



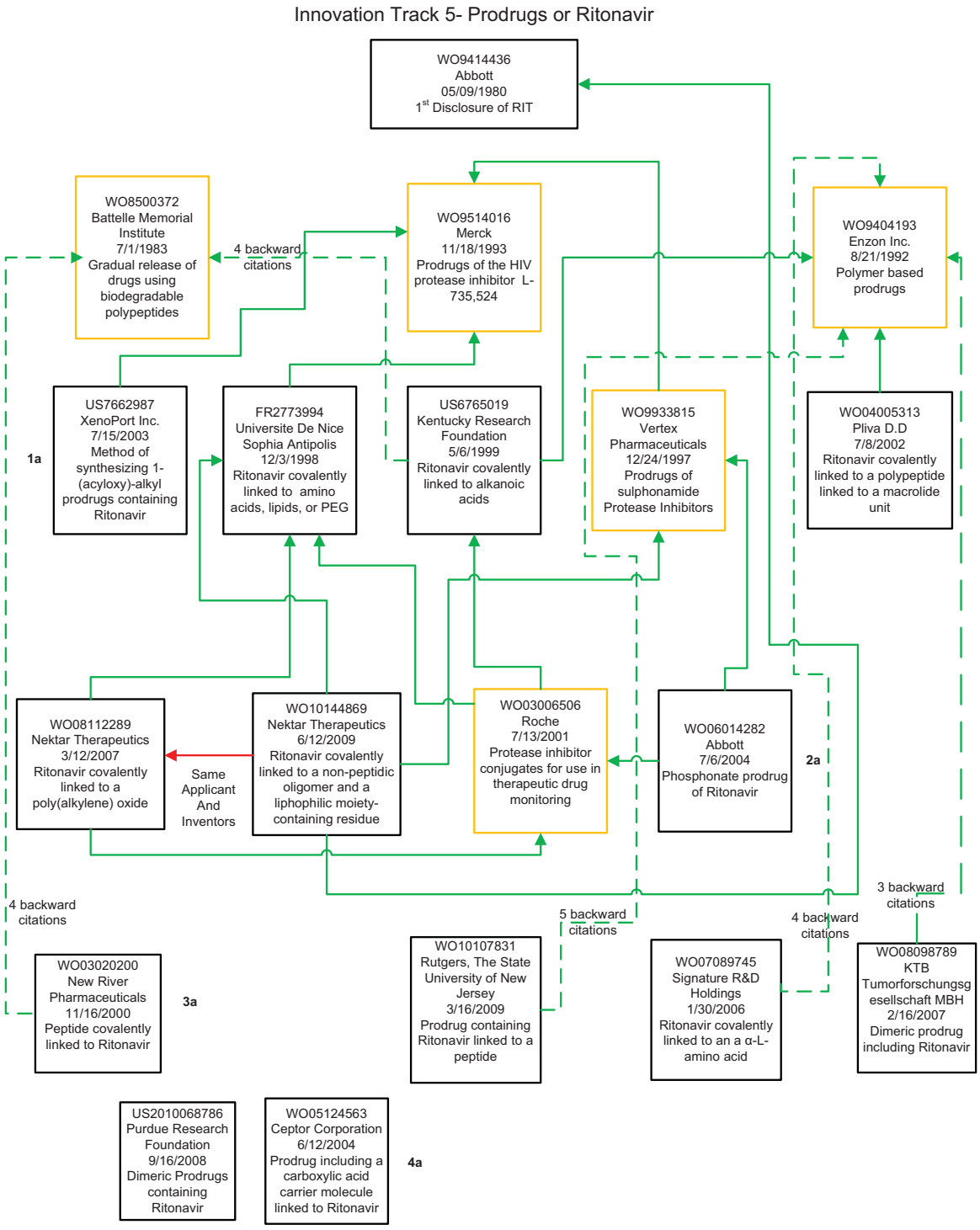
1.3 Polymorphs



1.4 Solid Dosage Forms



1.5 Prodrugs of Ritonavir



Appendix 2 - Glossary of Important Terms and Concepts

Search Operators:

Search Operator			Function
Search Platform			
Patbase	*Total Patent*	*Thomson Innovation*	
CTB			Identifies documents cited by a document (or results set)
CTF			Identifies documents that cited a document (or results set)
PN			Patent number search
PA			Patent Assignee search
PD		DP	Publication date
Ti			Search in Title only
CL	CLAIMS	CL	Search in Claims only
TAC	TITLE-ABST-CLAIM	CTB	Search in Title, Abstract and Claims only
W#	W/#	Near#	Proximity operator to find where words are within # of each other
		ADJ	Searches two words adjacent and in order written
%	*	?	Wildcard represents 1 or 0 characters
* (e.g. suspen*)	!	*	* allows for unlimited truncation
UC			UPC classification code search
IC			IPC classification code search
RF			Results Folder- used to add tagged documents to search query list to reduce redundancies during review

Dictionary

Citation Searching

Backward Citation Search: Backward citation search is defined as identifying all documents that are cited by the document in question.

Forward Citation Search: Forward citation search is defined as identifying all documents that cited the document in question.

Conformational Polymorphism: Polymorphs are different crystalline conformations of the same chemical substance. The conformational chance of the crystalline structure alters Ritonavir from the therapeutically effective polymorph to a lower energy polymorph. The lower energy conformation is not therapeutically effective.

ECLA Classification System: ECLA stands for European Classification, and was designed in-house by the European Patent Office as an enhancement to the IPC classification system; as such it is compatible with the IPC (see below). The ECLA classifications are useful because they are assigned to patent documents by the highly skilled examiners of the EPO. As the body of patent literature expands, IPC subgroupings naturally grow in size. Because a sub categorization that still contains thousands of documents hinders the ultimate purpose of a classification scheme, ECLA classes are defined to split these large IPC subgroups into even smaller divisions. More information about IPC and ECLA classifications can be found at the following web-based resources:

Intellixir: Intellixir is a software package available as stand alone software or through the Questel Orbit platform. This software through Orbit was used in the current study to explore forward and backward citations of one or more INPADOC family members. More information on the functions of Intellixir can be found at http://www.intellixir.com/en/default.asp.

IPC: http://www.wipo.int/classifications/ipc/en/

ECLA: http://www.epo.org/searching/essentials/classification/ecla.html

Comparative descriptions of the ECLA and IPC as well as other classification systems can be found at

http://www.intellogist.com.

INPADOC: acronym for International Patent Documentation Center. INPADOC is an international patent collection. The database of patent families is produced and maintained by the European Patent Office and was founded by WIPO.

Additional Information about FAMPAT families can be found at

http://www.intellogist.com/wiki/Patent_Families#INPADOC

IPC Classification System: IPC stands for the International Patent Classification and is administered by the World Intellectual Property Organization (WIPO). The scheme was conceived as an indexing system to organize patent documents from around the world based on the technical field of the invention, thereby providing a retrieval system by subject matter, independent of keyword searching.

IUPAC Naming: Systematic method of naming organic chemical compounds as recommended by the International Union of Pure and Applied Chemistry.

Markush Structures: A term used to describe the series of compounds covered by a patent claim, where the compound is defined as a basic structure with a variable list of possible substitutions (e.g. where R=H, methyl, ethyl, OH, etc)

Merck Index: Encyclopedia of chemicals, drugs and biological containing over 10,000 single substances or groups of related compounds. The index also contains an appendix with descriptions of organic name reactions. The Merck Index was first published in 1889 and the most current 14th edition was published in 2006.

Non-Active Ingredients: Ingredients that are present in pharmaceutical dosages that do not have pharmaceutical activity, i.e. are not considered medicine. Also referred to as excipients,

are ingredients included in pharmaceuticals that are needed to prepare the tablet, pill, capsule or liquid. Some common examples of non-active ingredients include binders, fillers, disintegrants, lubricants, coatings, sweeteners, flavors and coloring agents.

Orange Book: The Orange Book is prepared by the United States Food and Drug Administration (FDA) to provide states with a list of drugs approved for safety and effectiveness, as well as therapeutic equivalence determinations for multisource drugs which are available from more than one manufacturer. The Orange Book is a list of drugs approved under section 505 of the Federal Food, Drug and Cosmetic Act for interstate commerce within the United States. The Orange Book is updated daily with new generic drug approvals. WEBSITE: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm

Patent Family: Patent families are groups of patents, which like a family, are all related to each other, in this case by way of the priority or priorities of a particular patent document. There are several different systems for grouping families. In Espacenet a patent family is defined as comprising all documents having exactly the same priority or combination of priorities. An INPADOC family member is defined as comprising all the documents having the same priority or combination of priorities. This includes all the patent documents resulting from a patent application submitted as a first filing with a patent office and from the same patent application filed within the priority year with a patent office in any other country. This information was obtained from the espacenet website. More information about patent families can be found at the European Patent Office website: http://www.epo.org/searching/essentials/patent-families.html

STN: Acronym for Scientific & Technical Information Network. STN is operated by Chemical Abstracts Service (CAS). STN is an interface to access CAS databases and many additional databases not covered in Chemical Abstracts database.

Additional CAS Databases searched using STN:

1) Registry: database of more than 50 million organic and inorganic substances and more than 60 million protein and DNA sequences. Each compound is given a unique CAS registry number, index name, and graphic representation of its chemical structure. Chemical names are assigned to each according to the rules of IUPAC.

2) CAplus: database of bibliographic information and abstracts for all articles in chemical journals worldwide, and chemistry related articles from all science journals, patents, and other scientific publications.

3) MARPAT: comprehensive database for structure searches of chemical patents. MARPAT contains more than 830,000 searchable Markush structures from patents covered by CAS from 1961 to the present. Database is crucial to identify documents that may disclose “prophetic structures”. A prophetic structure is a Markush structure that represents a core chemical compound with a large number of potential substitutions. Each of the potential chemicals is not independently represented but are all covered by the definition of the Markush structure.

Synthetic Intermediate: A compound which is produced in the course of a chemical synthesis, which is not itself the final product, but is used in further reactions to produce the final product.

Appendix 3 – Ritonavir Patent Database Description

The accompanying Excel database contains all 805 patent families identified as of March 5, 2011. The database comprises a master sheet which contains bibliographic information and family information and is fully sortable by any of the headings. Each family is identified by one family member, preferably a PCT application where available. The publication number of the document identifying the family is linked to Espacenet. This link permits immediate online access, e.g., to all INPADOC patent family information and to the legal status information of these family members as far as it is available in the INPADOC database. Espacenet further includes links to the national publications of the family members where available.

The Excel database further contains several columns that permit to sort the families according to different subject matter, such as:

1) *Synthesis and Crystalline Forms*: Subset of relevant patent families from Master Sheet describing synthesis of RIT as well as crystallization procedures for preparing crystalline RIT. These primarily focus on the synthesis and characterization of RIT and not pharmaceutical dosage forms.

2) *Methods of Treating HIV*: Subset of relevant patent families from Master Sheet describing methods of treating HIV including modulating expression of nucleic acids, inhibiting and determining resistance, reducing viral load, quantifying HIV virus, quantifying plasma concentrations.

3) *Derivatives*: Subset of relevant patent families from Master Sheet that are related to derivatives of RIT. These derivatives include different protecting groups to help storage as well as prodrugs. Prodrugs are compounds that are metabolized by the body to produce the active ingredient, in this case RIT. Several of the prodrugs consist of RIT attached to polypeptides or cellulose delivery agents.

4) *Combinations*: Subset of relevant patent families from Master Sheet describing pharmaceutical formulations containing an active pharmaceutical agent and RIT as a secondary active agent. This sheet contains a large number of families because RIT has been shown to be a useful protease inhibitor and is widely used as a booster for other protease inhibiting compounds.

5) *Stabilized Forms*: Subset of relevant patent families from Master Sheet related to preparation of stabilized forms of RIT. The stabilized forms typically involve crystallizing RIT in appropriate organic solvents and using these stabilized forms in pharmaceutical preparations.

Appendix 4 - Search History

Ritonavir Collection Search History

Minesoft Patbase Search History

1	PN=WO94014436	1
2	Combine_family=VLF30560186	77
3	ctb=1	4
4	PN=(us5142056)	1
5	ctb=4	15
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	US4725583 OR US4725584 OR US4826815)	
7	PN=(US5151438 OR US5256677 OR US5354866 OR US5670675 OR US5541334 OR US5545750 OR US5597926 OR US5616714 OR US5648497 OR US5539122 OR US5552558 OR US5696270 OR US5679797 OR US5580984 OR US5597927 OR US5583232 OR US5674882 OR US5583233 OR US5625072 OR US5591860 OR US5659045 OR US5565418 OR US5635523 OR US5616720 OR US5554783 OR US5541206 OR US5362912 OR US6531610)	28
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26	PN=(BG65150 OR EP1248600 OR EP1418174 OR EP1733725 OR EP1917958 OR EP2017269 OR US5786500 OR US6221400 OR US6232333 OR US6407252 OR US6458818 OR US6521651 OR US6894171 OR US6911214 OR US7148359 OR US7183416 OR US7364752 OR US7659405 OR US7820671 OR WO08055136 OR WO08055146 OR EP1729730 OR WO9857648 OR CZ299728 OR CZ301308 OR EP0942721 OR EP1002065 OR EP1090914 OR EP1170289 OR EP1283041 OR EP1284140 OR EP1302468 OR EP1677827 OR EP1800681 OR EP1944042 OR EP2130534 OR EP2141172 OR US6045829 OR US6068858 OR US6667404 OR US6703403 OR US7141593 OR US7208600 OR US7279582 OR US7378422 OR US7432294 OR US7494660 OR US7666834 OR US7705138 OR US7745444 OR WO0074677 OR WO06090264 OR WO9822106 OR WO9902665 OR WO9208701 OR EP0486948 OR EP0490667 OR EP0532466 OR EP0541168 OR US3903297 OR WO9307128 OR WO9405639 OR WO94014436 OR US5206219 OR EP1773850 OR US7718633 OR WO06014282 OR WO06037827 OR WO06129276 OR WO08041176 OR US7790905 OR US3536809 OR US3598123 OR US3845770 OR US3916899 OR US4008719 OR US5059595 OR US5073543 OR US5120548 OR US5354556 OR US5541206 OR US5591767 OR US5635523 OR US5639476 OR US5674533 OR US5733566 OR US5846987 OR US5886036 OR US6037157 OR US6284767 OR US6977723 OR US7061605 OR WO0004016 OR WO0151919)	62
27	PN=(WO06014282 OR WO06014282 OR WO0182919 OR US5559158 OR WO9509614 OR WO9507696 OR WO94014436 OR WO10037402 OR WO02097114 OR WO10151495 OR WO10150100 OR WO10148006 OR WO10144869 OR WO10143207 OR WO10135690 OR WO10132664 OR WO10132511 OR WO10127272 OR WO10127099 OR WO10122087 OR WO10117276 OR WO10116248 OR WO10115981 OR WO10111196 OR WO10107831 OR WO10100381 OR WO10099527 OR WO10099458 OR WO10096462 OR WO10091413 OR WO10086844 OR WO10077740 OR WO10077734 OR WO10077317 OR WO10077061 OR WO10075065 OR WO10068899 OR WO10065118 OR WO10059883 OR WO10057048 OR WO10047819 OR WO10045266 OR WO10041241 OR WO10038237 OR WO10037566 OR WO10033614 OR WO10030343 OR WO10020799 OR WO10017432 OR WO10014130 OR WO10012466 OR US2010316607 OR US2010304998 OR US2010291688 OR US2010290983 OR US2010273733 OR US2010267635 OR US2010261731 OR US2010227838 OR US2010226943 OR US2010183707 OR US2010179169 OR US2010167268 OR US2010160262 OR US2010158859 OR US2010152147 OR US2010150829 OR US2010137844 OR US2010137843 OR US2010137787 OR US2010137247 OR US2010137246 OR US2010136097 OR US2010136096 OR US2010136095 OR US2010136094 OR US2010135984 OR US2010135983 OR US2010135960 OR US2010135908 OR US2010129357 OR US2010120786 OR US2010113589 OR US2010113359 OR US2010081713 OR US2010069383 OR US2010068786 OR US2010056622 OR US2010041133 OR US2010041014 OR US2010040576 OR US2010021505 OR US2010021427 OR	776

	US2010009970 OR US7785879 OR US7700076 OR IN2008MU01366 OR FR2942717 OR FR2942409 OR EP2239582 OR EP2172193 OR WO09153654 OR WO09153346 OR WO09145956 OR WO09134987 OR WO09134401 OR WO09134120 OR WO09133188 OR WO09129470 OR WO09128947 OR WO09124755 OR WO09123768 OR WO09121997 OR WO09118356 OR WO09115652 OR WO09115594 OR WO09111638 OR WO09111040 OR WO09110940 OR WO09108865 OR WO09105781 OR WO09105776 OR WO09105774 OR WO09105430 OR WO09100532 OR WO09098475 OR WO09098469 OR WO09097670 OR WO09094443 OR WO09094438 OR WO09094205 OR WO09094191 OR WO09094190 OR WO09092897 OR WO09089295 OR WO09089263 OR WO09084036 OR WO09082819 OR WO09082818 OR WO09082448 OR WO09081174 OR WO09079412 OR WO09076195 OR WO09075960 OR WO09073843 OR WO09073713 OR WO09073686 OR WO09064975 OR WO09061856 OR WO09059243 OR WO09058924 OR WO09058923 OR WO09058921 OR WO09058919 OR WO09056818 OR WO09055006 OR WO09053828 OR WO09051840 OR WO09051782 OR WO09048594 OR WO09047264 OR WO09045975 OR WO09042960 OR WO09040818 OR WO09038663 OR WO09037855 OR WO09036341 OR WO09035662 OR WO09027644 OR WO09020457 OR WO09014638 OR WO09009531 OR WO09006203 OR WO09006199 OR WO09005693 OR WO09005674 OR US2009269305 OR US2009257979 OR US2009239831 OR US2009192205 OR US2009175820 OR US2009170880 OR US2009149491 OR US2009143761 OR US2009130059 OR US2009123425 OR US2009098085 OR US2009087483 OR US2009054503 OR US2009053203 OR US2009005387 OR US7491819 OR IN2008MU00496 OR IN2007CH01730 OR IN2007CH01605 OR IN2006MU01872 OR FR2923160 OR EP2135601 OR EP2113510 OR DE102008019916 OR DE102007030695 OR CN101613325 OR CN101569617 OR CN101342185 OR WO09002829 OR WO09002826 OR WO09002821 OR WO08157330 OR WO08157273 OR WO08156632 OR WO08154271 OR WO08153610 OR WO08149228 OR WO08145733 OR WO08145606 OR WO08143500 OR WO08140461 OR WO08140460 OR WO08140459 OR WO08134578 OR WO08133982 OR WO08131505 OR WO08129106 OR WO08118991 OR WO08118849 OR WO08116135 OR WO08115525 OR WO08113364 OR WO08113177 OR WO08112289 OR WO08112156 OR WO08109483 OR WO08109462 OR WO08109154 OR WO08106139 OR WO08106058 OR WO08103949 OR WO08103899 OR WO08101665 OR WO08100867 OR WO08098789 OR WO08097924 OR WO08092006 OR WO08090287 OR WO08073138 OR WO08067164 OR WO08063493 OR WO08062429 OR WO08059046 OR WO08057402 OR WO08055995 OR WO08052737 OR WO08051039 OR WO08041176 OR WO08034039 OR WO08033466 OR WO08033389 OR WO08029417 OR WO08027932 OR WO08022956 OR WO08022242 OR WO08021456 OR WO08017867 OR WO08016522 OR WO08011117 OR WO08011116 OR WO08011045 OR WO08010953 OR WO08010921 OR WO08009689 OR WO08006085 OR WO08005511 OR WO08005276 OR US2008311162 OR US2008292584 OR US2008286344 OR US2008286343 OR US2008260837 OR US2008187516 OR US2008184618 OR US2008124407 OR US2008114065 OR US2008113984 OR US2008113946 OR US2008107749 OR US2008086198 OR US2008069850 OR US2008051323 OR US2008045495 OR US2008039428 OR US2008039393 OR US2008026062 OR US2008026040 OR US2008020370 OR US7364752 OR KR2008083890 OR IN2006MU01934 OR FR2910327 OR EP2003120 OR EP1894559 OR DE102007026701 OR WO07147884 OR WO07144720 OR WO07143433 OR WO07133865 OR WO07129274 OR WO07128349 OR WO07127683 OR WO07126812 OR WO07124383 OR WO07124104 OR WO07121418 OR WO07121416 OR WO07121415 OR WO07121125 OR WO07121124 OR WO07120595 OR WO07115381 OR WO07113856 OR WO07112357 OR WO07112352 OR WO07112345 OR WO07111866 OR WO07106450 OR WO07104748 OR WO07104747 OR WO07103740 OR WO07094825 OR WO07092616 OR WO07090721 OR	

	WO07089907 OR WO07089030 OR WO07087549 OR WO07087548 OR WO07086039 OR WO07083316 OR WO07079260 OR WO07076372 OR WO07073583 OR WO07072503 OR WO07070695 OR WO07070694 OR WO07070643 OR WO07068383 OR WO07068380 OR WO07065256 OR WO07065016 OR WO07064691 OR WO07062528 OR WO07060682 OR WO07056214 OR WO07054085 OR WO07049265 OR WO07042037 OR WO07036671 OR WO07035957 OR WO07034312 OR WO07033208 OR WO07027999 OR WO07025307 OR WO07024678 OR WO07019130 OR WO07019101 OR WO07019100 OR WO07019098 OR WO07016589 OR WO07015824 OR WO07014926 OR WO07014923 OR WO07014922 OR WO07014921 OR WO07014920 OR WO07014919 OR WO07014918 OR WO07013047 OR WO07011833 OR WO07011810 OR WO07009397 OR WO07008780 OR WO07008539 OR WO07008499 OR WO07008496 OR WO07002173 OR WO07002172 OR WO07000779 OR US2007292355 OR US2007264265 OR US2007219239 OR US2007207122 OR US2007203149 OR US2007197646 OR US2007196453 OR US2007196452 OR US2007196325 OR US2007196323 OR US2007191406 OR US2007191335 OR US2007190130 OR US2007190124 OR US2007189977 OR US2007148124 OR US2007128278 OR US2007099941 OR US2007099877 OR US2007098802 OR US2007088053 OR US2007078128 OR US2007036834 OR US2007032477 OR US7288265 OR US7186506 OR JP2007139554 OR IN2005MU01013 OR IN2005MU01012 OR IE2005000699 OR FR2899815 OR EP1832281 OR AU2007231808 OR WO06136175 OR WO06133194 OR WO06130477 OR WO06130426 OR WO06129276 OR WO06129134 OR WO06125042 OR WO06120495 OR WO06119353 OR WO06114001 OR WO06108879 OR WO06108666 OR WO06108556 OR WO06104646 OR WO06101920 OR WO06097323 OR WO06096444 OR WO06091798 OR WO06091692 OR WO06091534 OR WO06090270 OR WO06090264 OR WO06076131 OR WO06066414 OR WO06065947 OR WO06065377 OR WO06060919 OR WO06060918 OR WO06058920 OR WO06057945 OR WO06050999 OR WO06050165 OR WO06041900 OR WO06039488 OR WO06039356 OR WO06037827 OR WO06037617 OR WO06037418 OR WO06037335 OR WO06036816 OR WO06030297 OR WO06028229 OR WO06026924 OR WO06026703 OR WO06024354 OR WO06023400 OR WO06021456 OR WO06020742 OR WO06020415 OR US2006287244 OR US2006241017 OR US2006222627 OR US2006199956 OR US2006172945 OR US2006154857 OR US2006121080 OR US2006105964 OR US2006105045 OR US2006099246 OR US2006084628 OR US2006058286 OR US2006057149 OR US2006046967 OR US2006025726 OR US2006024685 OR US2006024368 OR US2006024365 OR US7141593 OR US7058616 OR IN2005KO00084 OR IN2004MU00256 OR IE2005000643 OR EP1656951 OR EP1637885 OR DE102005053679 OR DE102005012681 OR CN1768733 OR CN1727337 OR WO05124563 OR WO05122741 OR WO05121378 OR WO05116081 OR WO05115469 OR WO05113059 OR WO05112929 OR WO05111006 OR WO05097818 OR WO05082385 OR WO05082331 OR WO05077969 OR WO05077925 OR WO05077050 OR WO05076892 OR WO05074575 OR WO05072706 OR WO05070901 OR WO05063213 OR WO05062979 OR WO05062952 OR WO05061487 OR WO05060663 OR WO05058248 OR WO05054297 OR WO05051419 OR WO05051358 OR WO05051354 OR WO05043118 OR WO05042517 OR WO05042045 OR WO05042020 OR WO05039587 OR WO05037246 OR WO05037196 OR WO05035525 OR WO05030790 OR WO05028502 OR WO05027979 OR WO05018530 OR WO05016386 OR WO05007681 OR WO05007656 OR WO05007070 OR WO05001027 OR WO05000405 OR US2005281868 OR US2005276836 OR US2005267105 OR US2005244818 OR US2005244339 OR US2005239880 OR US2005215545 OR US2005215544 OR US2005215543 OR US2005209287 OR US2005203150 OR US2005203129 OR US2005187267 OR US2005182105 OR US2005176703 OR US2005176658 OR US2005171038 OR US2005171037 OR US2005159469 OR US2005148623 OR US2005143404 OR US2005131216 OR US2005131042 OR US2005131017 OR US2005129777 OR US2005101561 OR	

	US2005084529 OR US2005079200 OR US2005079138 OR US2005064517 OR US2005059578 OR US2005048112 OR US2005033132 OR US2005031713 OR US2005031620 OR US2005026902 OR US2005025761 OR US2005020580 OR US2005020548 OR US2005015039 OR US2005013863 OR US2005009848 OR US2005009810 OR US2005009766 OR US2005009756 OR IN2004MU01092 OR GB2407089 OR FR2869045 OR FR2865133 OR EP1604697 OR DE10333099 OR DE10333098 OR CN1565442 OR WO04112747 OR WO04112724 OR WO04101512 OR WO04098531 OR WO04092162 OR WO04092161 OR WO04091578 OR WO04089423 OR WO04089182 OR WO04087140 OR WO04087139 OR WO04085406 OR WO04084892 OR WO04084876 OR WO04074257 OR WO04069166 OR WO04065563 OR WO04064846 OR WO04064845 OR WO04062600 OR WO04060370 OR WO04058253 OR WO04056770 OR WO04056181 OR WO04055163 OR WO04055016 OR WO04055012 OR WO04055011 OR WO04055010 OR WO04054974 OR WO04054586 OR WO04054581 OR WO04052862 OR WO04052296 OR WO04046309 OR WO04045586 OR WO04045519 OR WO04041818 OR WO04033663 OR WO04029201 OR WO04028455 OR WO04024683 OR WO04022066 OR WO04013110 OR WO04012732 OR WO04011019 OR WO04010937 OR WO04009073 OR WO04006847 OR WO04004660 OR WO04004658 OR WO04003514 OR WO04003512 OR WO04002428 OR WO04002410 OR US2004265889 OR US2004229908 OR US2004219155 OR US2004214764 OR US2004213779 OR US2004197321 OR US2004192704 OR US2004192624 OR US2004171568 OR US2004167123 OR US2004167096 OR US2004162254 OR US2004162253 OR US2004161429 OR US2004131622 OR US2004131621 OR US2004131610 OR US2004127689 OR US2004106136 OR US2004081957 OR US2004077859 OR US2004024031 OR US2004022873 OR US2004019027 OR US2004009124 OR JP2004244347 OR JP2004161625 OR FR2841785 OR EP1452605 OR EP1382692 OR DE202004009061 OR DE202004009060 OR CN1554647 OR AU2004201149 OR WO03105826 OR WO03101481 OR WO03099851 OR WO03090690 OR WO03082248 OR WO03082241 OR WO03080120 OR WO03075010 OR WO03070976 OR WO03066830 OR WO03062238 OR WO03057173 OR WO03051361 OR WO03051301 OR WO03049746 OR WO03046559 OR WO03041694 OR WO03035111 OR WO03035074 OR WO03024932 OR WO03020716 OR WO03020200 OR WO03014105 OR WO03013535 OR WO03013534 OR WO03012131 OR WO03006506 OR US2003236255 OR US2003206909 OR US2003180279 OR US2003152913 OR US2003147952 OR US2003138483 OR US2003109468 OR US2003105121 OR US2003082594 OR US2003073069 OR US2003045501 OR US2003027867 OR US2003007983 OR TW550073 OR DE10145361 OR DE10131036 OR CA2607992 OR WO02099387 OR WO02096395 OR WO02090993 OR WO02087585 OR WO02087583 OR WO02081456 OR WO02079157 OR WO02078628 OR WO02074777 OR WO02072109 OR WO02070470 OR WO02062123 OR WO02056902 OR WO02056861 OR WO02053138 OR WO0234237 OR WO0233638 OR WO0230514 OR WO0227321 OR WO0223186 OR WO0222781 OR WO0222076 OR WO0220057 OR WO0210124 OR WO0208226 OR WO0206292 OR WO0206190 OR WO0200168 OR US2002198231 OR US2002151542 OR US2002147197 OR US2002142050 OR US2002128301 OR US2002119916 OR US2002119444 OR US2002114848 OR US2002099013 OR US2002094522 OR US2002068761 OR US2002064838 OR US2002061836 OR US2002048748 OR US2002031558 OR US2002022034 OR US2002016293 OR US6489098 OR US6419934 OR US6391919 OR JP2002371042 OR JP2002214195 OR JP2002191399 OR JP2002138080 OR JP2002020283 OR EP1207394 OR EP1166782 OR DE10040592 OR CN1334122 OR CN1330922 OR WO0197749 OR WO0196611 OR WO0196329 OR WO0192288 OR WO0182927 OR WO0181926 OR WO0180896 OR WO0178681 OR WO0168086 OR WO0156547 OR WO0154729 OR WO0154701 OR WO0154652 OR WO0152821 OR WO0151014 OR WO0147511 OR WO0141742 OR WO0137808 OR WO0134119 OR WO0134118 OR WO0129037 OR WO0128555 OR WO0128532 OR WO0125200 OR WO0125199 OR WO0121603 OR WO0112168 OR WO0110456 OR WO0110454 OR WO0110387 OR WO0103708 OR	

	US2001041706 OR US6232333 OR JP2001187746 OR IT99MI1661 OR EP1109019 OR CA2608807 OR CA2293913 OR WO0079268 OR WO0078996 OR WO0074677 OR WO0072827 OR WO0069255 OR WO0068203 OR WO0067801 OR WO0066173 OR WO0059486 OR WO0059475 OR WO0056303 OR WO0052034 OR WO0051641 OR WO0050043 OR WO0050007 OR WO0045844 OR WO0043515 OR WO0043017 OR WO0042211 OR WO0040269 OR WO0038679 OR WO0038650 OR WO0035472 OR WO0035419 OR WO0033820 OR WO0033654 OR WO0027196 OR WO0025784 OR WO0021514 OR WO0009150 OR WO0006143 OR WO0004016 OR WO0000479 OR US6143742 OR US6068858 OR US6040434 OR JP2000309598 OR WO9967428 OR WO9967427 OR WO9966936 OR WO9964001 OR WO9963998 OR WO9961658 OR WO9959585 OR WO9955843 OR WO9955370 OR WO9948526 OR WO9948504 OR WO9947146 OR WO9939732 OR WO9938961 OR WO9933795 OR WO9933477 OR WO9925352 OR WO9913914 OR WO9908676 OR US5948436 OR US5945413 OR JP11239486 OR FR2773994 OR WO9857648 OR WO9852571 OR WO9847492 OR WO9846241 OR WO9833067 OR WO9822106 OR WO9820888 OR WO9808539 OR WO9804290 OR US5849793 OR US5723490 OR DE19703131 OR WO9746222 OR WO9742962 OR WO9727856 OR WO9727480 OR WO9708180 OR WO9701349 OR WO9626734 OR WO9604913 OR WO9604232 OR US5567823 OR GB2292146 OR EP0728481 OR EP0691345 OR WO9533464 OR WO9520384 OR WO9511224)	
28	20 and 27	657
29	20 or 27	968
30	PN=(US5484801 OR US5541206 OR US5635523 OR US5648497 OR US5674882 OR US5886036 OR US5914332 OR US5948436 OR US6037157 OR US6284767 OR US6703403 OR US6911214 OR US7432294 OR US7141593 OR US6521651 OR US6458818 OR US6284767 OR US6232333)	12
31	20 and ((heat or thermal*) w4 stabili*)	13
32	(PA=("ABBOTT_LAB" OR "ABBOTT_LAB_INC" OR "ABBOTT_LAB_LTD" OR "ABBOTT_LABOR" OR "ABBOTT_LABOR_US" OR "ABBOTT_LABORATORIES" OR "ABBOTT_LABORATORIES_A_CORP" OR "ABBOTT_LABORATORIES_ABBOTT_PARK" OR "ABBOTT_LABORATORIES_ABBOTT_PARK_IL" OR "ABBOTT_LABORATORIES_ABBOTT_PARK_IL_A_CORP" OR "ABBOTT_LABORATORIES_ABBOTT_PARK_ILL" OR "ABBOTT_LABORATORIES_ABBOTT_PARK_ILL_US" OR "ABBOTT_LABORATORIES_ABBOTT_PARK_ILLINOIS" OR "ABBOTT_LABORATORIES_AN_IL_CORP" OR "ABBOTT_LABORATORIES_CHAD" OR "ABBOTT_LABORATORIES_PATENT_AND_TRADEMARK_DEPARTMEN"))	6271
33	(PA=("GLAXOSMITHKILNE_CONSUMER_HEALT" OR "GLAXOSMITHKLINE" OR "GLAXOSMITHKLINE_BIOLOG_S_A" OR "GLAXOSMITHKLINE_BIOLOG_S_A" OR "GLAXOSMITHKLINE_BIOLOG_SA" OR "GLAXOSMITHKLINE_BIOLOG_SA" OR "GLAXOSMITHKLINE_BIOLOGICALS_S_A" OR "SMITH_KLINE_BECKMAN_CORP" OR "SMITH_KLINE_BEECHAM_CORP" OR "SMITH_KLINE_BEECHAM_CORP" OR "SMITH_KLINE_BEECHAM_CORPORATION" OR "SMITH_KLINE_BEECHAM_CORPORATION" OR "SMITH_KLINE_BEECHAM_P_L_C" OR "SMITH_KLINE_BEECHAM_P_L_C" OR "SMITH_KLINE_BEECHAM_PLC" OR "SMITHKLIN_BEECHAM_CORP" OR "SMITHKLINE_AND_FRENCH_LABORATORIES_LIMITED"))	1890
34	(PA=("HOFFMANN_LA_ROCHE_CO" OR "HOFFMANN_LA_ROCHE_CO_AG" OR "HOFFMANN_LA_ROCHE_CO_AG_F" OR "HOFFMANN_LA_ROCHE_CO_F_AG" OR "HOFFMANN_LA_ROCHE_ET_CIE_SA" OR "HOFFMANN_LA_ROCHE_ET_CIE_SA_CH" OR "HOFFMANN_LA_ROCHE_ET_CO" OR "HOFFMANN_LA_ROCHE_F" OR "HOFFMANN_LA_ROCHE_F_AND_CIE_SA" OR	9040

	"HOFFMANN_LA_ROCHE_F_AND_CO_A_G" OR "HOFFMANN_LA_ROCHE_F_AND_CO_AG" OR "HOFFMANN_LA_ROCHE_INC" OR "HOFFMANN_LA_ROCHE_INC_US" OR "HOFFMANN_LA_ROCHE_LIMITED" OR "HOFFMANN_LA_ROCHE_LTD" OR "ROCHE_DIAGNOSTICS_CORP" OR "ROCHE_DIAGNOSTICS_GMBH" OR "ROCHE_DIAGNOSTICS_INT" OR "ROCHE_DIAGNOSTICS_OPERATIONS" OR "ROCHE_DIAGNOSTICS_OPERATIONS_I" OR "ROCHE_DIAGNOSTICS_OPERATIONS_INC" OR "ROCHE_HOLDINGS_INC" OR "ROCHE_MOLECULAR_SYSTEMS_INC" OR "ROCHE_PALO_ALTO_LLC" OR "ROCHE_PRODUCTS_LIMITED" OR "ROCHE_PRODUCTS_LTD"))	
35	(PA=("BRISTOL_MYERS" OR "BRISTOL_MYERS" OR "BRISTOL_MYERS_CANADA_LIMITED" OR "BRISTOL_MYERS_CANADA_LTD" OR "BRISTOL_MYERS_CANADA_LTD" OR "BRISTOL_MYERS_CO" OR "BRISTOL_MYERS_CO" OR "BRISTOL_MYERS_CO_NEW_YORK_N_Y_US" OR "BRISTOL_MYERS_CO_NEW_YORK_N_Y_US" OR "BRISTOL_MYERS_CO_NEW_YORK_N_Y_V_ST_A" OR "BRISTOL_MYERS_SQIBB_CO" OR "BRISTOL_MYERS_SQUIBB" OR "BRISTOL_MYERS_SQUIBB_CO" OR "BRISTOL_MYERS_SQUIBB_CO_N_D_GES_D_STAATES__" OR "BRISTOL_MYERS_SQUIBB_CO_NEW_YORK" OR "BRISTOL_MYERS_SQUIBB_CO_NEW_YORK_N_Y_US" OR "BRISTOL_MYERS_SQUIBB_CO_PRINCE" OR "BRISTOL_MYERS_SQUIBB_CO_PRINCETON" OR "BRISTOL_MYERS_SQUIBB_COMPANY" OR "BRISTOL_MYERS_SQUIBB_COMPANY_PRINCETON" OR "BRISTOL_MYERS_SQUIBB_PHARMA_COMPANY" OR "SQUIBB_BRISTOL_MYERS_CO"))	5845
36	(PA=("SCHERING_A_G" OR "SCHERING_A_G_A_BERLIN_ET_A_BERGKAMEN_ALLEMAGNE" OR "SCHERING_AG_1000_BERLIN_UND_4619_BERGKAMEN" OR "SCHERING_AG_1000_BERLIN_UND_4709_BERGKAMEN_DE" OR "SCHERING_AG_BERLIN" OR "SCHERING_AG_BERLIN_BERGKAMEN_1000_BERLIN_DE" OR "SCHERING_AG_BERLIN_UND_BERGKAMEN" OR "SCHERING_AG_BERLIN_UND_BERGKAMEN_1000_BERLIN_DE" OR "SCHERING_AG_WB" OR "SCHERING_AG_WB_DE" OR "SCHERING_AGROCHEMICALS_LIMITED" OR "SCHERING_AGROCHEMICALS_LTD" OR "SCHERING_AKTIENGESELLSCHAFT" OR "SCHERING_AKTIENGESELLSCHAFT_BERLIN" OR "SCHERING_CORP" OR "SCHERING_CORP_US" OR "SCHERING_CORPORATION" OR "SCHERING_KAHLBAUM_A_G" OR "SCHERING_KAHLBAUM_AG" OR "SCHERING_KAHLBAUM_AKTIENGESELLSCHAFT" OR "SCHERING_PLOUGH_CORP" OR "SCHERING_PLOUGH_CORPORATION" OR "SCHERING_PLOUGH_HEALTHCARE" OR "SCHERING_PLOUGH_HEALTHCARE_PRODUCTS_INC"))	8849
37	(PA=("SCHERING_A_G" OR "SCHERING_A_G_A_BERLIN_ET_A_BERGKAMEN_ALLEMAGNE" OR "SCHERING_AG_1000_BERLIN_UND_4619_BERGKAMEN" OR "SCHERING_AG_1000_BERLIN_UND_4709_BERGKAMEN_DE" OR "SCHERING_AG_BERLIN" OR "SCHERING_AG_BERLIN_BERGKAMEN_1000_BERLIN_DE" OR "SCHERING_AG_BERLIN_UND_BERGKAMEN" OR "SCHERING_AG_BERLIN_UND_BERGKAMEN_1000_BERLIN_DE" OR "SCHERING_AG_WB" OR "SCHERING_AG_WB_DE" OR "SCHERING_AGROCHEMICALS_LIMITED" OR "SCHERING_AGROCHEMICALS_LTD" OR "SCHERING_AKTIENGESELLSCHAFT" OR "SCHERING_AKTIENGESELLSCHAFT_BERLIN" OR "SCHERING_CORP" OR	8849

	"SCHERING_CORP_US" OR "SCHERING_CORPORATION" OR "SCHERING_KAHLBAUM_A_G" OR "SCHERING_KAHLBAUM_AG" OR "SCHERING_KAHLBAUM_AKTIENGESELLSCHAFT" OR "SCHERING_PLOUGH_CORP" OR "SCHERING_PLOUGH_CORPORATION" OR "SCHERING_PLOUGH_HEALTHCARE" OR "SCHERING_PLOUGH_HEALTHCARE_PRODUCTS_INC"))	
38	29 and 32	46
39	29 and 33	6
40	29 and 34	31
41	29 and 35	35
42	29 and 36	21
43	29 and 37	21
44	29 and ((heat or thermal*) w4 stabili*)	17
45	29 and cl=(synthes*)	64
46	45 and (crystal* or polymorph*)	49
47	29 and TAC=(stabil*)	87
48	29 and (stabil*)	690
49	29 and ((heat or thermal*) w20 stabili*)	24
50	29 and tac=(polymorph*)	42
51	29 and tac=(solution* or liquid or solvent*)	322
52	51 and 47	62
53	29 and tac=(solution* or liquid or solvent* or suspen* or dispers*)	356
54	53 and 47	66
55	29 and tac=(tablet* and (solid* or dispersed* or layer*))	60
56	29 and tac=(pharmacokinetic* or ((improv* or enhanc* or increas*) w10 (absorp* or absorb* or bioavailab*)))	100
57	29 and ((improv* or enhanc* or increas*) w10 (absorp* or absorb* or bioavailab*))	429
58	57 and (aqueous or gel* or solution* or liquid*)	429
59	56 and (aqueous or gel* or solution* or liquid*)	100
60	57 and tac=(aqueous or gel* or solution* or liquid*)	180
61	56 and tac=(aqueous or gel* or solution* or liquid*)	45
62	29 and tac=((sustain* or different*) w4 (deliver* or release*))	43
63	UC=("424/489" OR "424/451" OR "424/497" OR "424/468" OR "424/455" OR "424/490" OR "424/456")	10480
64	IC=("A61K47/38" OR "A61K47/10" OR "A61K47/42" OR "A61K47/36" OR "A61K9/14" OR "A61K9/10" OR "A61K9/16" OR "A61K9/22" OR "A61K9/20" OR "A61K9/00" OR	more than

	"A61K9/50" OR "A61K9/52" OR "A61K9/08" OR "A61K9/48" OR "A61K31/70" OR "A61K9/70")	100,000
65	(63 or 64) and 29	306
66	65 not 62	271
67	UC=("424/464" OR "424/400" OR "424/450" OR "424/465" OR "424/486")	12911
68	(63 or 64 or 67) and 29 not 62	279
69	29 and TAC=(liposom*)	64
70	29 and tac=(emulsion* or cream*)	66
71	29 and TAC=(microparticl* or nanoparticl*)	45
72	29 and TAC=(transdermal* or mucos* or vagin*)	113
73	UC=(424/451 OR 424/433 OR 424/434 OR 424/436)	3017
74	29 and 73	21
75	29 and (liposom*)	336
76	29 and (emulsion* or cream*)	606
77	29 and (transdermal* or mucos* or vagin*)	578
78	29 and tac=((drug* or therap*) w20 (resist*))	108
79	29 and tac=((detect* or measur* or quantif* or assess*) w5 (HIV or AIDS or viral or virus))	45
80	29 and tac=(apopt* or cancer* or prolifer*)	224
81	UC=("435/5" OR "514/220" OR "514/269" OR "424/85.5" OR "514/365" OR "514/3.8" OR "514/1.1" OR "514/2")	27611
82	IC=("A61P31/00" OR "A61P31/18" OR "A61P31/12" OR "A61P31/14" OR "A61K31/427" OR "A61K31/00" OR "A61K31/426" OR "A61K38/00" OR "A61K9/00")	more than 100,000
83	tac=(protease inhibitor*) and (81 or 82)	2815
84	83 and peptid*	2095
85	83 and (HIV OR AIDS or retroviral or anti*retroviral* or immunodefic*)	1952
86	84 and 85	1453
87	86 and 29	268
88	RF=(122302)	931
89	87 not 88	18
90	tac=((antiviral* or protease inhibitor* or ant*retroviral*) and (CYP3A4 or cytochrome p*450))	169
91	90 and (heterocycl* or thiazo*)	96
92	91 not 88	29

93	86 and (carbamate or urea)	714
94	pn=(US20080312300)	1
95	pn=US20070244168	1
96	PN=(US5541206 OR US5567823 OR US5914332)	3
97	PN=(US7758886 OR US2009098200 OR US2008286344 OR US2007292355 OR US2007116729 OR US2005244339 OR EP1712220 OR WO09040818 OR WO10037402 OR WO09040818 OR WO08140461 OR WO08097924 OR WO08075207 OR WO07117482 OR WO07061529 OR WO06108556)	11
98	PN=(WO07068383 OR US2005089840 OR WO10107831 OR US7572456 OR WO08100867 OR US2010260709 OR EP1808177 OR US7589233 OR US2005187267 OR WO06091798 OR US2009105187 OR US2006141033 OR EP1709037 OR WO06020742 OR WO10045266 OR WO09051840 OR US2008292584 OR WO09088719 OR US2006122166 OR WO07089907 OR WO08118849 OR US7127285 OR US2005203152 OR US6946469 OR EP1880715 OR WO07103934 OR US2005009768 OR EP2172193 OR US7018650 OR US2007010489 OR US2007112003 OR US2009098085 OR US2010003214 OR US2010056622 OR US2009270336 OR US2008069850 OR US7659275 OR EP2130534 OR EP1421946 OR WO08005276 OR WO08022956 OR US2008045514 OR WO05042045 OR WO09134401 OR EP1418174 OR US2010069383 OR US2006040257 OR US2007219239 OR WO07061529 OR US2006160045 OR EP2269657 OR US7008946 OR US2009291952 OR US7320961 OR WO09094443 OR US2010022578 OR US7208600 OR WO09056818 OR WO07124224 OR WO08059046 OR WO09040818 OR WO07022255 OR WO05097818 OR US2005244816 OR EP1810976 OR US2009149947 OR WO07035957 OR US2008113984 OR US2007099941 OR US2008154210 OR US2009137495 OR US2008027144 OR WO08029417 OR US2005020517 OR US2007087048 OR US2010098678 OR US2010331331 OR US2008187516 OR WO05063213 OR WO09014638 OR US2006057149 OR US2006052408 OR US7696226 OR US2006040867 OR US2009257979 OR US2009306224 OR US2011009411 OR US2008260837 OR US2008261978 OR WO05028502 OR US2009076045 OR US2008234231 OR US2005244819 OR WO06039488 OR US2006121080 OR WO05027855 OR US2010111930 OR WO09005674 OR US7183416 OR WO08140461 OR WO08133982 OR US2006068027 OR EP1800681 OR WO05062952 OR WO10132511 OR WO07019101 OR WO09073686 OR WO07070695 OR US2010261731 OR US7758886 OR WO08057402 OR US2008311162 OR US2005137213 OR US2005009810 OR US2009093454 OR WO07124104 OR WO05102392 OR US2010068786 OR WO07079260 OR US7098213 OR WO08021456 OR US6932983 OR US7776863 OR WO07073583 OR US6896900 OR US7364752 OR WO07014921 OR US2009143761 OR EP2258344 OR WO09042960 OR WO06066958 OR WO10054042 OR EP1002065 OR US2007190067 OR WO09036341 OR WO05018530 OR WO06017341 OR WO09082819 OR WO08106139 OR US2008312300 OR US7157561 OR US2009239831 OR US2007232536 OR US2008200533 OR US2010298209 OR WO08016522 OR US2007167380 OR US7157489 OR US2010183707 OR WO07121415 OR WO07079260 OR US2010075914 OR US7189718 OR US2008045537 OR US2005013854 OR WO08156632 OR US2006099170 OR EP1591444 OR WO10096462 OR WO08011045 OR US2005276842 OR WO05039587 OR US7666834 OR EP1569647 OR US2010029566 OR US2005244339 OR WO06066958 OR US2007116729 OR WO07002173 OR US2008293711 OR US2009324593 OR WO08011117 OR WO08054454 OR US2009317418 OR WO08140460 OR WO07112352 OR WO07097936 OR WO10068899 OR US2007128278 OR US2010135984 OR WO07126812 OR US2010226882 OR US2009143314 OR WO07014919 OR US2005244818 OR US2005239880 OR WO09153654 OR US2008214527 OR EP1886994 OR WO06052452 OR WO07120595 OR US2011008430 OR WO07056215 OR	645

	WO08051039 OR US2006205697 OR WO05004873 OR US2009130059 OR WO05102392 OR WO10121351 OR EP1708740 OR US2005020548 OR US2010221259 OR US2010119479 OR US2005215545 OR EP1284140 OR US2007179157 OR WO05077050 OR US2008181948 OR WO08109483 OR US2009105147 OR EP1458447 OR US2010124543 OR US2009238794 OR US2007059360 OR US2005119189 OR US2008306019 OR US7288265 OR WO07115181 OR US2010172993 OR WO06037418 OR US2007161611 OR EP2266971 OR US7759336 OR WO06050165 OR WO09094190 OR US2009075939 OR US2006084628 OR US2009036357 OR WO07086039 OR US2009170856 OR WO05077969 OR US2010137247 OR WO07143847 OR US2010069489 OR US7148243 OR EP1583542 OR WO06076131 OR US2011003735 OR US2010136129 OR WO09059243 OR US2010144804 OR US2006100139 OR US2006223874 OR US2006264618 OR WO09076173 OR US2007189977 OR EP0988042 OR WO07002238 OR EP1083898 OR WO05110411 OR US7335727 OR WO09094438 OR WO09005693 OR US7785879 OR WO08154271 OR US2010135960 OR WO07000234 OR US2009197888 OR US2010183716 OR US2007191335 OR WO08103949 OR US2005215543 OR US2010021540 OR WO07056215 OR EP1248600 OR US2005202094 OR US2005148548 OR US2005090450 OR WO10111196 OR US2007026056 OR EP1171137 OR WO09058919 OR US2007141643 OR WO05042517 OR WO09105776 OR US2009232886 OR WO10143207 OR EP1604697 OR US2005075326 OR WO07112357 OR US7820681 OR US2007249692 OR US2008096848 OR WO05102328 OR WO06076131 OR US7012129 OR WO05007070 OR US2010152214 OR WO06120495 OR US2010226990 OR US2010120786 OR WO06129134 OR WO08140459 OR US2010048559 OR WO06090270 OR US2009012034 OR EP1637528 OR US2005065319 OR WO07127683 OR EP2206500 OR US2007218486 OR US2006105964 OR US2008113946 OR US2009016990 OR US2011003764 OR EP1912999 OR US2008039393 OR EP1637885 OR US2008045530 OR US2007088053 OR WO09134120 OR US2005009766 OR WO08113177 OR WO06130477 OR WO06044968 OR US2008214575 OR WO09058921 OR WO06105374 OR US6911214 OR US2010136097 OR US2006193888 OR WO05079752 OR US6878728 OR WO05042570 OR WO07133865 OR US2008280849 OR WO07011707 OR US2009131414 OR WO09048594 OR US2006025715 OR US7745444 OR WO07100739 OR WO07056208 OR WO09064975 OR WO08017867 OR WO05111006 OR US2009306130 OR US2006193887 OR WO06028896 OR WO07115181 OR WO09055006 OR US2006172945 OR US2010129321 OR US2007181133 OR WO07111866 OR WO10122087 OR WO07014925 OR US7317029 OR WO05000405 OR WO07016589 OR WO07065016 OR WO07015824 OR WO10009335 OR WO05058248 OR WO09002829 OR WO05035525 OR WO07056214 OR US2008138315 OR WO09079412 OR US2009123515 OR US2006068389 OR EP2223929 OR US2009068719 OR WO06125042 OR WO07060682 OR WO08033389 OR WO10065079 OR WO08097924 OR US2009170880 OR WO09142842 OR WO08145733 OR US2009208576 OR US2008267915 OR US2005009756 OR US2010189687 OR WO05001027 OR US2007148124 OR US2006241150 OR US2007253957 OR US2009258011 OR US2010015090 OR WO09108865 OR WO10132494 OR WO06060918 OR EP1542012 OR WO06023400 OR US2010291034 OR EP1569933 OR US2010152147 OR US2007093456 OR US2008184618 OR US2006287316 OR WO09094205 OR US2006287244 OR US2006018934 OR US2009143427 OR US2010173921 OR US2010113589 OR US2006154857 OR US2007190124 OR US2009209583 OR EP1441735 OR US2005031713 OR WO06037827 OR WO07112345 OR WO07087548 OR WO06041900 OR WO10127272 OR US2005171037 OR US7569678 OR WO10047819 OR US2007190130 OR US2006205674 OR US2010144647 OR WO06026703 OR US2010062970 OR US2008214503 OR US2009170806 OR US7109172 OR US2009099154 OR WO05082331 OR US2009274765 OR US2005080017 OR US2007043000 OR US2010226883 OR US2007203520 OR US2008161324 OR US2009005387 OR US6967023 OR WO06041900 OR WO07042037 OR WO10115981 OR	

	US2007148684 OR US2008220441 OR WO07087549 OR US2005182105 OR US7741345 OR WO06005720 OR WO09038663 OR US2010041014 OR WO10132163 OR US7625897 OR US2008267906 OR US2006134646 OR WO05062979 OR WO07117482 OR WO07119006 OR WO09084036 OR US7718633 OR US2009274650 OR WO05107742 OR WO09094191 OR EP1180020 OR WO10099458 OR US7629337 OR EP1175205 OR US2006264434 OR US7527973 OR US2008070951 OR US2006099246 OR EP1712231 OR US2006193890 OR US7157433 OR WO05082364 OR US2010255032 OR WO08118991 OR WO08116165 OR US2005287597 OR WO06066414 OR WO09126293 OR WO08116165 OR US2007270383 OR WO07089906 OR US2006025462 OR US7157495 OR US2007264265 OR EP1786363 OR US2010021505 OR US7517992 OR WO09121997 OR WO07014923 OR US2007078187 OR EP1284741 OR US2007202051 OR US7825121 OR WO08112289 OR WO10065118 OR US2009324543 OR EP1765337 OR WO06108666 OR EP1242426 OR WO05051358 OR WO05060663 OR WO07100376 OR WO09083042 OR WO09081174 OR EP1194141 OR US2005074414 OR WO09082818 OR WO06133194 OR US2006246130 OR US2005261364 OR US2007167497 OR US7511124 OR US2008262058 OR US2008293664 OR EP2189159 OR WO08115525 OR US2009098200 OR EP1762567 OR US2005276836 OR US2009306112 OR US2010260715 OR US2009087841 OR US2010286032 OR WO08131505 OR WO05007656 OR US2009269305 OR WO05102391 OR US2005250764 OR EP1068219 OR US2010113359 OR US2009022823 OR EP1676551 OR US2008241289 OR WO07076372 OR US2010227774 OR US7622497 OR US7378422 OR US2006229336 OR WO06058920 OR WO09134616 OR WO07106450 OR WO08090287 OR US2009011013 OR US7635722 OR US2006223821 OR US2007244113 OR US2011008288 OR US2007197646 OR US2010221217 OR WO10017432 OR EP2153826 OR US2007287664 OR US2005048116 OR WO10077317 OR EP1712220 OR US6884576 OR US2005070489 OR EP1524988 OR US7553844 OR US2009202485 OR US2009192205 OR US2007082883 OR US2009123425 OR US2005214749 OR WO06002248 OR WO09051782 OR EP2258346 OR WO09058924 OR US2005176703 OR US2009074721 OR US2009087483 OR WO09111040 OR US2005075331 OR WO05011709 OR US7547678 OR EP2003120 OR WO10148006 OR US2007190558 OR US2008220079 OR US2008200503 OR WO09105774 OR WO07143433 OR US2010256041 OR US2010048500 OR US2008020981 OR US2007009533 OR WO10116248 OR US2008194523 OR US2008248126 OR US2010273733 OR WO07025307 OR US2008113046 OR WO05004881 OR US2005148561 OR US2007031408 OR US2008311079 OR US2007032477 OR WO06057637 OR US2005215544 OR WO08127291 OR WO08144458 OR US2007124152 OR US2007078128 OR WO09040818 OR US2008124407 OR US2010136096 OR EP1919899 OR WO06057945 OR US2008286355 OR US2006142241 OR US2007232532 OR US2007232531 OR US2006067940 OR US2010330086 OR US7666419 OR US2009281141 OR WO05111112 OR WO08055995 OR US2008286343 OR US2010305172 OR EP1560827 OR WO07019130 OR US2005171038 OR EP1892530 OR EP0876387 OR EP1624899 OR US2006025441 OR WO07047371 OR EP1701942 OR WO07121418 OR US2005009848 OR US2007196453 OR US2005143404 OR US2005015039 OR WO08034039 OR WO10041241 OR EP2003120 OR US2010040561 OR WO06014282 OR WO10075065 OR US2005009767 OR US2010221214 OR US2010183715 OR WO07014926 OR WO08147468 OR EP1677827 OR WO09002823 OR WO08101665 OR US2008085918 OR US7384909 OR EP1733725 OR WO07070643 OR US7754718 OR WO06041538 OR US2010221215 OR US2006088545 OR WO09075960 OR US2007009593 OR US6844340 OR WO07090721 OR WO07087548 OR WO05009413 OR US2007264334 OR WO09115652 OR WO05051419 OR WO10089767 OR US2008125376 OR US7501455 OR US2008107749 OR US2011008429 OR US2005033132 OR US7354906 OR WO06030297 OR WO07134037 OR US7662987 OR US2007196323 OR US2005084529 OR US2009105302 OR US2006127938 OR WO05058841 OR WO05062979 OR US2007054842 OR WO05016386 OR WO05042020 OR	

	WO09045975 OR US2009226431 OR WO07129274 OR US2009105791 OR EP1944300 OR WO09002821 OR US7141593 OR US2009274657 OR US2010202963 OR WO06050930 OR EP1658052 OR WO08011116 OR US2010015727 OR US7659405 OR US2005013863 OR US2011015149 OR WO08109154 OR US2008299203 OR US2007031822 OR US2010034827 OR EP0933372 OR WO05046575 OR WO09134987 OR EP1733725 OR US2009297476 OR US2007259014 OR US2008207620 OR US2006241017 OR WO10037402 OR WO06114001 OR US2007292355 OR WO08041176 OR US2010320099 OR US2009202486 OR US2009110720 OR US2005032042 OR US2009247544 OR WO06135480 OR US2005048112 OR EP1632479 OR US2009018162 OR US2007142365 OR US2010173282 OR US2008076669 OR WO09089295 OR US2007249601 OR US2010136094 OR US2009175820 OR US2006193886 OR US2009053305 OR WO05039551 OR US2008287488 OR WO07124383 OR US2009093467 OR WO07129274 OR WO07062528 OR EP1183026 OR WO05037860 OR US2006024685 OR US2007032435 OR EP2017269 OR WO05082362 OR US2005020580 OR WO09129470 OR WO08010953 OR WO06060919 OR US2009053203 OR WO09123768 OR WO06091534 OR US2009318519 OR US2006046967 OR US2005131042 OR US6962900 OR WO09014638 OR WO06053255 OR WO06031825 OR WO07014922 OR WO07064691 OR US2010178340 OR US2007203149 OR EP1806157 OR WO06026703 OR WO06108879 OR WO09008989 OR WO09058923 OR WO10059883 OR WO06130426 OR WO07092616 OR US2007208009 OR US2008181868 OR EP1591444 OR US2010272682 OR WO08075207 OR US2009281132 OR WO07121124 OR WO09145956 OR US2008146595 OR US7592368 OR WO09098469 OR US7244716 OR US7625949 OR US2010221216 OR EP2177523 OR US2007105781 OR US2009149491 OR US2010150829 OR EP1133485 OR EP2080511 OR US2008255073 OR US2007059308 OR US2007099877 OR WO05061487 OR WO07019100 OR US2005148623 OR US2007099276 OR WO05077925 OR WO09118356 OR WO09089263 OR WO06022759 OR US2008004242 OR WO07011810 OR EP1894559 OR WO08033466 OR US2010297271 OR US2007213305 OR US2006234982 OR WO05066131 OR WO08157273 OR US2010004481 OR WO07070694 OR WO08060578 OR EP1732575 OR EP1571146 OR US2009247512 OR US2005159469 OR US2006211107 OR WO07121125 OR WO09153346 OR WO08092006 OR US7468274 OR EP2058006 OR WO10132664 OR US2007098802 OR US2007088015 OR US2007149565 OR US6929803 OR US2010316607 OR WO08067164 OR EP1732604 OR US2006276885 OR EP2103623 OR US2009131363 OR US2005176658 OR WO05122741 OR US2006276884 OR WO06097323 OR US2010167268 OR WO07121416 OR WO06096444 OR US2011015216 OR US2009155209 OR US2010266543 OR WO08052737 OR WO06119353 OR WO08008120 OR US6946465 OR US7348345 OR US2007117859 OR WO07065256 OR WO07054085 OR WO07089030 OR WO08103899 OR WO08109462 OR EP2144599 OR US2008014228 OR US7365221 OR US7292944 OR US2006003942 OR WO07128349 OR WO08112156 OR WO06108556 OR WO09002826 OR EP1373206 OR US2006199772 OR US2010267635 OR WO08153610 OR US2005069566 OR EP1569934 OR WO08157330 OR US2010221264 OR WO07000779 OR US2008161287 OR US2005064517 OR US7829665 OR US7205413 OR WO09134401 OR US2008249151 OR US2008139495 OR US2006235023 OR WO07049265 OR US2008045511 OR US7815936 OR US2007232530 OR WO08009689 OR US2007196325 OR EP1659111 OR WO10091413 OR US7378441 OR WO10014130 OR US2007054922 OR US2006047116 OR US2007027172 OR US7432294 OR US2005014759 OR EP1964569 OR WO09006203 OR US2007010486 OR US2005148523 OR WO09020457 OR US2009142300 OR US2009047246 OR US7713573 OR US2008207634 OR WO10150100 OR US2006003317 OR EP1632479 OR WO06020415 OR EP1937639 OR US7166299 OR US2005131216 OR US7048924 OR EP2135601 OR US7419967 OR US2005079200 OR US2005048002 OR EP1519192 OR WO10057048 OR EP1402924 OR WO08149228 OR US2005203150 OR WO10144869 OR WO07098247 OR WO08073558 OR US2009011052 OR	

	WO09117594 OR US2009011007 OR EP2258345 OR WO07089745 OR US2008095740 OR US2010137246 OR WO05086871 OR US2010272681 OR EP1907444 OR WO07011833 OR WO07103740 OR WO09027644 OR US2008026040 OR WO05043118 OR WO05039551 OR WO05061450 OR US2006252795 OR EP1340075 OR WO08113364 OR WO10038237 OR US2007244114 OR EP1219605 OR US2008161246 OR WO10127099 OR WO10111238 OR US2009093482 OR US7700076 OR WO05037196 OR WO07068380 OR WO10086844 OR WO07147884 OR US2009036408 OR WO06078876 OR US2008086198 OR US2006014767 OR US2010029755 OR US7204980 OR WO09142842 OR US2008228051 OR EP1637139 OR US2008103125 OR EP1227797 OR US7871991 OR US6838474 OR WO07013047 OR US2010178339 OR US2007032436 OR WO09097670 OR US2007249643 OR WO05007681 OR EP1293207 OR US2009233964 OR US2005064028 OR WO05115469 OR US6930093 OR WO10100381 OR US2005020495 OR WO06091529 OR WO05012276 OR WO05113059 OR EP1136479 OR US2009054503 OR WO06050165 OR WO08106058 OR US2009227637 OR US2008194554 OR US2009060871 OR US2007179167 OR WO05116081 OR US2005181049 OR US2009181902 OR US7632853 OR US2007021454 OR WO09102487 OR US2009053294 OR US2008021201 OR US2007207122 OR WO10132663 OR US2010280055 OR US7176234 OR US2010129357 OR US2007155959 OR WO09082448 OR EP1656951 OR WO08145606 OR EP1519192 OR US2009035324 OR WO09076195 OR US2010135983 OR US2006063771 OR WO09035662 OR US2010099885 OR WO07014918 OR US2010034840 OR US2007043076 OR US2008112978 OR WO08027932 OR WO09105781 OR WO09006199 OR US2007167459 OR WO06065947 OR WO07002172 OR WO06031825 OR WO09105430 OR US7745432 OR WO07094825 OR US2008269161 OR US2008318876 OR WO08073138 OR US2008070920 OR US2010290983 OR WO06090264 OR WO08115525 OR US2009105279 OR EP1917958 OR US7357930 OR US2009053172 OR WO05116081 OR US6849605 OR WO06129276 OR WO08062429 OR US2008227959 OR WO07008499 OR US2007286842 OR US7611704 OR US2006025726 OR EP1673092 OR US2008096832 OR US2005163857 OR US2009099096 OR US2009215712 OR US2006058284 OR US2005123514 OR US2010285115 OR WO07115381 OR US2006280430 OR WO05021003 OR US2006058286 OR WO06044968 OR WO10037566 OR WO05122741 OR US2006264511 OR WO09009531 OR US6900315 OR WO09111638 OR US2008039428 OR WO05120393 OR WO07034312 OR US2010240698 OR US2008112943 OR US2007219243 OR WO06021456 OR US2009148407 OR US2010040576 OR EP1923063 OR US2008286344 OR US2007037249 OR WO09061856 OR US7119124 OR EP1180020 OR WO06048300 OR WO05030790 OR WO05082385 OR US2005191324 OR WO06027711 OR WO06101920 OR US2007244168 OR US2006264475 OR US2005131017 OR WO09100532 OR WO06104646 OR EP1889839 OR EP1637139 OR WO08010921 OR US2006024365 OR WO07008496 OR WO07050375 OR US2007172469 OR EP2075011 OR WO06065377 OR US2009068144 OR EP1597235 OR US7312221 OR EP1583542 OR WO05124563 OR US2010305173 OR US2011009355 OR WO10099527 OR US2005158408 OR EP1686113 OR WO05077406 OR US2006009651 OR US2007274951 OR US2005215554 OR EP1809672 OR WO08129106 OR EP2269591 OR WO09098475 OR WO06091692 OR US2010247635 OR WO10151495 OR US2010317855 OR WO07033208 OR WO07004236 OR US2010209391 OR EP1637528 OR US7148359 OR US2005222043 OR WO07008780 OR US2006018933 OR US2007191406 OR US2010160262 OR US2010136095 OR US2006223856 OR WO09128947 OR WO07083316 OR WO09053828 OR US2008167353 OR US2005119338 OR US2006052595 OR EP1418432 OR EP1239840 OR WO07072503 OR US2009062227 OR US2007015804 OR EP2003120 OR EP1569931 OR WO10020799 OR US2010226885 OR WO07008539 OR US2005019409 OR US2008026062 OR EP1194404 OR WO10012466 OR US2005026902 OR EP1207394 OR US2010260922 OR WO08005511 OR US2010233122 OR US2010092427 OR US7470506 OR US7183273 OR US2005107304 OR	

	WO08141227 OR WO08098789 OR WO09047264 OR US2008287429 OR US2008019942 OR US2009047238 OR US2005153907 OR US7860545 OR US6995283 OR US2010216746 OR US7455833 OR WO05076892 OR US2005137139 OR US2005153908 OR US2005085464 OR US2008108617 OR WO08063493 OR WO05011567 OR WO05120473 OR US2006222627 OR US2010249181 OR US2010041133 OR US7812034 OR US7192961 OR US2007265281 OR US2007208044 OR EP1421075 OR WO08137779 OR WO09092897 OR US2008066741 OR US2010305171 OR US2010239690 OR US2009062311 OR US2005209197 OR WO05072706 OR US2008167513 OR WO10033614 OR WO08062385 OR US2007196452 OR WO06046134 OR WO07014924 OR US2010120855 OR US2005137140 OR WO07027999 OR WO07014920 OR WO10089763 OR US2006024368 OR WO06136175 OR WO07113856 OR US2007196396 OR US2008045495 OR US2010226943 OR WO07019098 OR US2010286212)	
99	98 not 29	1
100	PN=(US2006293334 OR WO07068383 OR US2008207647 OR WO10107831 OR US2008207699 OR US2005171038 OR WO07019130 OR WO08020024 OR WO06027346 OR US2006122166 OR US2008280849 OR US2009131414 OR WO07039218 OR WO05061450 OR US2009131403 OR US2007135335 OR WO06075012 OR US2010221214 OR EP1219605 OR WO06027346 OR US2008085918 OR WO07111866 OR US2009325992 OR WO05019176 OR US2008213217 OR US2010221215 OR US2010016361 OR US2010104659 OR US2006014767 OR WO09075960 OR US2010074862 OR US2010240623 OR US2008312278 OR US2010292232 OR EP1861365 OR WO08042240 OR EP2033952 OR US7759372 OR WO06116764 OR US2008249097 OR US2009093501 OR US7462721 OR EP1569933 OR US2009227637 OR EP1961744 OR US2008194554 OR US2010234369 OR WO05105843 OR US2006052408 OR US2010285149 OR US7696226 OR US2005288294 OR WO09102487 OR US7589092 OR US2010034827 OR US2008234231 OR US2006269478 OR WO10011959 OR EP1375486 OR US2009118233 OR US2008214503 OR WO10118009 OR US2006217345 OR US2007292355 OR WO07019101 OR US2008220441 OR US2005197320 OR US2007142365 OR WO05028478 OR US2005004232 OR EP1739082 OR US2008114026 OR EP2055705 OR WO09146555 OR US2008070920 OR US2009124633 OR US2008287488 OR US2005209301 OR EP0762880 OR US2009053172 OR EP1682548 OR US2008057074 OR US2007232527 OR EP1673092 OR WO07117482 OR US2010267801 OR US2007293488 OR WO09123768 OR US2007141096 OR US2005131042 OR US2006058284 OR EP1621540 OR WO05021003 OR US2010144825 OR US2005080260 OR WO05003351 OR WO06108879 OR US7148237 OR WO10059883 OR WO06066414 OR WO06130426 OR EP1557468 OR WO10117939 OR WO07149031 OR WO08016522 OR WO08075207 OR US7189718 OR US2009028818 OR EP1809630 OR WO09061856 OR US2006205765 OR WO10033226 OR WO05039587 OR EP1569647 OR US2006026704 OR US2007043001 OR US2008153783 OR EP1995246 OR WO09100532 OR WO06104646 OR US2007155713 OR EP1790637 OR WO08042240 OR US2010291032 OR WO07019100 OR WO05014634 OR WO08101905 OR US2009324543 OR EP1515724 OR US2005222155 OR US2009318421 OR US2005239880 OR US2010179122 OR US2006009651 OR US2008214527 OR EP1886994 OR US2005250707 OR US2005215554 OR US2008176848 OR EP1762567 OR US2010240676 OR EP1220842 OR US2007225347 OR US2007179157 OR WO05007656 OR WO05077050 OR US2010249132 OR WO05035548 OR WO06123182 OR WO07115670 OR WO08006883 OR US2009105186 OR WO10132852 OR EP1326865 OR EP1165070 OR US2007191406 OR US2008146560 OR US2006229336 OR WO05003150 OR US2010022508 OR US2005282839 OR US2006205671 OR EP2266971 OR WO10149257 OR US2006052595 OR US2007207949 OR US2009169567 OR WO09037001 OR US2007287664 OR US2006105997 OR EP1569931 OR US7348345 OR US2005137199 OR WO06097474 OR US2007117859 OR	137

	US2007254046 OR US2009215799 OR US2005026902 OR US2008214582 OR WO09058924 OR WO06040056 OR US2007185007 OR WO05011709 OR WO05070901 OR US7183273 OR US2007191335 OR EP1569934 OR US2010234355 OR EP1541558 OR US2010222341 OR US2009221571 OR US2008064714 OR US2007286856 OR US2008020981 OR US2010048500 OR US2008207596 OR US2008194523 OR WO10091413 OR US2007099910 OR WO07002481 OR US6890942 OR US2005075326 OR US2006047116 OR US2006128692 OR EP2045242 OR US2006128669 OR WO05087728 OR US2007032477 OR WO06129134 OR US2007021354 OR WO10117936 OR WO08127291 OR US2007124152 OR WO09036299 OR US2006241301 OR EP1799679 OR WO07027999 OR US2008207682 OR WO07019098)	
101	100 not 29	76
102	tac=((antiviral* or protease inhibitor* or ant*retroviral*) (peptid*) and (thiazol*))	1269
103	cl=((antiviral* or protease inhibitor* or ant*retroviral*) (peptid*) and (thiazol*))	812
104	PN=(US2011015149 OR US2011015216 OR US7871991 OR US2011008429 OR US2011009355 OR US2011009411 OR US2011008430 OR US2011008288 OR US2011003764 OR US2011003735 OR US2010330086 OR US2010331331 OR EP1560827 OR EP1732575 OR WO10150100 OR WO10151495 OR US7860545 OR WO10148006 OR US2010320099 OR WO10143207 OR WO10144869 OR US2010316607 OR US2010317855 OR CU23604 OR US2010305172 OR US2010305173 OR US2010305171 OR US2010297271 OR US2010298209 OR WO10132163 OR WO10132494 OR WO10132663 OR US2010291034 OR US2010290983 OR EP1624899 OR US2010286212 OR US2010285115 OR US7829665 OR WO10127272 OR WO10127099 OR US2010280055 OR WO10122087 OR WO10121351 OR US2010272681 OR US2010273733 OR US2010272682 OR US7820681 OR US2010267635 OR US2010266543 OR WO10115981 OR WO10116248 OR US2010260922 OR US2010260709 OR US2010260715 OR US2010261731 OR US7812034 OR US2010255032 OR US2010256041 OR CN101854919 OR WO10111196 OR WO10111238 OR US2010249181 OR US2010247635 OR WO04076687 OR US6787573 OR US2004167123 OR US2004167139 OR WO04069166 OR WO04065563 OR US2004152625 OR WO04062600 OR US2004146551 OR WO04060370 OR EP1438962 OR WO04058253 OR US2004138153 OR WO04056770 OR WO04056181 OR US2004131629 OR US2004131604 OR AU2004202466 OR WO04054974 OR WO04055016 OR WO04055012 OR US2004127521 OR US2004127689 OR US2004122000 OR US2004122064 OR US2004116411 OR US2004110733 OR US2004106106 OR WO04041247 OR US2004092583 OR US2004092745 OR US2004092539 OR US2004082066 OR US2004081957 OR CN1491665 OR AU2004201149 OR US2004077859 OR US2004077612 OR US2004077601 OR US2004073259 OR US2004071757 OR US2004073378 OR US6720001 OR US2004062802 OR US2004063734 OR EP1402924 OR WO04025267 OR WO04024683 OR AU2004200629 OR EP1395249 OR AU770801 OR US2004039016 OR US2004033489 OR EP1163256 OR WO04010937 OR US2004023955 OR US2004022844 OR US2004024031 OR US2004022873 OR AU769538 OR US2004019027 OR US2004019047 OR WO10107831 OR US2010239690 OR US2010240698 OR WO10100381 OR US2010226885 OR US2010226943 OR US2010226990 OR US2010226882 OR US2010226883 OR US2010227774 OR WO10099458 OR WO10099527 OR US2010221214 OR US2010221215 OR US2010221216 OR US2010221217 OR US2010221264 OR EP2223929 OR US7785879 OR WO10096462 OR US2010216746 OR IN2536DELNP2009 OR JP2010527996 T OR US2010209391 OR US7776863 OR WO10089763 OR WO10089767 OR WO10091413 OR CN101801348 OR CN101801414 OR WO10086844 OR EP2144599 OR CN101796040 OR CN101795674 OR US2010189687 OR CN101790313 OR US2010183716 OR US2010183715 OR US2010183707 OR EP1732604 OR CN101784549 OR CN101784532 OR US2010178339 OR US2010178340 OR US2010179169 OR	856

	US7754718 OR WO10077317 OR US2010173921 OR US2010173282 OR US2010172993 OR WO10075065 OR US2010167268 OR US7745432 OR US7745444 OR WO10070611 OR US2010160262 OR US7741345 OR WO10068899 OR US2010152147 OR US2010150829 OR US2010152214 OR WO10065118 OR US2004014655 OR US2004014030 OR CA2491466 OR WO04004660 OR WO04004658 OR WO04004711 OR US2004009890 OR US2004010008 OR WO04002410 OR US2004002498 OR US2003236255 OR WO03101481 OR EP1058687 OR WO03099851 OR US2003219472 OR US2003220327 OR AU2003254711 OR US2003211180 OR US2003211545 OR US6645528 OR US2003207843 OR EP1359147 OR US2003202961 OR US2003199808 OR US2003195350 OR US6627651 OR US2003181436 OR US2003180279 OR US2003175690 OR WO03075010 OR US2003171406 OR US2003162800 OR US6610542 OR US2003157138 OR DE69624136 OR US2003152913 OR US2003152917 OR US2003147952 OR US6602885 OR US2003144217 OR US2003144220 OR US2003138483 OR US2003138399 OR US2003138423 OR EP1053012 OR US2003124518 OR US2003124513 OR WO03051361 OR US2003119881 OR US2003114443 OR US6579898 OR US2003109468 OR US2003108857 OR US6576231 OR DE10131036 OR WO03046559 OR EP1315487 OR WO03043602 OR US2003100088 OR US2003100755 OR WO03041694 OR US2003095988 OR US2003092722 OR WO10065079 OR US2010144647 OR US2010144804 OR US2010137246 OR US2010135983 OR US2010135984 OR US2010136097 OR US2010136129 OR US2010136094 OR US2010136096 OR US2010137247 OR US2010136095 OR EP2003120 OR EP2190413 OR WO10059883 OR US2010129357 OR US2010129321 OR WO09040818 OR WO10057048 OR US2010124543 OR CN101711237 OR US7718633 OR WO10054042 OR US2010119479 OR US2010120855 OR US2010120786 OR US7713573 OR US2010111930 OR US2010113589 OR CN101702908 OR WO10047819 OR WO10045266 OR US2010098678 OR US2010099885 OR WO10041241 OR US2010092427 OR US7696226 OR WO10038237 OR WO10037402 OR EP2172193 OR WO10033614 OR US2010075914 OR CN101679325 OR CN101679277 OR CN101679021 OR IN4044KOLNP2009 OR US2010068786 OR US2010069383 OR US2010062970 OR EP2160394 OR US2010056622 OR EP1937639 OR WO10020799 OR US2010048559 OR US2010048500 OR US7666419 OR US2010040576 OR US2010041014 OR US2010041133 OR US7662987 OR WO10017432 OR US2010034840 OR US2010034827 OR US6562848 OR US2003087912 OR US6559137 OR US2003082594 OR US2003083369 OR US2003083485 OR US2003073069 OR US2003069252 OR DE10145361 OR EP1295874 OR EP1284140 OR CA2429345 OR WO03020200 OR US2003050620 OR US2003045534 OR WO03013535 OR US2003032619 OR US2003027867 OR US2003018015 OR US2003018039 OR US6509371 OR EP1275373 OR US6506555 OR US2003007983 OR US2003008891 OR US2003004185 OR WO02102436 OR US2002198231 OR US2002198160 OR US2002192273 OR US2002193828 OR WO02099387 OR WO02097114 OR US6489320 OR US2002177603 OR US6486183 OR WO02085365 OR US2002151542 OR WO02079157 OR US2002147197 OR WO02077186 OR US2002142050 OR WO02074777 OR WO02072109 OR US2002132347 OR EP1240903 OR US6451339 OR US2002128301 OR US2002119444 OR US6440946 OR US2002115665 OR US2002114848 OR US6436989 OR WO02062123 OR US2002107261 OR WO02056902 OR US6423718 OR US6419934 OR US2002090445 OR US6415797 OR US7659405 OR US7659275 OR WO10012466 OR US2010029566 OR US2010029755 OR US2010021540 OR US2010022578 OR US2010021505 OR WO10009335 OR US2010015090 OR US2010015727 OR US7649085 OR CN101627044 OR US2010003214 OR US2009324593 OR US2009324543 OR EP1207394 OR CN101613386 OR US2009317418 OR EP2135601 OR WO09153654 OR US7635722 OR AU2003231765 OR US2009306130 OR US2009306224 OR US2009306112 OR EP1701942 OR US7629337 OR WO09145956 OR US2009297476 OR US7625949 OR WO09142842 OR US2009291952 OR US7622497 OR CN101583379 OR US2009281141 OR US2009281140 OR US2009281132 OR WO09134616 OR WO09134987 OR	

	WO09134401 OR WO09134120 OR US2009274765 OR US2009274650 OR EP2112925 OR CN101569617 OR US7611704 OR DE102008019916 OR US2009270352 OR US2009269305 OR US2009270336 OR WO09128947 OR WO09129470 OR IN496MUM2008 OR WO09126293 OR US2009258011 OR US2009257979 OR WO09121997 OR WO09123768 OR WO09118356 OR US2009247512 OR US2009247544 OR WO09115652 OR CL200102143 OR US2002082249 OR US6407252 OR US2002071863 OR EP1044000 OR US2002068761 OR US2002068749 OR US2002064838 OR US2002061836 OR US2002061896 OR US6391919 OR US6383471 OR WO0234284 OR WO0233402 OR WO0233638 OR US2002048748 OR US2002042394 OR US2002040138 OR WO0222076 OR US2002031558 OR EP1186604 OR DE10040592 OR US2002028791 OR US2002022742 OR US2002022659 OR US2002022054 OR US2002022034 OR EP1180513 OR CN1336934 OR US6347633 OR WO0210124 OR US2002016293 OR WO0206190 OR WO0206292 OR WO0203879 OR CN1330922 OR US2002004503 OR WO0200168 OR EP1166782 OR CA2312644 OR WO0197749 OR US2001049372 OR LU90839 OR US2001041706 OR WO0182919 OR WO0180896 OR US2001036472 OR EP1133485 OR KR1020010086449 OR US6284767 OR EP1126847 OR CA2337616 OR EP1125936 OR US6277879 OR WO0156547 OR WO0154733 OR WO0154729 OR US2001011088 OR US6268393 OR US2001009922 OR US6265406 OR WO0151014 OR WO0147511 OR WO09117594 OR US2009239831 OR US7592368 OR US2009233964 OR US2009232886 OR US7589233 OR WO09111638 OR WO09111040 OR IN1730CHE2007 OR US2009227637 OR US2009226431 OR WO09108865 OR CN101522174 OR WO09105430 OR WO09105776 OR WO09105774 OR WO09105781 OR US2009215712 OR CN101516369 OR WO09102487 OR WO09100532 OR US2009209583 OR US2009208576 OR EP1907444 OR CA2224008 OR WO09098475 OR WO09097670 OR US7572456 OR US2009197888 OR JP4307252 B2 OR US7569678 OR WO09094438 OR WO09094443 OR WO09094205 OR WO09094191 OR US2009192205 OR CN101495457 OR EP2080511 OR WO09089295 OR WO09089263 OR WO09088719 OR WO09083042 OR WO09084036 OR WO09082819 OR WO09082818 OR JP2009525265 T OR US2009175820 OR US2009176983 OR CA2710605 OR WO09082448 OR US2009170856 OR US2009170880 OR US2009170806 OR EP2075011 OR US7553844 OR WO09079412 OR EP1180020 OR WO09076173 OR WO09075960 OR WO09076195 OR NZ335639 OR WO0141742 OR US6242461 OR WO0138332 OR US6235771 OR WO0134118 OR US6232333 OR EP1097148 OR CA2387919 OR WO0128532 OR US6221400 OR CA2289365 OR US6210712 OR US6194391 OR WO0110454 OR WO0110387 OR US6172110 OR US6172061 OR US6172110 OR WO0078996 OR WO0072827 OR WO0073284 OR US6147095 OR US6143742 OR CA2364690 OR WO0059486 OR US6127375 OR WO0056303 OR WO0052034 OR WO0051641 OR CL199902515 OR CA2281133 OR WO0047561 OR US6103462 OR WO0045844 OR US6096780 OR WO0042060 OR WO0040269 OR WO0038679 OR WO0038650 OR US6083958 OR EP1013276 OR WO0035472 OR WO0035419 OR WO0033654 OR US6068851 OR US6068858 OR WO0027196 OR WO0021514 OR CL199901611 OR ECSP993206 OR US6040434 OR US6037157 OR WO0009150 OR WO0006143 OR WO0003998 OR CA2330110 OR WO0000478 OR US2009155209 OR US7547678 OR WO09073686 OR US2009149491 OR US2009148407 OR US2009149947 OR CN101454086 OR US2009143427 OR US2009142300 OR US2009143761 OR US2009137495 OR CN100490811 OR CN101440091 OR WO09064975 OR US2009131363 OR US2009131414 OR WO09061856 OR US2009123515 OR US2009123425 OR EP2058006 OR WO09059243 OR WO09058919 OR WO09058921 OR WO09058923 OR WO09058924 OR CA2703591 OR WO09053828 OR WO09055006 OR US2009110720 OR WO09051840 OR WO09051782 OR US2009105279 OR US2009105147 OR US2009105187 OR US2009105791 OR US2009105302 OR EP1733725 OR WO09047264 OR US2009098200 OR US2009099154 OR US7517992 OR WO09045975 OR US2009093482 OR US2009093454 OR US2009093467 OR WO09040818 OR US2009087483 OR US2009087841 OR US7511124 OR WO09038663 OR WO09035662 OR WO09036341 OR	

	US2009075939 OR US2009074721 OR US2009076045 OR US2009068719 OR WO09027644 OR US2009060871 OR US2009062227 OR US2009062311 OR CN101378729 OR US2009054503 OR US2009053305 OR WO0000475 OR WO0000479 OR WO9966936 OR WO9964001 OR US5994299 OR WO9959585 OR US5985867 OR EP0955054 OR WO9955843 OR WO9955370 OR WO9948504 OR WO9948526 OR US5945413 OR WO9939732 OR JP11508884 T OR US5932570 OR FR2773994 OR ITMI991661 OR WO9933792 OR WO9933795 OR WO9933793 OR WO9925352 OR WO9908676 OR US5874430 OR WO9908112 OR WO9857648 OR US5849793 OR US5843990 OR WO9852571 OR EP0878194 OR WO9848021 OR WO9847492 OR EP0871465 OR WO9843969 OR WO9833067 OR WO9832442 OR WO9820009 OR US5750493 OR WO9817282 OR US5723490 OR WO9804290 OR EP0810873 OR US5691372 OR WO9742962 OR CA2244735 OR EP0719142 OR WO9524385 OR CH156745 OR AU2001245508 OR AU200113690 OR AU2010257200 OR AU200039414 OR CA002442227 OR CA002300876 OR CA002633489 OR CA02633489 OR BR410360 OR BR415023 OR BR415686 OR BR509140 OR US2009053203 OR US2009053294 OR US2009053172 OR EP2026771 OR US2009047246 OR US2009047238 OR WO09020457 OR US2009035324 OR US2009036357 OR HR20080612 OR WO09014638 OR JP2009502889 T OR EP1340075 OR WO09008989 OR US2009016990 OR US2009018162 OR DE102007030695 OR WO09006199 OR WO09005674 OR WO09005693 OR WO09006203 OR US2009011007 OR US2009011013 OR US2009011052 OR US2009005387 OR EP2007381 OR CN101336107 OR US7470506 OR US2008318876 OR EP1373206 OR WO08157273 OR WO08157330 OR US7468274 OR WO08154271 OR WO08153610 OR US2008312300 OR US2008311162 OR US2008306019 OR WO08145733 OR WO08147468 OR WO08144458 OR US2008293664 OR US2008292584 OR WO08140460 OR WO08140459 OR WO08141227 OR WO08140461 OR US2008287488 OR US2008287429 OR US2008286343 OR US2008286344 OR US2008286355 OR EP1284741 OR CN101309675 OR CA2686138 OR WO08137779 OR US2008280849 OR WO08133982 OR WO08131505 OR US2008269162 OR US2008269161 OR US2008267906 OR US2008267915 OR BR515293 OR BR415470 OR BRPI99149400 OR ES2186787 OR NL1012825 OR WO08127291 OR US2008261978 OR US2008260837 OR US2008262058 OR US2008255073 OR US2008249151 OR US2008248126 OR EP1976517 OR CN101282978 OR CA2681718 OR WO08118991 OR WO08118849 OR US2008241289 OR CN101277684 OR WO08113177 OR WO08115525 OR WO08113364 OR WO08116165 OR US2008234231 OR CN101273027 OR CN101273042 OR WO08112156 OR WO08112289 OR US2008227959 OR US2008228051 OR WO08109154 OR WO08109462 OR WO08109483 OR US2008220079 OR US2008220441 OR CN101263156 OR WO08106139 OR US2008214503 OR US2008214527 OR US2008214575 OR EP1964569 OR US7419967 OR CA2678907 OR WO08101665 OR WO08103949 OR WO08103899 OR US2008207620 OR US2008207634 OR WO08100867 OR US2008200503 OR US2008200533 OR CN101245058 OR WO08097924 OR US2008194523 OR US2008194554 OR US2008184618 OR US2008187516 OR US2008181948 OR US2008181868 OR CN101233137 OR CN101233147 OR EP1569933 OR CN101228169 OR IN1269MUM2006 OR US2008167353 OR US2008167513 OR US2008161287 OR US2008161324 OR HU800266 OR HU800267 OR US2008154210 OR WO08073138 OR US2008146595 OR US2008138315 OR US2008139495 OR US7384909 OR WO08063493 OR WO08062385 OR US2008124407 OR US7378441 OR WO08057402 OR WO08055995 OR US2008113946 OR US2008113984 OR US2008112978 OR US2008112943 OR US2008113046 OR EP1919899 OR DE102006051516 OR WO08052737 OR US2008108617 OR US2008107749 OR EP1917958 OR WO08051039 OR US2008103125 OR US7364752 OR US2008096848 OR US7357930 OR US2008085918 OR US7354906 OR US2008076669 OR WO08034039 OR WO08033389 OR US2008070920 OR US2008069850 OR US2008066741 OR WO08027932 OR EP1894559 OR WO08022242 OR WO08021456 OR US2008045495 OR US2008045511 OR US2008045537 OR US2008045530 OR US2008045514 OR EP1889839 OR US2008039428 OR	

	US2008039393 OR EP1886994 OR US2008026040 OR US2008027144 OR US2008026062 OR AU2002329238 OR CA2658395 OR WO08011117 OR WO08010953 OR WO08011116 OR WO08010921 OR US2008019942 OR IN9874DELNP2007 OR US2008014228 OR WO08005276 OR EP0988042 OR US2008004242 OR EP1171137 OR KR1020070120619 OR WO07143847 OR AU2007234580 OR WO07143433 OR US2007286842 OR US2007287664 OR AU2007231810 OR AU2007231808 OR US2007274951 OR BRPI0511144 OR IN1638MUMNP2007 OR US2007270383 OR CN100349913 OR WO07128349 OR WO07129274 OR US2007264334 OR US2007265281 OR US2007264265 OR WO07127683 OR US2007259014 OR WO07124383 OR WO07124224 OR WO07124104 OR US2007253957 OR EP1242426 OR CN101065110 OR US7288265 OR WO07121415 OR WO07121416 OR WO07120595 OR WO07121418 OR US2007249692 OR WO07117482 OR WO07115381 OR US2007244168 OR US2007244114 OR WO07115181 OR CN101052635 OR US2007232532 OR US2007232530 OR US2007232531 OR WO07106450 OR US2007218486 OR US2007219239 OR US2007219243 OR CN101039701 OR US2007213305 OR US2007207122 OR US2007208009 OR US2007208044 OR US2007202051 OR US2007203149 OR US2007203520 OR WO07094825 OR US2007196396 OR US2007197646 OR US2007196323 OR US2007196452 OR CN101022834 OR US2007191406 OR US2007190558 OR US2007190067 OR US2007190130 OR US2007189977 OR US2007191335 OR EP1597235 OR WO07089030 OR US2007181133 OR MX2007003431 OR WO07087548 OR WO07087549 OR US2007179167 OR WO07083316 OR AU2007202956 OR US2007167459 OR US2007167380 OR US2007167497 OR EP1808177 OR US7244716 OR US2007161611 OR WO07076372 OR WO07073583 OR WO07072503 OR US2007148684 OR US2007148124 OR EP1800681 OR WO07068383 OR WO07070694 OR WO07070695 OR WO07070643 OR US2007142365 OR US2007141643 OR WO07065256 OR WO07064691 OR WO07065016 OR WO07062528 OR US2007128278 OR WO07060682 OR US2007124152 OR IE20050699 OR US2007116729 OR WO07054085 OR US2007105781 OR WO07050375 OR US2007099276 OR US2007099877 OR US2007099941 OR US2007098802 OR WO07047371 OR WO07042037 OR US2007088053 OR US2007088015 OR US2007087048 OR EP1658052 OR KR100708581 OR US7205413 OR US2007082883 OR US2007078128 OR US2007078187 OR WO07035957 OR WO07033208 OR US2007059360 OR EP1762567 OR WO07027999 OR US2007054842 OR US2007054922 OR CN1926108 OR WO07022255 OR US2007043076 OR WO07019098 OR WO07019130 OR WO07019101 OR WO07014925 OR US2007032436 OR US2007031408 OR US2007031822 OR US2007032477 OR US2007026056 OR US2007027172 OR CN1906208 OR CN1905859 OR WO07011707 OR US2007021454 OR CN1899289 OR WO07008499 OR WO07008539 OR WO07008496 OR WO07008780 OR US2007015804 OR US2007010486 OR US2007009593 OR US2007009533 OR US2007010489 OR WO07002238 OR WO07000234 OR WO07002172 OR WO07002173 OR US7157561 OR US7157433 OR DE102005053679 OR WO06136175 OR US2006287244 OR US2006287316 OR WO06133194 OR US2006280430 OR WO06130426 OR WO06130477 OR WO06129134 OR US7141593 OR US2006264511 OR US2006264475 OR WO06120495 OR WO06119353 OR US2006252795 OR US2006241150 OR CN1852920 OR WO06108666 OR WO06108879 OR US2006234982 OR US2006235023 OR EP1712220 OR US2006229336 OR US7119124 OR US2006223856 OR US2006222627 OR US2006223874 OR US2006223821 OR WO06101920 OR DE102005012681 OR WO06097323 OR WO06096444 OR US2006199772 OR WO06090264 OR WO06090270 OR WO06091798 OR US2006193890 OR WO06052373 OR AU2002301207 OR US2006172945 OR WO06078876 OR US2006160045 OR US2006154857 OR DE60022047 OR WO06066958 OR WO06066414 OR US2006141033 OR US2006142241 OR CN1795188 OR WO06065377 OR US2006134646 OR CN1791437 OR WO06060918 OR US2006122166 OR US2006121080 OR BRPI0108433 OR CA2588168 OR WO06057637 OR WO06057945 OR WO06053255 OR US2006099246 OR	

	US2006099170 OR EP1219605 OR CN1768733 OR EP1194404 OR US2006088545 OR WO06041538 OR US2006084628 OR CA2581489 OR WO06037418 OR WO06036816 OR WO06035418 OR CN1754559 OR US2006068027 OR US2006067940 OR US2006068389 OR US7018650 OR WO06031825 OR WO06030297 OR US2006058284 OR US2006057149 OR US2006058286 OR US7012129 OR WO06026703 OR US2006052595 OR US2006052408 OR US7008946 OR WO06023400 OR WO06021456 OR US2006046967 OR US2006047116 OR WO06020415 OR EP1441735 OR WO06017341 OR CN1735612 OR DE60017444 OR US2006025726 OR US2006024685 OR US2006025462 OR US2006024365 OR US2006025715 OR US2006025441 OR US2006024368 OR CN1727337 OR US2006018934 OR US2006014767 OR US2006003317 OR US2006003942 OR WO05124563 OR US2005287597 OR EP1608366 OR US2005276836 OR US2005276842 OR RU2265439 OR WO05115469 OR WO05116081 OR WO05113059 OR WO05111112 OR WO05110411 OR US2005261364 OR US2005250764 OR US6962900 OR WO05102391 OR US2005244339 OR US2005244816 OR US2005244818 OR US2005244819 OR US2005239880 OR WO05097818 OR CA2503754 OR US2005222043 OR US2005214749 OR US2005215545 OR US2005215543 OR US2005215544 OR US2005215554 OR US2005209197 OR US2005209196 OR EP1002065 OR US6946469 OR US2005202094 OR US2005203150 OR US2005203152 OR WO05082331 OR DE60008353 OR EP1569659 OR US2005191324 OR WO05077969 OR WO05077050 OR WO05077925 OR US2005187267 OR US6932983 OR US2005182105 OR US2005181049 OR WO05072706 OR US2005176703 OR US2005176658 OR US2005171038 OR US2005171037 OR US2005163857 OR US2005159469 OR WO05063213 OR WO05062952 OR WO05061487 OR WO05060663 OR US2005148523 OR US2005148561 OR US2005148623 OR WO05058248 OR US2005137213 OR US2005137140 OR US2005137139 OR US2005131017 OR US2005131216 OR US2005131042 OR WO05051419 OR US2005123514 OR US2005119189 OR US2005119338 OR WO05046575 OR US6896900 OR US2005107304 OR CN1617731 OR US6894171 OR WO05043118 OR WO05042045 OR WO05042570 OR WO05037196 OR US2005089840 OR US2005085464 OR US2005084529 OR US2005079200 OR US6878728 OR US2005075326 OR US2005075331 OR US2005074414 OR US2005069566 OR US2005070489 OR US2005065319 OR WO05018530 OR US2005048002 OR US2005048112 OR US2005048116 OR WO05016386 OR DE10333098 OR DE10333099 OR WO05011709 OR WO05012276 OR US2005031713 OR US2005033132 OR US2005032042 OR KR1020050014802 OR US2005026902 OR US6849605 OR WO05007070 OR US2005020517 OR US2005020580 OR US2005020548 OR US2005020495 OR US2005019409 OR US2005014759 OR US2005013863 OR US2005013854 OR US2005015039 OR CN1565442 OR US2005009766 OR US2005009848 OR US2005009768 OR US2005009810 OR US2005009767 OR US2005009756 OR US2004265320 OR WO04112747 OR WO04112724 OR WO04110401 OR US2004259876 OR CN1554647 OR JP2004346077 A OR US2004248789 OR US2004242509 OR WO04101512 OR US2004235781 OR US2004235823 OR US2004235779 OR US2004229908 OR US2004228839 OR US2004224916 OR US2004224917 OR US2004224960 OR DE69913499 OR WO04092161 OR WO04092162 OR CA2521048 OR WO04089182 OR CA2425495 OR WO04084876 OR US2004197770 OR US2004198736 OR US6800280 OR US6800668 OR US2004192624 OR US2004192666 OR US2004192704 OR US6797283 OR US2004186066 OR DE202004009061 OR DE202004009060)	
105	104 not 29	19
106	PN=(US20070116729)	1
107	pn=(US20030207813 or WO9533464)	1
108	UC=("435/5" OR "514/45" OR "514/274" OR "435/6" OR "514/230.5" OR "514/43" OR "514/220" OR "514/269" OR "514/253.09" OR "514/49" OR "514/50" OR "514/365" OR	62786

	"514/81" OR "514/275" OR "514/307" OR "514/2" OR "514/357")	
109	UC=("435/5" OR "514/220" OR "435/6" OR "514/43" OR "514/44" OR "514/2")	56429
110	pn=(EP1418174)	1
111	73 and tac=((HIV OR AIDS or retroviral or anti*retroviral* or immunodefic*) and pep-tid*)	34
112	111 not 29	32
113	(108 or 109) and tac=((HIV OR AIDS or retroviral or anti*retroviral* or immunodefic*) and peptid*)	1997
114	113 and (thiazol*)	296
115	114 not 29	278
116	PN=(EP1733725 OR US6506555 OR US5484801 OR EP2269591 OR US6703403 OR US6232333 OR WO05007070 OR US7632853 OR WO9746222 OR WO9857648 OR US7018650 OR US2005031713 OR DE10131036 OR US6967023 OR US2009306224 OR DE10145361 OR US2007059360 OR US2005020495 OR US2004146551 OR EP1240903 OR US2006222627 OR US2006024368 OR WO0220057 OR US2007167380 OR US2010173921 OR WO05011567 OR US2007264334 OR US2007249692)	28
117	PN=(EP1733725 OR US6506555 OR US5484801 OR EP2269591 OR US6703403 OR US6232333 OR WO05007070 OR US7632853 OR WO9746222 OR WO9857648 OR US7018650 OR US2005031713 OR DE10131036 OR US6967023 OR US2009306224 OR DE10145361 OR US2007059360 OR US2005020495 OR US2004146551 OR EP1240903 OR US2006222627 OR US2006024368 OR WO0220057 OR US2007167380 OR US2010173921 OR WO05011567 OR US2007264334 OR US2007249692)	28
118	29 and tac=((heat or thermal*) w4 stabili*)	1
119	pn=(WO02096395)	1
120	PN=(us5484801)	1
121	ctb=120	13
122	121 and 1	1
123	ctf=120	39
124	117 and 123	6
125	PN=(EP0346847 OR EP0441307 OR US5296604 OR WO9520384)	4
126	125 and 2	0
127	ctf=2	337
128	127 and 125	1
129	RF=(122302) and tac=(stab* and (solution* or liquid* or aqueous or solvent*))	71
130	129 and 127	1
131	PN=(EP1733725 OR US6506555 OR US5484801 OR EP2269591 OR US7141593 OR US6703403 OR US6232333 OR WO9822106 OR WO05007070 OR US7141593	202

	OR US7632853 OR WO9746222 OR US7364752 OR EP1002065 OR WO9857648 OR US2010247635 OR US2010267635 OR US7018650 OR US2008286344 OR US7012129 OR WO09153654 OR WO07106450 OR US2007190130 OR WO03043602 OR US6383471 OR US2005031713 OR DE10131036 OR WO06030297 OR US6440946 OR US2009105791 OR US6967023 OR WO10037402 OR ITMI991661 OR US2003138483 OR WO10077061 OR US2009306224 OR US2010062970 OR US2007264265 OR WO07115381 OR US6682759 OR US2004138153 OR WO09115652 OR US2010227774 OR WO08113364 OR US7553844 OR US2007190067 OR US2011008429 OR DE10145361 OR US6797283 OR WO08059046 OR IN01730CH2007 OR US2005287597 OR US7501455 OR US2005244816 OR US2010183716 OR US2008311162 OR WO07083316 OR US2007059360 OR US2009317418 OR WO10089767 OR US2009281132 OR US2010178339 OR US2010021540 OR US2004224960 OR US6720001 OR US2008026040 OR US2008200533 OR US2008026062 OR US2008181948 OR US2009011007 OR US2004151774 OR EP1583542 OR US2009123425 OR US2005181049 OR EP1125936 OR WO07060682 OR US7815936 OR US7713573 OR US2009232886 OR US2002071863 OR US2008248126 OR US2010135984 OR US2008184618 OR US7629337 OR IN00496MU2008 OR US2005020495 OR US2004146551 OR US2009087451 OR US2003050620 OR WO04091578 OR WO10075065 OR WO10038237 OR US2005129777 OR US2007124152 OR US2006024365 OR US2006018934 OR WO0203879 OR US2010172993 OR US2005084529 OR US2002198160 OR WO08133982 OR EP1240903 OR US2006222627 OR US2006099170 OR WO07124104 OR WO02087583 OR US7635722 OR WO09073843 OR US2007087048 OR US2006287316 OR US6929803 OR WO08157330 OR WO0051641 OR US2009274765 OR US2006024368 OR US7354906 OR US2007116729 OR WO9847492 OR EP1800681 OR US2008287429 OR WO06057637 OR US2010226990 OR US2009208576 OR US2009076045 OR US2004197321 OR EP0988042 OR WO06017341 OR WO9626734 OR US2005276836 OR WO0220057 OR US2007167380 OR US2007202051 OR WO10089763 OR US7758886 OR US2008154210 OR WO08073558 OR WO10107831 OR WO09121997 OR US2010152147 OR US2010183715 OR WO08140459 OR WO08140460 OR WO08140461 OR US2010173921 OR US2002068749 OR WO06035418 OR US6932983 OR US2006099246 OR US2007196396 OR WO07002238 OR US2007196323 OR US2010178340 OR US2009098200 OR WO05082331 OR WO08005276 OR US2010143472 OR EP1227797 OR WO09111040 OR US2008220079 OR WO03005826 OR US2008066741 OR US2010226943 OR WO10059883 OR WO05018530 OR WO05011567 OR US2008014228 OR US7700076 OR US2005069566 OR WO10111238 OR US2010034840 OR US2010160262 OR US2007292355 OR EP2172193 OR US2004019027 OR WO0056303 OR WO09027644 OR WO08075207 OR WO09123768 OR US2005202094 OR US2002192273 OR US2007259014 OR WO04112747 OR US2010239690 OR WO02056861 OR US6210712 OR WO06108556 OR US6232333 OR WO10132664 OR WO0166123 OR US2004073259 OR WO09084036 OR WO10033614 OR US2010136129 OR US2009011013 OR US7357930 OR WO09098469 OR US2004062802 OR US2009099154 OR US2010255032 OR US2008286343 OR WO10068899 OR US2005013863 OR US2007264334 OR US2007249692)	
132	123 and 131	9
133	PN=(EP0490667 OR EP0532466 OR EP0541168 OR EP0560268 OR EP0580402 OR US4997851 OR US5196438 OR US5413999 OR US5484801 OR US5484926 OR US5541206 OR US5559158 OR US5725878 OR US5914332 OR US5948436 OR WO9208701 OR WO9307128 OR WO9323368 OR WO9405639 OR WO9506061 OR WO9509614 OR WO9509843 OR WO9520384 OR WO9530670 OR WO9603113 OR WO9701349 OR WO9720554 OR WO9721685 OR US5643878)	23
134	PN=(EP2103623 OR EP2177523 OR US6864369 OR US7141593 OR US7205413 OR US7432294 OR US7632853 OR US7781474 OR WO02096395 OR WO05007070	10

	OR WO08137779 OR US7014866)	
135	RF=(122302) and 134	9
136	135 not 132	8
137	PN=(WO08010921 OR WO08103949 OR WO09008989 OR AU2006235895 OR EP1248600 OR EP1663183 OR EP1917958 OR US7364752 OR US7432294 OR WO0152821 OR WO02096395)	7
138	RF=(122302) and 137 not 132	3
139	PN=(US7364752 OR BG65150 OR CZ301308 OR EP0989851 OR EP0999838 OR EP1248600 OR EP1333810 OR EP1418174 OR EP1660522 OR EP1712231 OR EP1733725 OR EP1917958 OR EP2017269 OR US6121313 OR US6147095 OR US6231887 OR US6448245 OR US6531139 OR US6894171 OR US6911214 OR US6956048 OR US7141593 OR US7148359 OR US7183416 OR US7432294 OR US7659405 OR WO0074677 OR WO0141742 OR WO0152821 OR WO0182919 OR WO02096395 OR WO08002121 OR WO9906024 OR WO9906043 OR WO9906044)	16
140	RF=(122302) and 139 not 132	7
141	PN=(US7750153 OR US7432294)	2
142	PN=(EP1565153 OR GB2423711 OR US7364752)	3
143	ctf=(us56147095)	0
144	ctf=(us6147095)	0
145	CTF=(ep141874)	0
146	pn=(ep141874)	1
147	pn=EP0942721	1
148	CTF=(ep1418174)	0
149	pn=(ep1418174)	1
150	PN=(CZ301308 OR WO08041176 OR US7205413 OR WO02096395 OR WO06129276)	5
151	pn=(us6911214)	1
152	PN=(US7579032 OR WO04047663 OR WO05099473 OR WO06130132 OR WO07041035)	5
153	pn=(us7432294)	1
154	PN=(US7750153 OR US7432294)	2
155	pn=us7364752	1
156	pn=us7364752	1
157	pn=wo0500707	1
158	pn=wo05007070	1
159	pn=us7632853	1
160	PN=(WO09087474)	1

161	PN=(WO2007071055 OR US5747490 or wo9720820 or ep255710)	4
162	PN=(EP2269591 OR US7141593 OR US7141593 OR US7364752 OR EP1002065 OR US2008286344 OR US7012129 OR WO09153654 OR WO07106450 OR US2007190130 OR WO03043602 OR US6383471 OR WO06030297 OR US6440946 OR ITMI991661 OR US2003138483 OR US2009306224 OR US2010062970 OR US2007264265 OR WO07115381 OR US6682759 OR US2009306224 OR US2010062970 OR US2007264265 OR WO07115381 OR US6682759 OR US6797283 OR WO08059046 OR IN01730CH2007 OR US2005287597 OR US2008311162 OR WO07083316 OR WO10089767 OR US2009281132 OR US2010178339 OR US2010021540 OR US2004224960 OR US2008026040 OR US2008200533 OR US2008026062 OR EP1583542 OR US2009123425 OR US2005181049 OR EP1125936 OR WO07060682 OR US7815936 OR US7713573 OR US2009232886 OR US2002071863 OR US2008248126 OR US2008184618 OR US2005020495 OR WO10075065 OR WO10038237 OR US2005129777 OR US2007124152 OR US2006024365 OR US2010172993 OR US2002198160 OR EP1240903 OR US2006222627 OR US7635722 OR US2007087048 OR US2006287316 OR US6929803 OR WO08157330 OR WO0051641 OR US2009274765 OR US2006024368 OR US7354906 OR US2007116729 OR WO9847492 OR EP1800681 OR US2008287429 OR WO06057637 OR US2010226990 OR US2009208576 OR US2009076045 OR WO9626734 OR WO08073558 OR WO10107831 OR WO09121997 OR US2010152147 OR US2010183715 OR WO08140459 OR WO08140460 OR WO08140461 OR WO06035418 OR US6932983 OR US2006099246 OR US2007196396 OR WO07002238 OR US2010178340 OR US2009098200 OR WO05082331 OR US2010143472 OR EP1227797 OR US2008220079 OR US2008014228 OR US2005069566 OR WO09027644 OR US6210712 OR US6232333 OR WO09084036 OR WO10033614 OR US2010136129 OR US2004062802 OR US2009099154 OR US2010255032 OR US2008286343 OR US2005013863 OR US2007264334 OR US2007249692)	107
163	162 not 2	107
164	127 and 163	5
165	ctf=127	1785
166	163 and 165	12
167	166 not 164	7
168	PN=(FR2878747 OR US6004968 OR US6113920 OR US6506555 OR US6544961 OR WO06058920 OR WO9963998 OR EP0513917 OR WO9210496 OR WO9323021 OR WO9402155 OR WO9533464)	10
169	168 and 127	2
170	PN=(CZ300031 OR US6503898 OR US6538006 OR US6696488 OR US7026333 OR US7157489 OR WO05058248 OR AU759386 OR CZ297676 OR CZ297719 OR EA000578 OR EA001457 OR EA001517 OR EA1457 OR EA1517 OR EA578 OR EP0813519 OR EP0813542 OR EP0833826 OR EP0846110 OR EP0871465 OR EP0910386 OR EP0955054 OR EP1052250 OR EP1076062 OR EP1188766 OR EP1210941 OR EP1258491 OR EP1273298 OR EP1293207 OR EP2130534 OR US5705500 OR US5753660 OR US5776971 OR US5863950 OR US5972989 OR US5985870 OR US6037157 OR US6063795 OR US6113920 OR US6143788 OR US6150556 OR US6169085 OR US6172101 OR US6180634 OR US6214861 OR US6316496 OR US6380188 OR US6388132 OR US6407134 OR US6486136 OR US6544961 OR US6617310 OR US6667307 OR US6673822 OR US6683210 OR US6703403 OR US6861539 OR US7045518 OR US7141594 OR US7161033 OR US7339078 OR WO05061450 OR WO9626734 OR WO9628418 OR WO9628463 OR	47

	WO9628464 OR WO9628465 OR WO9633184 OR WO9701349 OR WO9749410 OR WO9749411 OR EP0580402 OR WO9317003 OR EP0337714 OR EP0342541 OR EP0346847 OR EP0393445 OR EP0402646 OR EP0541168 OR EP0617968 OR EP0691345 OR GB2209752 OR US4644055 OR US4652552 OR US4857511 OR US5122517 OR US5157041 OR US5413999 OR US5458889 OR US5476874 OR US5484926 OR US5504104 OR US5527799 OR US5585397 OR USH1649 OR WO9208688 OR WO9309096 OR WO9604913 OR WO9404493)	
171	169 and 170	0
172	168 and 167	0
173	pn=us7364752	1
174	ctb=173	136
175	ctf=173	0
176	174 and 1	0
177	174 and 2	2
178	pn=ep1800681	1
179	PN=(WO09002821 OR WO09002829 OR WO10070611)	3
180	pn=wo9626734	1
181	PN=(FR2878747 OR US6004968 OR US6113920 OR US6506555 OR US6544961 OR WO06058920 OR WO9963998)	5
182	PN=(WO06039488 OR DE10051716 OR EP1112741 OR WO02087583 OR WO03051361)	5
183	PN=(WO09108814 OR AU2009219240 OR CA2716578 OR KR2010122937 OR EP2252148 OR CN101959412)	1
184	PN=(WO11008546 OR US2011021484)	2
185	PN=(US7871598 OR EP2276491 OR US2009258069 OR US2011020454 OR US2011020412 OR US2011014133 OR US2009281156 OR US2009281156 OR US2009137540 OR US2009131386 OR US2009149433 OR WO09061273 OR US2009149432 OR US2009181100 OR US2011011959 OR US2006142241 OR US2009238828 OR WO05115464 OR US2008241251 OR US7110803 OR US7442388 OR US2007259037 OR US7871598 OR US6630169 OR US7871598 OR US2002002154 OR US7435745 OR US7160538)	22
186	PN=(CN101954021 OR WO11006938 OR US2010086645 OR US2011014306 OR WO09129316 OR US2011021466 OR US2009214712 OR WO09090085 OR US2009130284 OR US2011015759 OR US2011015125 OR US2009105319 OR US2008227829 OR US2008131559 OR US7270835 OR US7833553 OR US2004204617 OR US6638971)	17
187	PN=(WO11008546 OR EP2276508 OR US2011021484 OR WO09087410 OR US7517886 OR WO09064084 OR US2011021481 OR US2009238828)	8
188	PN=(WO09134336 OR US7875618 OR US2010087381 OR US2011014117 OR US7871645 OR US7871611 OR US2011014122 OR US6337328 OR US2007148235)	9

Total Patent

Authorities : US, EP, WO, JP, DE, FR, GB, CA, CN, RU, AT, AU, BE, BR, CH, DD, DK, EA, ES, FI, IE, IN, IT, LU, MC, MX, NL, PT, SE, SU, AP, AR, BA, BG, BN, BO, BY, CL, CO, CR, CS, CU, CY, CZ, DO, DZ, EC, EE, EG, GC, GR, GT, HK, HN, HR, HU, ID, IL, IS, KE, KR, KZ, LB, LT, LV, MA, MD, MN, MT, MW, MY, NI, NO, NZ, OA, PA, PE, PH, PL, PY, RO, SG, SI, SK, SM, SV, TH, TJ, TR, TT, TW, UA, UY, UZ, VE, VN, YU, ZA, ZM, ZW

Search Query	Results
TITLE-ABST-CLAIM(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)))	1395
TITLE-ABST-CLAIM((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and (HIV OR AIDS or retroviral or anti*retroviral! or immunodefic!)))	927
TITLE-ABST-CLAIM((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and ((heat or thermal!) w/4 stabili!)))	1
TITLE-ABST-CLAIM((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and (synthes!)))	88
TITLE-ABST-CLAIM((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and (solution! or liquid or solvent! or suspen! or dispers!)))	431
TITLE-ABST-CLAIM((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and (pharmacokinetic! or ((improv! or enhanc! or increas!) w/10 (absorp! or absorb! or bioavailab!)))))	143
TITLE-ABST-CLAIM((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and (emulsion! or cream! or liposom!)))	127
CLAIMS((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and (transdermal! or mucos! or vagina!)))	149
CLAIMS(((retroviral! protease inhibitor!) and (peptid!) and (thiazol!) and (polymorph!)))	0
CLAIMS(((retroviral! protease inhibitor!) and (peptid!) and (thiazol!) and (HIV or AIDS)))	2
CLAIMS((((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB "7160") OR (Norvir) OR (TMC 114r) OR (UNII-O3J8G9O825)) and (apopt! or cancer! or prolifer!)))	259
CLAIMS(((retroviral! protease inhibitor!) and (carbamate or urea or thiazol!)))	10
CLAIMS(((antiviral! or protease inhibitor! or anti!retroviral!) and (HIV or AIDS or viral or virus) and (!butanamido! or thiazol!)))	846

CLAIMS(((antiviral! or protease inhibitor! or anti!retroviral!) and (HIV or AIDS or viral or virus) and (!butanamido! or thiazol!) and (peptid! or valin!)))	126
CLAIMS(((antiviral! or protease inhibitor! or anti!retroviral!) and (HIV or AIDS or viral or virus) and HAART))	74

Thomson Innovation

Collection: US Grant,US App,WO App,EP

Search Query	Results
CTB=(((antiviral* or protease ADJ inhibitor* or ant*retroviral*) and (CYP3A4 or cytochrome ADJ p?450)) and (thiazo*)) AND DP>=(20050101);	8
CTB=(((antiviral* or protease ADJ inhibitor* or ant*retroviral*) and (thiazo*) and (peptid*))) AND DP>=(20050101);	141
CTB=(((antiviral* or protease ADJ inhibitor* or ant*retroviral*) and (thiazo*) and (peptid*) and (HIV OR AIDS or retroviral or anti*retroviral* or immunodefic*))) AND DP>=(20050101);	31
CTB=(((antiviral* or protease ADJ inhibitor* or ant*retroviral*) and (thiazo* or heterocycl*) and (peptid*) and (HIV OR AIDS or retroviral or anti*retroviral* or immunodefic*))) AND DP>=(20050101);	101
CL=(((antiviral* or protease ADJ inhibitor* or ant*retroviral*) and (thiazo* or heterocycl*) and (peptid*) and (HIV OR AIDS or retroviral or anti*retroviral* or immunodefic*))) AND DP>=(20050101);	73
CTB=((protease ADJ inhibitor*) and (carbamoyl* or carbamate or urea) and (AIDS or HIV or anti?retro?viral)) AND DP>=(20050101);	300
CL=((protease ADJ inhibitor*) and (carbamoyl* or carbamate or urea) and (AIDS or HIV or anti?retro?viral)) AND DP>=(20050101);	219
ALL=((retroviral* ADJ protease ADJ inhibitor*) and (peptid*) and (thiazol*)) AND DP>=(20050101);	162
CL=((retroviral* ADJ protease ADJ inhibitor*) and (peptid*) and (thiazol*) and (carbamate* or urea* or carbamoty*)) AND DP>=(20050101);	0
CL=((retroviral* ADJ protease ADJ inhibitor*) and (peptid*) and (thiazol*) and (polymorph*)) AND DP>=(20050101);	0
CTB=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825))) AND DP>=(20050101);	1274
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825))) AND DP>=(20050101);	1217
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and (solution* or liquid or solvent* or suspen* or dispers*)) AND DP>=(20050101);	358
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and (heat* or thermal*) and (stabil* or stabl*)) AND DP>=(20050101);	16
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and (HIV OR AIDS or retroviral or anti*retroviral* or immunodefic*) and (protease ADJ inhibitor*)) AND DP>=(20050101);	498
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ	38

"7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and ((improv* or enhanc* or increas*) near10 (absorp* or absorb* or bioavailab*))) AND DP>=(20050101);	
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and (aqueous or gel* or solution* or liquid*)) AND DP>=(20050101);	344
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and (aqueous or gel* or solution* or liquid*) and (stabl* or stabil*)) AND DP>=(20050101);	72
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and (transder-mal* or mucos* or vagin*)) AND DP>=(20050101);	131
CL=(((155213-67-5) OR (C37-H48-N6-O5-S2) OR (Kaletra) OR (Ritonavir) OR (A-84538) OR (Abbott ADJ "84538") OR (ABT-538) OR (DRG-0244) OR (HSDB ADJ "7160") OR (Norvir) OR (TMC ADJ 114r) OR (UNII-O3J8G9O825)) and (emulsion* or cream* or liposom*)) AND DP>=(20050101);	87

STN- Transcript of Search History

```
=> fil caplus
FILE 'CAPLUS' ENTERED AT 14:14:37 ON 13 JAN 2011

FILE COVERS 1907 - 13 Jan 2011  VOL 154 ISS 3
FILE LAST UPDATED: 12 Jan 2011  (20110112/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Oct 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Oct 2010

This file contains CAS Registry Numbers for easy and accuratesubstance identification.

=> s 155213-67-5/rn
         4035 155213-67-5
           38 155213-67-5D
L1         4009 155213-67-5/RN
              (155213-67-5 (NOTL) 155213-67-5D )

=> s l1 and patent/dt
      7531919 PATENT/DT
L2         889 L1 AND PATENT/DT

=> fil caslink
FILE 'CAPLUS' ENTERED AT 14:15:09 ON 13 JAN 2011
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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CHARGED TO COST=122302

CLUSTER 'CASLINK' ENTERED

 Predefined command sequences will be executed in
 REGISTRY, MARPAT, and CAPLUS.


=>
Uploading C:\Documents and Settings\al02\My Documents\STN Express 8.4\Queries\Ritonavir-
WIPO.str
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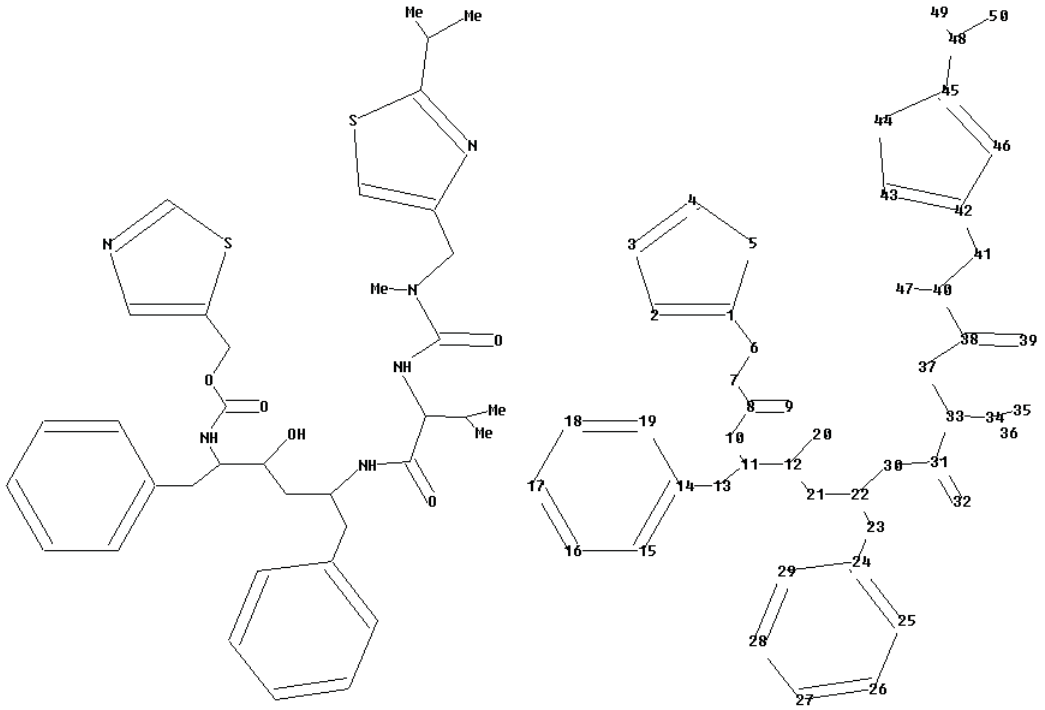

chain nodes :
6 7 8 9 10 11 12 13 20 21 22 23 30 31 32 33 34 35 36 37 38 39
40 41 47 48 49 50
ring nodes :
1 2 3 4 5 14 15 16 17 18 19 24 25 26 27 28 29 42 43 44 45 46

chain bonds :
1-6 6-7 7-8 8-9 8-10 10-11 11-12 11-13 12-20 12-21 13-14 21-22 22-23
22-30 23-24 30-31 31-32 31-33 33-34 33-37 34-35 34-36 37-38 38-39 38-40 40-41 40-47
41-42 45-48 48-49 48-50
ring bonds :
1-2 1-5 2-3 3-4 4-5 14-15 14-19 15-16 16-17 17-18 18-19 24-25 24-29
25-26 26-27 27-28 28-29 42-43 42-46 43-44 44-45 45-46
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 6-7 7-8 8-9 8-10 10-11 12-20 22-30 30-31 31-32
33-37 37-38 38-39 38-40 40-41 42-43 42-46 43-44 44-45 45-46
exact bonds :
1-6 11-12 11-13 12-21 13-14 21-22 22-23 23-24 31-33 33-34 34-35 34-36
40-47 41-42 45-48 48-49 48-50
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19 24-25 24-29 25-26 26-27 27-28 28-29

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom
30:CLASS 31:CLASS
32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS
40:CLASS 41:CLASS
42:Atom 43:Atom 44:Atom 45:Atom 46:Atom 47:CLASS 48:CLASS 49:CLASS 50:CLASS

L3 STRUCTURE UPLOADED

```
=> s l3

S L3 SSS SAM FILE=REGISTRY
SAMPLE SEARCH INITIATED 14:15:37 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       30 TO ITERATE

100.0% PROCESSED       30 ITERATIONS                          2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         272 TO      928
PROJECTED ANSWERS:              2 TO      124

L4           2 SEA SSS SAM L3
  1 FILES SEARCHED...

S L4 SSS SAM FILE=MARPAT
SAMPLE SEARCH INITIATED 14:15:38 FILE 'MARPAT'
SAMPLE SCREEN SEARCH COMPLETED -      748 TO ITERATE

100.0% PROCESSED      748 ITERATIONS                          1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       13349 TO    16571
PROJECTED ANSWERS:              1 TO       80

L5           1 SEA SSS SAM L3
  1 FILES SEARCHED...

=> s l3 full

S L3 SSS FUL FILE=REGISTRY
FULL SEARCH INITIATED 14:15:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      620 TO ITERATE

100.0% PROCESSED      620 ITERATIONS                         42 ANSWERS
SEARCH TIME: 00.00.01

L6          42 SEA SSS FUL L3
  1 FILES SEARCHED...

S L6 SSS FUL FILE=MARPAT
FULL SEARCH INITIATED 14:15:44 FILE 'MARPAT'
FULL SCREEN SEARCH COMPLETED -    16239 TO ITERATE

100.0% PROCESSED    16239 ITERATIONS                          6 ANSWERS
SEARCH TIME: 00.00.02

L7           6 SEA SSS FUL L3
  1 FILES SEARCHED...

S L6 FILE=CAPLUS
L8        4140 FILE CAPLUS
  1 FILES SEARCHED...

SET DUPORDER FILE
```

```
SET COMMAND COMPLETED

DUP REM L7 L8
PROCESSING COMPLETED FOR L7
PROCESSING IS APPROXIMATELY  48% COMPLETE FOR L8
PROCESSING IS APPROXIMATELY  95% COMPLETE FOR L8
PROCESSING COMPLETED FOR L8
L9        4135 DUP REM L7 L8 (11 DUPLICATES REMOVED)
               ANSWERS '1-6' FROM FILE MARPAT
               ANSWERS '7-4135' FROM FILE CAPLUS

=> s l9 and patent/dt

S L8 AND PATENT/DT FILE=CAPLUS
L10        916 FILE CAPLUS
  1 FILES SEARCHED...

S L7 AND PATENT/DT FILE=CAPLUS
L11          6 FILE CAPLUS
  1 FILES SEARCHED...

S L11 AND L7 FILE=MARPAT
L12          6 FILE MARPAT
  1 FILES SEARCHED...

DUP REM L12 L10
PROCESSING COMPLETED FOR L12
PROCESSING COMPLETED FOR L10
L13        913 DUP REM L12 L10 (9 DUPLICATES REMOVED)
               ANSWERS '1-6' FROM FILE MARPAT
               ANSWERS '7-913' FROM FILE CAPLUS

=> s l13 or l2

S L10 OR L2 FILE=CAPLUS
L14        916 FILE CAPLUS
  1 FILES SEARCHED...

S L12 OR L2 FILE=CAPLUS
L15        889 FILE CAPLUS
  1 FILES SEARCHED...

S L15 AND L12 FILE=MARPAT
L16          6 FILE MARPAT
  1 FILES SEARCHED...

DUP REM L16 L14
PROCESSING COMPLETED FOR L16
PROCESSING COMPLETED FOR L14
L17        913 DUP REM L16 L14 (9 DUPLICATES REMOVED)
               ANSWERS '1-6' FROM FILE MARPAT
               ANSWERS '7-913' FROM FILE CAPLUS
```

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