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BASTION

"From Basic to Translational Research in Oncology"

Deliverable D5.6

Final report on achieved innovation capacity and IP protection using TTO metrics

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Introduction

Detailed analysis of patents and patent applications' portfolio allows to estimate the value of intellectual property owned by the University and to fit the strategy of commercialization to the strongest sides of research done at the University. Identification of potential markets helps in reaching to desired business partners and in taking appropriate marketing and sales activities.

Deliverable 5.6 description

Deliverable D5.6 reported hereby corresponds to the task T5.3 in WP5. The aim of this task was implementation of efficient IP protection and innovation managements schemes at the Medical University of Warsaw.

Task performance

Medical University of Warsaw patents and patent applications statistics

The statistics and analysis took into account the information provided by MUW Legal Office and Project Office. Patent applications filed within BASTION project under supervision of Innovation Manager are described in detail in D 5.4 report. MUW's patent portfolio for the years 2006-2013 (the applications already published) consists of:

- ✓ **14 patent** applications,
- ✓ **3 national patents granted**
- ✓ **6 international patent applications** (PCT procedure), which are a direct consequence of Polish patent applications

Among the Polish entries, shared ownership of the use of technical solutions include:

- ✓ **8 applications** evaluated by the Polish Patent Office,

Among the 3 patents granted the two are shared with another entity or business research.

Of patent applications in the international phase (PCT process) 3 inventions are shared with other applicants, the others are independent and fully belong to the MUW.

Technologies life span

For the purpose of this analysis lifetime of technology was arbitrary value. In accordance with the generally accepted principle, the lifetime of medical technology is mature about 7 years. Patent portfolio analysis presented does not allow to state that any of these technologies is mature. Therefore, it was assumed, based on the time of protection, to divide patent applications / patents according to a scale based on the time that elapses until expiration of this protection. Maximum lifetime of a patent was set at 20 years, and each was given the following frames:

- ✓ The **short** lifetime (from 4 to 0 years left until the expiry of patent protection),
- ✓ The **average** lifetime (from 10 to 5 years left until the expiry of patent protection),
- ✓ The **long** lifetime (from 20 to 10 years left to the expiration of patent protection)

NOTE: The presented framework is based on the assumption that for each of these applications patent will be granted.

A separate analysis was performed for Polish applications and separate for international applications.

Polish patent applications and patents

The analysis showed that all the Polish patent applications and granted patents have a long life of 10 years or more. Summary of time remaining until expiration of protection are shown in the table below.

Patent application/patent number	Years until expiration of protection
P 380177	11
P 380929	11
P 382945	12
P 385712	13
P 384978	13
P 385059	13
P 385197	13
P 392292	15
P 391482	15
P 394063	16

P 397231	16
P 392651	16
P 395069	16
P 396618	16
P 398193	17
P 398434	17

Table 1. Projected Polish patents/patent applications lifetime (based on Polish and International Patent Acts)

At the same time the analysis showed that all international patent applications also have a long lifetime of 10 years or more. Summary of time remaining until expiration of protection are shown in the table below.

Patent application/patent number	Years until expiration of protection
PA 2007 015 19	12
P/45.DK-P	13
WO 2009/052830 A1	14
PCT/PL2009000035	14
PCT/PL2011/050041	16
PCT/PL2011/050041	16

Table 2. Projected international patents/patent applications life time (based on polish and international patent acts)

Analyzed patent portfolio is relatively young. This makes it possible for beneficial exclusive rights management and encourages to take appropriate marketing and sales activities. Due to the high cost of maintaining patents (if granted) it should be pursued as soon as possible to license technology. The second alternative is to look for possibilities of financing the development of technology in the model of co-development with a business partner or a confirmation of their application by the nature of the additional public funding.

The biggest drawback is the lack of real portfolio of measures to support the financing or development.

Target markets for technologies

Without a doubt, there are inventions at MUW within the developing areas of medical technologies. All target market segments are both lucrative and highly competitive.

The following outlines the areas of commercial sector with assigned patent applications / patents:

Market sector	IP assets
Infectious diseases	P 380177
Medical imaging	P 380929
Immunotherapy of cancer	P 382945
Regenerative and reconstructive medicine	PCT/PL2011/050041, P 398434, P 391482, P 385197, P 385712
Cosmetics	P 384978, PCT/PL2009000035
Oncology	P 385059, P 392292. P 394063, P 392651, P 398193, PA 2007 015 19, P/45.DK-P, WO 2009/052830 A1, PCT/PL2011/050041,
Immunosuppression	P 397231
Analgesics	P 395069
Cardiovascular	P 396618

Characterization of target markets for technologies are presented below:

Active Pharmaceutical Ingredients Market

The invention P 380177 is related to infectious diseases market. There is a rationale for sustaining the patent protection for aforementioned patent application, since there is a growing need for novel antibacterial compounds.

According to the report prepared by Transparency Market Research[1] anti-infective agents are drugs used for the purpose of killing and/or suppressing the infection causing organisms from invading the host organism by means of its replication or releasing variety of toxins in the host. Such infection causing micro-organisms include viruses, bacteria, fungi, viroids and macro parasites. Infections thus can be classified depending on the type of organism causing infection and the symptoms and medical signs shown by the host.

The global market for anti-infectives is classified by product type as antifungal, antiviral and antibacterial depending on the type of organism they fight. Geographically, North America is the most dominating region in the anti-infectives market and is followed by Europe. The emerging economies of Asia-Pacific regions are also showing growth potential in the global anti-infectives market. India forecasts high potential for growth in demand for anti-infectives due to existence of large patient pool, the government initiatives undertaking various control programs and private partnership projects and rising cost containment initiatives by drug manufacturers.

Some of the major driving factors for the anti-infectives market include

- ✓ increase in patient population,
- ✓ large number of vaccines gaining approvals and
- ✓ newer drug introductions.

The growing resistance of infection causing organisms to the existing drug therapies could pose a major challenge to the anti-infectives market.

Furthermore:

- ✓ high price of drugs,
- ✓ dicey reimbursement policies
- ✓ competition between generic manufacturers

The anti-infectives market is highly fragmented with a large number of domestic and international players. Developmental focus of anti-infective agents has shifted to antiviral agents due to requirement of longer treatment regimens in large number of patient population with chronic indications as compared to antifungal and antibacterial agents requiring shorter treatments.

Some of the key players contributing to the growth of this market include Abbott Laboratories Limited, Cipla Ltd., Claris Life Sciences Ltd., GlaxoSmithKline Pharmaceuticals Ltd., Glenmark

[1] Anti-Infectives Market - Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2012 - 2018

Pharmaceuticals Ltd., Lupin Ltd., Novartis AG, Panacea Biotech Ltd., Pfizer Ltd., Ranbaxy Laboratories Ltd. and Sun Pharmaceutical Industries Ltd.

Therefore, if activity and safety profile will be confirmed as positive, this invention is likely to be outlicensed to one of the major players.

Medical Imaging Market

This an extremely absorbant market, however, its major need are the mature technologies, at least representing the prototype-related state of technology.

The global medical imaging equipment market was valued at $24.4 billion in 2012 and will reach a market value of $35.4 billion by 2019, according to Medical Imaging Equipment Market –according to the report published by Transparency Market Research[2].

The projected 2019 figure represents a compound annual growth rate of 5.4 percent, driven by the global rise of various conditions such as cardiovascular diseases (CVDs), brain disorders, lung disorders and oral conditions such as gingivitis. Medical imaging equipment helps in diagnosing these and other complex diseases such as chromosomal abnormalities, atherosclerosis and Parkinson's disease. Growth of this market will also be supported by the increasing geriatric population worldwide because elderly people are highly susceptible to diseases such as osteoporosis, stroke and CVDs, the company noted.

The market comprises various imaging modalities, from X-ray to SPECT (single-photon emission computed tomography), and from MRI to CT and beyond. CT and nuclear imaging are expected to show the highest growth at more than 5 percent apiece.

Support from various private and government bodies will also trigger the growth of the medical imaging equipment market. In the US, for example, the Medicare Benefit Schedule (MBS) was introduced in 2011 to provide rebates for various categories of items, including medical devices. But an imposition of excise tax on the sale of medical devices will hamper the growth of this market: Medical device manufacturers are expected to pay an additional medical device excise tax (MDET) of 2.3 percent on the sale of every device, in accordance with the Patient Protection and Affordable Care Act (PPACA). Geographically, the North American region made up the largest share by revenue for medical imaging equipment in 2012, but the Asia-Pacific is predicted to see the highest growth rate of more than 7 percent from 2013 to 2019 because of the rise in the geriatric population and

[2] Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2013-2019

improving health care infrastructure in that region. In addition, the favorable demand-supply gap for diagnostic services in this region will also propel the growth of this market.

Again, this market expects the mature technologies, if the patent application covers only an initial stage of development and some more studies have not been conducted, it is not probable that this technology will be commercialized before the costs of patent protection will be higher than the developmental costs to the date.

Regenerative and reconstructive medicine (orthobiologics)

The matters of the aforementioned patents may be positioned in following submarkets of regenerative technologies sector.

Orthobiologics are biomaterials used in orthopedic surgery as an adjunct to faster fusion and healing of the bone. The orthobiologics category covers allografts, bone graft substitutes, bone growth stimulators and viscosupplementation products. Bone allografts are the transplanted bones, sourced from a genetically non-identical living or dead member of the same species. Bone allografts are usually harvested by bone banks from a cadaveric donor. Allografts are used for joint reconstruction, spinal, trauma, craniomaxillofacial and dental procedures. Allografts for dental procedures are not covered under this segment. Allografts in the form of bone, granules or crushed and cubes or block are covered. Bone graft substitutes are synthetic substances which are an alternative to bone allografts and autografts. Bone Morphogenetic Proteins (BMP), Demineralized Bone Matrix (DBM) and synthetic bone graft substitutes are covered under this segment.

The EU5 Orthobiologics market was valued at $433.2 million in 2005 grew at a CAGR of 4.9% from 2005-2012 to reach $605.8 million in 2012, according to the market forecast it is about to reach $1,029.8 million in 2020 with a CAGR of 6.9% (from 2012-20). The Orthobiologics Market in EU is dominated by Bone Graft Substitutes, bone allografts are placing way behind the bone graft substitutes and the revenue in 2012 reached roughly 65% of the one generated by the latter one. The EU Orthobiologics market valued at $433.1 million in 2005 grew at a CAGR of 4.9% from 2005-2012 to reach 605.8 million in 2012, according to the forecast it will reach $1,029.7 million in 2020 with a CAGR of 6.9% from 2012-2020.

Potential buyer need a custom made solution, ability to buy the patented matter that is biocompatible with custom made mechanical properties and has improved biocompatibility over existing products. The reconstructive/orthobiologics portfolio of MUW is composed of 4 Polish patent applications and one international document. This gives a chance for patent marketing and

showing a portfolio of patents instead of single technologies targeting the vast market. Nevertheless, there are some drawbacks and, above all, the lack of international protection of 3 technologies would be a problem in licensing process. This particular repertoire of technologies should enter the sales process after conducting a freedom-to-operate analysis.

Oncology Market[3]

The global oncology market reached $91Bn in 2013, marked by a slowing rate of growth; most sales continue to be in the U.S. and Europe although oncology is a dominant spend area for pharmerging nations; the shift in spend to targeted products and away from biologics is occurring globally:

- While incidence of cancer varies by tumor and geography, survival appears to be improving.
- Growth has been more steady in recent years, expanding at a compound annual growth rate (CAGR) of 5.4% from 2008 to 2013 when it reached $91Bn.
- Oncology spend is still dominated by the U.S. at $37.2Bn in 2013 although pharmerging nations have made cancer their fourth largest healthcare spend area and are poised for more growth.
- The advent of targeted therapies signaled the first explosion of growth in the global oncology market in the early 2000s and continues to shift the market away from biologics and other agents

Oncology market is attractive in terms of numbers, however, extremely competitive. Big Pharma oriented licensing or purchase of exclusive rights that cover new substances / biologics is real only in context of mature technologies that have, in the case of drugs, proofs of toxicological profile, pharmacokinetics, and dirty pharmacology. The only opportunity for these technologies is either selling/licensing the rights to smaller companies that are willing to bear the risks of research at an early stage or a co- development, most probably in the framework of projects financed from public funds. If both strategies fail, one should consider the abandonment of patent protection due to its high cost and low success probability.

Immunosupression market/ Cancer Immunotherapy Market

This fast growth will be seen across the US, France, Germany, Italy, Spain, UK and Japan, and the expected new treatments include four novel immune checkpoint inhibitors and five novel therapeutic vaccines, according to the research, from Decision Resources.

[3] http://www.obroncology.com/imshealth/content/IMSH_Oncology_Trend_Report_020514F4_screen.pdf

Taken together, Bristol-Myers Squibb's anti-CTLA-4 agent Yervoy (ipilimumab) and novel immune checkpoint inhibitors that target the anti-programmed cell death-1/programmed death-ligand-1 (PD-1/PD-L1) pathway – including BMS/Ono Pharmaceutical's nivolumab, Merck & Co's pembrolizumab (MK-3475), Roche/Genentech/Chugai's MPDL-3280A and AstraZeneca/MedImmune's MED14736 – will dominate the immunotherapy market and capture a colossal 85% market share in 2022, the study forecasts.

There are forecasts available showing that the therapeutic vaccines segment of the market will grow by an average of 13.6% a year from 2012 to 2022. However, with combined major-market sales reaching $1.2 billion in 2022, these agents will fall short of replicating the commercial success of immune checkpoint inhibitors.

The transplant marketplace in the United States is ideally suited for a small and well-focused selling effort and the clinical practice of transplant medicine leads to a unique commercialization opportunity. Transplants are generally performed at a small number of highly specialized centers, of which there are approximately 250 in the entire United States

Patients waiting for a transplant will often travel considerable distances for transplant at one of these few centers. As such, a limited number of sales representatives can cover the majority of the centers. During a sales visit, a representative can effectively call upon all professionals involved in the transplant process including surgeons, nephrologists, infectious diseases specialists and pharmacists. On a targeted basis, community nephrologists with large numbers of transplant patients would also be included for field force coverage. In 2012, more than 50,000 organ transplants were conducted in the US, Japan, the United Kingdom, France, Germany, Italy and Spain.

The immunosuppression market comprises several different classes of compounds. The main class of immunosuppressants is the calcineurin inhibitors (CNIs), which includes tacrolimus (Prograf® and Advagraf® / Astagraf XL (Astellas Pharma Inc.) and generics of Prograf®) and cyclosporine (Neoral® and Sandimmune® (Novartis AG) and generics). The worldwide sales of non-generic Prograf® and Advagraf® were reported by Astellas Pharma Inc. to be JPY 161.8 billion (approximately USD 1.95 billion) for 2012 (Astellas Pharma Inc. Annual Report FY 2012). Sales of non-generic cyclosporine (Neoral and Sandimmune), for which generic versions have been available since 2000, were reported to be USD 750 million for 2013 (Novartis AG Annual Report FY 2013). The CNIs are the principle class of agents that will compete with Envarsus® for sales, together with Nulojix® (belatacept), which was launched by Bristol-Myers Squibb Company ("BMS") in 2011 and achieved sales of USD 8 million in 2013 (BMS Annual Report 2013).

This market covers two patent applications. The only way to succeed with commercialization of these two technologies is to develop them and prepare a dossier for pharma licensing process. The easiest way to obtain a significant amount of money from public funds. Other opportunities would be co-development, where MUW has a different but complementary research capabilities as partner, so together they can further develop intellectual property, which is something that neither could do without the other.

Analgesics Market[4]

The global NP market was valued at an estimated $2.58 billion in 2012. GlobalData expects the market to grow at a Compound Annual Growth Rate (CAGR) of 3.19% to $3.53 billion by 2022, with more than 50% of sales coming from the US.

Major drivers of the growth of the NP market over the forecast period include:

- The increasing NP incidence due to the growing elderly population
- The increase in the prevalence and diagnosis of type 2 diabetes, which will lead to growth of the painful diabetic neuropathy (PDN) market, which is the largest NP segment
- The approval of novel formulations and first-in-class therapies in the pipeline for NP, which will drive sales in this market

Major barriers to the growth of the NP market over the forecast period include:

- The NP market will be dominated by generics, which raises the barrier to entry for novel drug therapies.
- An incomplete understanding of the disease mechanisms underlying NP has made appropriate target selection for drug development challenging.
- The lack of recognition for the trigeminal neuralgia (TN) indication has led to the off-label prescribing of all drugs, except carbamazepine.

Pharmaceutical therapies are facing competition from interventional therapies, that are more expensive to apply, but less expensive to undergo regulatory pathway. Therefore, there will be always a need for development of new drugs in the pain management. This particular application, no matter what stage of development it is on, should be presented to potential licensor.

[4] GlobalData, access 25-03-2015

Cardiovascular[5]

This is an interesting and lucrative market:

- ✓ The global cardiovascular market recorded sales of $170bn in 2010 and is set to grow to $187bn in 2016 at a CAGR of 1.6%. The US continued to be the largest market, with a share of 40% of the overall market. After a decline in sales in 2008 due to maturity of key drug categories and the increasing generic presence, the US witnessed a resurgence in 2009.
- ✓ Antihypertensives remained the largest drug class in 2010, with global sales of $37.6bn and a global market share of 22%. Novartis's Diovan led the antihypertensives segment with $3.6bn in sales, followed by Benicar with sales of $2.9bn. Pfizer's Norvasc, one of the blockbusters in this sub-category suffered strong sales erosion and lost significant market share to Diovan.
- ✓ Angiotensin receptor blockers (ARBs) remained the most prescribed therapeutic class within antihypertensives, driven by key brands such as Diovan, Cozaar, and Avapro. However, the advent Cozaar generics in 2010 is expected to erode sales significantly. Angiotensin converting enzyme (ACE) inhibitors have also been on the decline due to competition from ARBs and increased genericization.
- ✓ Antidyslipidemics remained the second largest therapeutic sub-category with $29.9bn in sales and a market share of 18% in 2010. The entry of Lipitor generics in 2011 is expected to negatively impact future prospects of sales in this segment. Dalcetrapib, manufactured by Roche, is a potential blockbuster in this category and could serve to offset the negative impact in the antidyslipidemic market created by the genericization of Lipitor.
- ✓ Antithrombotics recorded $18.7bn in sales in 2010 and a market share of 11%. This segment isforecast to deliver strong growth in the next two years owing to the commercialization of recently approved products such as Pradaxa and Xarelto and the expected launch of Pfizer/BMS's apixaban.
- ✓ The antiarrhythmic market is likely to remain a relatively smaller opportunity owing to the limitation of drug therapy. However, promising products such as Sanofi's Multaq are expected to provide a fillip to the segment by 2013

[5] http://download.bioon.com.cn/view/upload/201303/16084307_4163.pdf

Conclusions

MUW portfolio of patents and patent applications is very modest for now and for this reason it is hard to draw wide and long term strategy for commercialization. Due to an early stage of IP management and (still) low awareness in that field and also not much interest in commercialization among researchers it would be important to put some effort in creating an entrepreneurial spirit. It is also extremely important to stimulate translational research through a proactive approach and providing support in planning, preparation and execution of applied / translational projects. Very helpful could be implementation of a motivation system for researchers with affinity for technology transfer that would support their attempts and recognize their accomplishments in the following areas: collaboration and contracts with industry, invention disclosures, patent filings, granted patents, commercialized patents, etc. The motivation system should have both financial and career promoting elements.

Corresponding estimated/* budget

PERSONNEL, TRAVEL AND OTHER MAJOR DIRECT COST ITEMS FOR BENEFICIARY "1" FOR M19-M36			
WP no.	Item description	Amount [EUR]	Explanations
WP5	Personnel costs	9,146.80	Salary of the WP5 Leader (2,16 PM); fee of theWP5 Co-leader (0,31 PM),
	Travel	-	-
	Subcontracting	986,49	External Expert consultation
	Remaining direct costs	-	-
TOTAL DIRECT WP5 COST (D5.6)		10,133.29	

/* - exact costs for M19-M36 will be presented in the 2nd Period Report and Form C (October 2015)

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Warsaw, *August 2015*