PharmaLundensis AB

Quarterly Report
1st January 2017 to 30th September 2017
PharmaLundensis AB (publ)
556708-8074

The English text of the Quarterly Report is an unofficial office translation. In the event of any discrepancy between the Swedish and the English texts, the Swedish text shall prevail.

1. Summary

1st January 2017 to 30th September 2017 (9 month)

- ✓ Net sales amounted to 0 SEK (0).
- ✓ Loss after financial items amounted to -4 279 635 SEK (-3 017 428).
- ✓ Earnings per share* amounted to -0.21 SEK (-0.16).
- ✓ Equity ratio amounted 2017-09-30 to 91.1 %.

1st July 2017 to 30th September 2017 (3 month)

- ✓ Net sales amounted to 0 SEK (0).
- ✓ Loss after financial items amounted to -1 410 005 SEK (-1 061 575).
- ✓ Earnings per share* amounted to -0.07 SEK (-0,06).

** Loss for the period divided by 20 280 344 (18 796 418) outstanding shares.*

PharmaLundensis develops new treatments against three major lung diseases:
* Chronic obstructive pulmonary disease, COPD (IodoCarb).
* Chronic bronchitis
* Influenza-induced lung failure.

In addition, the company develops EcoFilter®, which is a system that eliminates all the release of pharmaceutical drugs and multi-resistant bacteria in hospital waste water.

* Several positive patent messages during the period

PharmaLundensis patent application for COPD treatment Iodocarb comp was granted in South Africa. Approvals are expected in additional nine markets. Furthermore, the patent protects the treatment against chronic bronchitis approved on the company's main market in Europe. More approvals are expected.

* More insider purchases by CEO during and after the period

In total, CEO Staffan Skogvall has acquired 22 511 PharmaLundensis shares in 2017.

* Licensing discussions are ongoing with a number of companies

PharmaLundensis has received inquiries about the company's COPD projects from a number of pharmaceutical companies in Europe and Asia. PharmaLundensis offers licensing of Iodocarb in most international markets, with the exception of core markets in the Nordic countries and some countries in continental Europe.

* Continued further development and improvement of Iodocarb

Modification of the Iodocarb manufacturing process continues. The purpose is to reduce the release of iodine without reducing the ability to bind heavy metals such as mercury. This new iodinated charcoal is called Iodocarb Novum. PharmaLundensis board estimates that a new improved iodinated charcoal can further improve the positive effect on lung function, and also significantly simplify and speed up the registration process of Iodocarb as a drug.

* Patient recruitment in the COPD study is currently halted

If the work on improving Iodocarb is successful, it may be appropriate to carry out future

clinical trials with Iodocarb Novum. For this reason, no new patients are currently recruited for the COPD study.

* Treatment for chronic bronchitis awaits the improved manufacturing process for the iodinated charcoal

A new and improved manufacturing process for iodinated activated charcoal will alwo have important positive effects for the chronic bronchitis treatment. Therefore, the project awaits the results of the optimization process.

* EcoFilter

Testing of the new EcoFilter system in lab environment continues. Clinical trials are being prepared for spring 2018.

* Influenza-induced lung failure

Test protocols are developed, equipment purchased and scheduling is carried out.

2. Important news during the third quarter

Insider Trading (14 July 2017)
CEO Staffan Skogvall purchased 5000 PharmaLundensis shares in July 2017.

First patent for Iodocarb comp granted (170908)
PharmaLundensis patent application protecting the combination of activated carbon impregnated with iodine or iodine salts in combination with perchlorate (Iodocarb comp) has now been granted in South Africa. The patent is sufficient for at least 16 years, with the possibility of renewal for another 5 years. PharmaLundensis has also filed national patent applications in nine other markets (USA, Europe, China, Japan, Chile, Israel, Saudi Arabia, South Korea and Russia). The company's strategy is to secure patent protection in the four major markets (EU, US, Japan and China), but also in at least one smaller country per continent outside the major markets. The plan is that a pharmaceutical company in that country licenses Iodocarb comp and then is responsible for sales across the region. A pharmaceutical company in South Africa will thus be responsible for the sale of Iodocarb in the majority of the African countries.

CEO Dr Staffan Skogvall: It is very positive that the first national patent for Iodocarb comp is now granted. Thus, one can expect great likelihood of positive messages even in other regions. I think we will benefit greatly from this patent, which will also be able to protect the new iodinated charocal that we are developing.

Patent for the treatment of chronic bronchitis is granted in Europe (170920)
The European Patent Office EPO has announced that it approves PharmaLundensis patent application "Activated carbon comprising an adsorbed iodide salt in a method for treating chronic bronchitis". The patent is valid until 2032 with the option of an additional 5 years extension. Patents for this project have previously been approved in Japan and are currently being processed in China and South Korea.

CEO Dr Staffan Skogvall: PharmaLundensen's patent portfolio is developing very well. Recently, the first national patent for COPD Iodocarb comp was granted and now it is the patent that protects the treatment against chronic bronchitis that is approved on the company's main market in Europe. I am pleased that the patent authorities understand and approve our innovative products!

Licensing discussions with multiple pharma companies on NLSD 2017
PharmaLundensis participated in September in Nordic Life Science Days 2017. In their Partnership event we met a number of pharmaceutical companies from Japan, South Korea and India who requested information about PharmaLundensis COPD projects. All companies expressed interest in the project after the meetings and wanted more information for their internal discussions, which has been transmitted.

The meetings closely fit PharmaLundensis strategy to outlicense Iodocarb in a number of international markets, while retaining sales rights in the core markets. All companies we met were "medium-sized" with about 500-2000 employees in their pharmaceutical division. All of the companies have considerable experience in registering drugs in their respective markets.

This is important as one can expect that a COPD developed in Europe needs to be supplemented with an additional clinical study performed on Asian patients.

3. Important news after the third quarter

Insider Trading (13 oct 2017)

CEO Staffan Skogvall bought 4,221 PharmaLundensis shares in October 2017. In total, he has acquired 22,511 PharmaLundensis shares during 2017.

Continued further development and improvement of Iodocarb

PharmaLundensis is currently conducting a further development and adjustment of the Iodocarb manufacturing process. The purpose is to reduce the release of iodine without reducing the ability to bind heavy metals such as mercury. This new iodinated charcoal is called Iodocarb Novum. If the project is successful, it can bring several significant benefits:

1. COPD patients with light-moderate symptoms may take Iodocarb Novum without the addition of perchlorate (Iodocarb comp), which can greatly facilitate and speed up the registration process of the COPD treatment.
2. A low iodine release from Iodocarb Novum may allow dose increase in the COPD treatment. The Iodocarb effect is most likely dose dependent, therefore a dose increase can be expected to significantly improve lung function even more than the 130 ml improvement obtained in a previous clinical study[1] (which in itself was a good improvement that is well in class with the best of current treatments).

However, it is probably appropriate to treat patients with severe COPD with addition of perchlorate, as this seems to provide an extra synergistic improvement in lung function.

1. Skogvall S, Erjefält JS, Olin AI, Ankerst J, Bjermer L. Oral iodinated activated charcoal improves lung function in patients with COPD. Respir Med. 2014 Jun;108(6):905-9

4. Message from the CEO

As stated in today's quarterly report, PharmaLundensis is currently implementing a further development and modernization of the iodinated activated charcoal. If development is successful, the new product “Iodocarb Novum” can have several crucial advantages:

* Faster and easier registration as a COPD drug.
* Faster and easier registration as a treatment for chronic bronchitis.
* Even greater improvement in lung function at COPD.
* Even greater improvement on cough and sleep production in chronic bronchitis.
* Even bigger market for COPD treatment.

If the thyroid side effects disappear, it may even be possible to use Iodocarb to PREVENT the development of COPD in healthy individuals who have an increased risk, for example due to air pollution. Then the market for the COPD is not just the 11.7% that today has COPD, but then the market is basically ALL people living in areas with bad air!

Due to these potentially great benefits, we have frozen the recruitment of new patients in the present clinical COPD study. If the development work is successful, we will instead start new clinical studies with Iodocarb Novum.

We have also decided to temporarily halt the development of the treatment for chronic bronchitis, because this treatment can also benefit from the new manufacturing process.

Clearly, there are big things going on in the company at present!

I hope to return soon with more information.

Dr Staffan Skogvall
CEO

5. Background of the projects

A. IodoCarb comp – a new effective treatment for COPD

Background

Chronic Obstructive Pulmonary Disease (COPD) is a common and severe lung disease affecting around 400 million people in the world, corresponding to a global prevalence of 11.7 % in the age group of 30 years or more[1]. Patients experience impaired physical fitness, increasing breathlessness, coughing, and a number of other symptoms. The disease is usually progressive in spite of all existing treatment. COPD caused an estimated 2.75 million deaths globally[2] in 2000 (fourth leading cause of death) and the morbidity rates are growing every year.

1. Davies Adeloye et al. Global and regional estimates of COPD prevalence: Systemic review and meta-analysis. J Glob Health. 2015 Dec; 5(2): 020415.
2. David M Mannino and Victor A Kiri. Changing the burden of COPD mortality. Int J Chron Obstruct Pulmon Dis. 2006 Sep; 1(3): 219–233.

Causes of COPD

COPD has traditionally been seen as mainly caused by tobacco smoke. Tobacco smoke contains many hazardous substances such as carbon monoxide, nicotine, tar, irritants and other noxious gases. There are also considerable amounts of heavy metals in the smoke such as lead, cadmium and mercury[1]. No one knows what component in the smoke that is the most harmful to the lungs.

Today, more and more people in the world are affected by COPD without smoking. It is now considered that air pollutants and various industrial emissions are also important risk factors for COPD[2].

1. M. Chiba and R. Masironi. Toxic and trace elements in tobacco and tobacco smoke. Bull World Health Organ. 1992; 70(2): 269–275.
2. Li Li, Jun Yang, Yun-Feng Song, Ping-Yan Chen & Chun-Quan Ou. The burden of COPD mortality due to ambient air pollution in Guangzhou, China. *Scientific Reports* **6**, Article number: 25900 (2016).

Hypothesis

PharmaLundensis project is based on the hypothesis that the tobacco smoke's content of heavy metals such as lead, cadmium and mercury play a key role in the development of COPD[1+2]. A significant association between obstructive lung disease and serum cadmium and lead concentrations has previously been found[3]. When smoke is inhaled, a considerable amount of heavy metals such as mercury (Hg) will be retained in the airway epithelial cells[4], because they have a high oxidative capacity. As a result, epitelial cells convert Hg0 to Hg2+ which is trapped within them. The build-up in the airways of heavy metals from the smoke impairs a crucial relaxant mechanism located in the epithelium. It has previously been shown by Dr Staffan Skogvall that a specific type of epithelial cells, so-called neuroepithelial endocrine (NEE) cells, release a powerful relaxing factor that normally keeps the airways open[5]. According to the hypothesis, the release of this relaxing factor decreases when heavy metals build up in the epithelial cells as a result of smoking, causing a gradual closure of mainly the small airways. This causes the airway obstruction that is typical for COPD.

1. M. Chiba and R. Masironi. Toxic and trace elements in tobacco and tobacco smoke. Bull World Health Organ. 1992; 70(2): 269–275.
2. Suzuki T, Shishido S, Urushiyama K. Mercury in cigarettes. Tohoku J Exp Med. 1976 Aug;119(4):353-6.
3. Haala K.Rokadia, ShikharAgarwal,Serum Heavy Metals and Obstructive Lung Disease: Results From the National Health and Nutrition Examination Survey. Volume 143, Issue 2, February 2013, Pages 388-397.
4. Khayat A, Dencker L.Whole body and liver distribution of inhaled mercury vapor in the mouse: influence of ethanol and aminotriazole pretreatment. J Appl Toxicol. 1983 Apr;3(2):66-74.

5. Skogvall S, Korsgren M, Grampp W. Evidence that neuroepithelial endocrine cells control the spontaneous tone in guinea pig tracheal preparations. J Appl Physiol. 1999 Mar;86(3):789-98.

New and effective treatment of COPD with Iodocarb

PharmaLundensis COPD treatment IodoCarb is a substance which effectively binds and removes heavy metals from the body. Iodocarb consists of activated charcoal with adsorbed iodine. Activated charcoal is widely used in medicine to remove toxic substances from patients exposed to them[1]. It is possible to further strongly increase the heavy metal binding capacity of activated charocal by impregnating it with iodine[2]. Impregnation with iodine increases the metal binding capacity by more than 100 times (10 000 %)[3].

1. Neuvonen PJ, Olkkola KT. Oral activated charcoal in the treatment of intoxications. Role of single and repeated doses. Med Toxicol Adverse Drug Exp. 1988 Jan-Dec;3(1):33-58.
2. Henning K-D and Schäfer S. Impregnated activated carbon for environmental protection. Gas Sep Purif 1993 Vol 7(4):235-240.
3. Yoshimi Matsumura. Adsorption of mercury vapor on the surface of activated carbons modified by oxidation or iodization. Atmospheric Environment (1967), Volume 8, Issue 12, December 1974, Pages 1321-1327.

Mechanism of action

It is considered that Iodocarb acts by binding and removing heavy metals from the body. How can oral Iodocarb, which is not absorbed in the body but merely passes through the intestine, improve the lung function? Heavy metals often display an enterohepatic recirculation where they are excreted by the liver in the bile, enters the small intestine and is subsequently readsorbed into the body again further down the small intestine[1+2]. As a result, it is very difficult for the body to excrete heavy metals. When Iodocarb is present in the small intestine, heavy metals excreted in the bile are adsorbed to the iodinated activated charcoal and excreted in the faeces, rather than being readsorbed back into the body. This breaks the enterohepatic recirculation, thereby allowing a greatly increased excretion of heavy metals.

1. Huang W, Zhang P, Xu H, Chang S, He Y, Wang F, Liang G. A novel route for the removal of bodily heavy metal lead (II). Nanotechnology. 2015 Sep 25;26(38):385101.
2. Clarkson TW. Factors involved in heavy metal poisoning. Fed Proc [01 Apr 1977, 36(5):1634-1639].

Significantly improved lung function by Iodocarb in clinical study

PharmaLundensis has conducted a double blind randomized placebo controlled parallel group clinical study with 40 patients with moderate COPD that were given Iodocarb or placebo[1]. In the Iodocarb group, patients showed a statistically significant improvement of FEV_1 baseline by 130 ml compared to placebo, corresponding to 8.2% improvement ($p = 0.031$*). Correlation statistics revealed that the improvement of FEV_1 baseline was significantly correlated both to FEV_1 post-bronchodilator ($p = 0.0020$**) and FEV_1 post-exercise (0.033*) values. Furthermore, Iodocarb improved Home CAT-score by ~20 % (Fig 1). No serious adverse effects directly related to the treatment were recorded. However, 8 patients in the Iodocarb group showed changes of the thyroid hormone levels. The thyroid side effects were caused by some iodine leaving the carbon and entering the body.

1. Skogvall S, Erjefält JS, Olin AI, Ankerst J, Bjermer L. Oral iodinated activated charcoal improves lung function in patients with COPD. Respir Med. 2014 Jun;108(6):905-9

Iodocarb comp

In order to reduce the absorption of iodine released from Iodocarb in the intestine, an inhibitor of the sodium/idodide symporter (iodine pump) can be added to the treatment. The iodine pump inhibitor potassium perchlorate has been used for many years to treat thyreotoxicosis in humans[1]. The iodine pump is responsible for absorption of iodide in the intestine[2], the thyroid[3] and the kidneys[4]. The combination of Iodocarb and the iodine pump inhibitor potassium perchlorate is called Iodocarb comp. Preliminary experiments suggest a reduction of the thyroid side effects. Surprisingly, they also suggest that Iodocarb comp give a

synergistic improvement of the lung function. One 80-year old caucasian male got almost the double improvement of the lung function by Iodocarb comp, compared to only Iodocarb. This synergistic improvement may be caused by potassium perchlorate reducing the release of iodine from the activated carbon as a result of the inhibition of the intestinal iodine pump, thereby allowing Iodocarb to bind heavy metals for a longer time.

1. Morgans, ME and Trotter, WR. Treatment of thyreotoxicosis with potassium perchlorate. Lancet. 1954 Apr 10;266(6815):749-51.
2. Nicola JP, Basquin C, Portulano C, Reyna-Neyra A, Paroder M, Carrasco N. The Na+/I- symporter mediates active iodide uptake in the intestine. Am J Physiol Cell Physiol. 2009 Apr;296(4):C654-62. doi: 10.1152/ajpcell.00509.2008.
3. Wolff J. Perchlorate and the thyroid gland. Pharmacol Rev. 1998 Mar;50(1):89-105.
4. Spitzweg C1, Dutton CM, Castro MR, Bergert ER, Goellner JR, Heufelder AE, Morris JC. Expression of the sodium iodide symporter in human kidney. Kidney Int. 2001 Mar;59(3):1013-23.

Iodocarb Novum

The method to produce Iodocarb is at present being modified, in order to reduce the leakage of iodine from the activated carbon. A high-quality Iodocarb which releases considerably less iodine will allow the administration of much larger amounts of Iodocarb to COPD patients. Since the Iodocarb airway relaxation most likely is dose-dependent, an increased dose will result in an even larger improvement of the lung function than what was found in the previous clinical stydy (130 ml improvement of FEV_1 baseline compared to placebo[1]).

1. Skogvall S, Erjefält JS, Olin AI, Ankerst J, Bjermer L. Oral iodinated activated charcoal improves lung function in patients with COPD. Respir Med. 2014 Jun;108(6):905-9

Use of Iodocarb comp and Iodocarb Novum depends on the severity of disease

When treating patients with light - moderate COPD, it will probably be sufficient to administer Iodocarb Novum as a single treatment to achieve an improved lung function. However, when treating patients with severe COPD it may be appropriate to add an iodine pump inhibitor such as potassium perchlorate to get the added benefit of the synergistic improvement of the lung function.

Future clinical COPD studies

In the coming year, Iodocarb will be tested in two clinical studies:

1. Dose-finding study regarding thyroid side effects (10-20 patients).
2. Phase 2 study to determine the effects of Iodocarb Novum on lung function and walk test (60-80 patients).

Treatment of air pollution-induced COPD

As mentioned above, an increasing number of patients today get COPD as a result of air pollution, rather than smoking. Air pollution, especially from the burning of fossil fuel, contain considerable amounts of heavy metals, just like tobacco smoke[1+2]. Since the toxic factors that cause COPD may be heavy metals in both cases, Iodocarb can also be expected to be able to treat air pollution-induced COPD. Interestingly, it may be possible to PREVENT the development of COPD if exposed to tobacco smoke or air pollution by taking a small amount of Iodocarb to remove the heavy metals from the airways. Thus, if you live in a city with heavy pollution, it may be possible to protect your lungs by regularly taking a low dose of Iodocarb, rather than leaving the polluted city.

1. Honda A, Tsuji K, Matsuda Y, Hayashi T, Fukushima W, Sawahara T, Kudo H, Murayama R, Takano H. Effects of air pollution-related heavy metals on the viability and inflammatory responses of human airway epithelial cells. Int J Toxicol. 2015 Mar-Apr;34(2):195-203.
2. https://www.epa.gov/international-cooperation/mercury-emissions-global-context#types

Patent protection
The main patent for Iodocarb (WO2009067067) is valid in most countries in the EU, China, Japan and Russia. Patent protection lasts at least until 2028 and is likely to be extended for another 5 years.
National patent to protect Iodocarb comp (WO2015075111) in South Africa has recently been granted, and patent is pending in USA, Europe, China, Japan, Chile, Israel, Saudi Arabia, South Korea and Russia. Patent protection lasts until 2033 and may be extended for another 5 years.

Patents for Iodocarb Novum will cover many more markets.

Business Plan
PharmaLundensis will retain marketing rights in core markets (Nordic countries and some countries in continental Europe). Pharma companies outside core markets can obtain exclusive license in their main market for the sale of Iodocarb.

Potential for large revenues from Iodocarb
There is a high and growing prevalence of COPD, both globally and regionally. The costs of treating COPD are massive. In the United States, the costs were $ 32.1 billion 2010, which is expected to increase to $ 49 billion by 2020[1]. In other parts of the world, costs are also very high. In 2012, the 10 largest drugs against lung diseases generated a total of $ 25 billion in sales[2]. After successful registration, Iodocarb (comp or Novum or both) may be an international blockbuster with annual sales exceeding 1 billion dollar globally.
1. http://www.cdc.gov/features/ds-copd-costs/
2. http://www.firstwordpharma.com/node/1145830#axzz3lTHHd2ng

The future
If the planned COPD studies during next year show as good improvement of the lung function as the previous clinical study without thyroid side effects, it is likely that IodoCarb becomes a valuable COPD drug. Through "Staggered registration" (Fast-track) Iodocarb may reach the market relatively quickly. PharmaLundensis ambition is to get IodoCarb on the market within 2-3 years.

B. EcoFilter®

Summary
PharmaLundensis is developing EcoFilter, which is a system that eliminates all release of drug residues and multi-resistant bacteria in hospital waste water. In addition, it removes all multi-resistant bacteria from hospital sewage pipes, thereby eliminating the risk of multi-resistant bacteria that are growing in the pipes infect patients in the hospital wards. Drug residues isolated from the sewage water will be sent for high-temperature destruction, while purified water can be released to the municipal waste-water system. We know of no other project or system that has all these capacities.

Background
The increasing resistance to antimicrobial medicinal products represents one of the major emerging threats to human health. Antibacterial medicinal products can be found with increasing frequency in wastewater and sewage sludge, and in parallel, an increased level and frequency of resistant bacteria in the environment has been observed. In a study on the occurrence of *E. coli* in sewage and sludge, it was shown that microorganisms with resistances to antibacterial medicinal products accumulated in the sludge. *E. coli* strains were found which were resistant to 16 out of 24 tested antibacterial medicinal products (penicillins, cephalosporins, aminoglycosides, quinolones, and others); the highest resistance rate (up to 57%) was found for tetracycline[1].

Current municipal sewage treatment plants are unable to remove drug residues and antibiotic resistant bacteria. On the contrary, it has been suggested that these plants promote the spread of antibiotic resistance[2+3]. If inadequately treated sludge is used as fertiliser, agricultural products used as food or animal feed may be contaminated, and such phenomena have been the sources of several outbreaks of enteropathogenic infections[4].

In particular, hospital effluents are important contributors to the medicines released in the environment through urban effluents. In the EU, hospitals contribution to medicinal products environmental load is estimated at about 10% of urban effluents[5]. However, this share can be higher, as shown for instance in Denmark, where it is estimated that 24% of the total antibiotic load in the Capital Region originates from hospitals. This figure rises to 43% if non-problematic penicillins are disregarded. When it comes to life-saving broad-spectrum antibiotics, most are used primarily in hospitals. As a result, hospitals are hotspots for antimicrobial-resistant bacteria and play a major role in both their emergence and spread[6]. Large numbers of resistant bacteria will be ejected from hospitals via wastewater systems. To make matters even worse, in waste-water treatment plants antibiotic resistance genes are transferred between bacterial species. Consequently, large amounts of multi-resistant bacteria are released in the environment.

1. Reinthaler FF, Posch J, Feierl G, Wüst G, Haas D, Ruckenbauer G, Mascher F, Marth E. Antibiotic resistance of E. coli in sewage and sludge. Water Res. 2003 Apr;37(8):1685-90.
2. Karen L. Jury , Stuart J. Khan , Tony Vancov , Richard M. Stuetz & Nicholas J. Ashbolt. Are Sewage Treatment Plant Promoting Antibiotic Resistance? Critical Reviews in Environmental Science and Technology Volume 41, 2011 - Issue 3, Pages 243-270.
3. Rizzo L, Manaia C, Merlin C, Schwartz T, Dagot C, Ploy MC, Michael I, Fatta-Kassinos D. Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: a review. Sci Total Environ. 2013 Mar 1;447:345-60.
4. Heaton JC, Jones K. Microbial contamination of fruit and vegetables and the behaviour of enteropathogens in the phyllosphere: a review. J Appl Microbiol. 2008 Mar;104(3):613-26. Epub 2007 Oct 9.
5. Kümmerer K. Antibiotics in the aquatic environment--a review--part I. Chemosphere. 2009 Apr;75(4):417-34.

6. Hocquet D, Muller A, Bertrand X. What happens in hospitals does not stay in hospitals: antibiotic-resistant bacteria in hospital wastewater systems. J Hosp Infect. 2016 Aug;93(4):395-402.

Problems with today´s hospital wastewater systems

Hospital sewage systems today have four important problems that must be addressed by a new wastewater treatment system:

1. Release of large amounts of pharmaceutical drugs in the hospital wastewater.
2. Release of multi-resistant bacteria and resistance genes in the hospital wastewater.
3. Epidemics in hospital patients caused by spread of multi-resistant bacteria from the hospital wastewater system.
4. Spread of multi-resistant bacteria from patients carrying them.

1. Release of antibiotics and other pharmaceutical drugs in the hospital wastewater.

Most patients are treated with pharmaceutical drugs at the hospital. The drugs are excreted in urine and faeces and flushed down the patients toilets. As a result, the wastewater contains high amounts of many pharmaceuticals which can have ecotoxic effects[1]. An especially important group is broad-spectrum antibiotics, which can lead to the development of multi-resistant bacteria in the nature[2].

1. Frédéric O, Yves P. Pharmaceuticals in hospital wastewater: their ecotoxicity and contribution to the environmental hazard of the effluent. Chemosphere. 2014 Nov;115:31-9.
2. Gullberg E, Cao S, Berg OG, Ilbäck C, Sandegren L, Hughes D, et al. (2011) Selection of Resistant Bacteria at Very Low Antibiotic Concentrations. PLoS Pathog7(7): e1002158.

2. Release of multi-resistant bacteria and resistance genes in the hospital waste water.

Large amounts of antibiotics are used in hospitals to treat patients with infections. The antibiotics are excreted in the urine and faeces and flushed down the patients toilets. This leads to a continuous presence of large amounts of antibiotics in the hospital sewage pipes. As is always the case when large amounts of bacteria are exposed to antibiotics for a long time, the bacteria in the hospital sewage system become resistant to the drugs. Consequentially, hospital sewage water contains large amounts of multi-resistant bacteria[1]. These bacteria can spread and infect humans and animals. In addition, resistant bacteria supply antibiotic resistance genes that can spread to other bacteria especially in municipal treatment plants, which subsequently can infect vegetables, animals and people[2]. Furthermore, it has been shown that animal vectors such as *Rattus norvegicus* living in hospital sewage systems carry pathogens responsible for fatal diseases in humans as a result of the large outflow of antibiotics and antibiotic-resistant bacteria into the wastewater systems[3].

1. Hocquet D, Muller A, Bertrand X. What happens in hospitals does not stay in hospitals: antibiotic-resistant bacteria in hospital wastewater systems. J Hosp Infect. 2016 Aug;93(4):395-402.
2. Rizzo L, Manaia C, Merlin C, Schwartz T, Dagot C, Ploy MC, Michael I, Fatta-Kassinos D. Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: a review. Sci Total Environ. 2013 Mar 1;447:345-60. doi: 10.1016/j.scitotenv.2013.01.032. Epub 2013 Feb 7.
3. Hansen TA, Joshi T, Larsen AR, Andersen PS, Harms K, Mollerup S, Willerslev E, Fuursted K, Nielsen LP, Hansen AJ. Vancomycin gene selection in the microbiome of urban Rattus norvegicus from hospital environment. Evol Med Public Health. 2016 Aug 3;2016(1):219-26.

3. Epidemics in hospital patients caused by multi-resistant bacteria from the hospital waste water system.

There are many factors that have been found to contribute to contamination of clinical areas resulting in serious epidemics in hospital patients, including faulty sink, shower and toilet design, clean items stored near sluices, and frequent blockages and leaks from waste pipes[1]. Blockages can be caused by paper towels, patient wipes, or improper use of bedpan macerators. Furthermore, it has been demonstrated that bacteria in standard sink water traps in

seven days form a bio-film that extends up to the sink valve. When the tap is flushed afterwards, bacteria sprout up to a meter around the sink, after which the bacteria can infect patients[2]. If the bacteria are multi-resistant, they can cause very serious epidemics.

1. Breathnach AS, Cubbon MD, Karunaharan RN, Pope CF, Planche TD. Multidrug-resistant Pseudomonas aeruginosa outbreaks in two hospitals: association with contaminated hospital waste-water systems. J Hosp Infect. 2012 Sep;82(1):19-24.
2. Shireen Kotay, Weidong Chai, William Guilford, Katie Barry and Amy J. Mathers. Spread from the Sink to the Patient: in situ Study Using Green Fluorescent Protein (GFP) Expressing- Escherichia coli to Model Bacterial Dispersion from Hand Washing Sink Trap Reservoirs. Appl Environ Microbiol. 2017 Mar 31;83(8).

4. Spread of multi-resistant bacteria from patients carrying them.
Many patients in hospitals, especially those receiving longer care, carry multi-resistant bacteria[1]. As a result, large amounts of multi-resistant bacteria are flushed down in hospital toilets every day. In the hospital sewage pipes these bacteria can spread and multiply and return to the hospital ward as describe above, infecting other patients. Furthermore, the multi-resistant bacteria can leave the hospital in the waste water and spread its resistant genes to other bacteria in the municipal treatment plant and infect even more people.

1. Hogardt M, Proba P, Mischler D, Cuny C, Kempf VA, Heudorf U. Current prevalence of multidrug-resistant organisms in long-term care facilities in the Rhine-Main district, Germany, 2013. Euro Surveill. 2015;20(26):pii=21171.

EcoFilter Technology
The EcoFilter technology consists of the use of evaporators to remove water from liquids containing drug residues, as described in PharmaLundensis Patent application 1. The basis for this separation is that water boils away at 100 degrees while drug needs 600-800 degrees or more to evaporate. By removing nearly all water from the waste water with dissolved drugs, the drug residues are isolated and can easily be sent for destruction. Compare with a teaspoon of salt poured into a pan of boiling water. First, the salt dissolves and disappears, but if you boil away all the water, the salt will deposit on the walls of the pan. It will then be easy to collect the salt deposits for further treatment. This is a robust and well-proven technology that we use in a new way.

However, the system generates large amounts of waste material and in Patent application 2 we describe how the amount of waste material can be reduced, making the process much more economical.

There are many other practical issues that also need to be solved to establish a functioning system in a hospital. This is protected in EcoFilter Patent Applications 3 + 4, which have not yet been published.

Positive results in clinical trials with EcoFilter prototype
Studies with a prototype to clarify the capacity of EcoFilter® to remove urinary antibiotics from patients treated with very high doses of broad spectrum antibiotics have been conducted in Lund in 2015-2017. The tests showed:

A. That untreated urine from these patients contained extremely high amounts of antibiotics with a very pronounced antibacterial effect. Thus, the antibiotics had not been broken down or metabolized to a significant extent as it passed through the body.
B. That urine treated with EcoFilter® completely lacked antibacterial effect - all antibiotics had been eliminated.

Thus, EcoFilter® fully meets all required cleaning requirements.

In these tests, the antibacterial effect was evaluated by a biological bioassay where the germicidal effect of urine on bacteria growing on culture plates was determined. The following broad spectrum antibiotics were included in the test: Bensylpenicillin, Cefotaxim, Cefuroxim, Cloxacillin, Erytromycin, Metronicazol, Rifampicin, Trimetoprim-sulfa and Piperacillin-tazobaktam.

The tests are described in greater detail here: Report 1 och Report 2

Similar technical solutions (competition)
The methods to eliminate drug residues from hospital effluents are just developing, and there is probably no company which at present can offer a fully functional system for removal pharmaceutical drugs and multi-resistant bacteria from hospital waste water systems. However, there are several groups that work with this problem using various methods.

Akademiska sjukhuset in Uppsala, Sweden has a pilot project with ozone.
http://www.akademiska.se/press#/pressreleases/reningsverk-paa-akademiska-ska-minska-antibiotikaresistens-1242668
It is not expected that this project can reduce the amount of multi-resistant bacteria or resistance genes in hospital sewage systems.

In Linköping, Sweden, a treatment plant for removal of drug residues from municipal waste water is being built. For the purpose, ozone is used. It is expected to remove 90 % of drug residues.
https://www.tekniskaverken.se/innovation/rening-av-lakemedelsrester/
It is not expected that this project can reduce the amount of multi-resistant bacteria or resistance genes in hospital sewage systems.

Herlev Hospital in Denmark uses several techniques to remove drugs from the wastewater (membrane bioreactor, ozone, activated carbon, and Ultraviolet (UV) rays). This results in a high level of purification, but the process is complicated and expensive. Furthermore, it is not expected that this project can reduce the amount of multi-resistant bacteria or resistance genes in hospital sewage systems.
https://www.dhigroup.com/global/news/2016/08/hospital-wastewater-from-a-pollution-problem-to-new-water-resources

C. Treatment for chronic bronchitis

Background

Chronic bronchitis is characterized by cough with mucus (sputum) production that lasts at least three months a year for 2 consecutive years[1]. Chronic bronchitis is a common disese with a prevalence of 5.4 % of the population[2]. Smoking and occupational exposure to welding fumes are both associated with an increased risk of chronic bronchitis. There is no effective treatment today. Smoking cessation may possibly alleviate some of the symptoms.

1. https://lunginstitute.com/blog/chronic-bronchitis-symptoms-what-to-look-for/
2. Holm M, Kim JL, Lillienberg L, Storaas T, Jögi R, Svanes C, Schlünssen V, Forsberg B, Gíslason T, Janson C, Torén K; RHINE Study Group, Northern Europe. Incidence and prevalence of chronic bronchitis: impact of smoking and welding. The RHINE study. Int J Tuberc Lung Dis. 2012 Apr;16(4):553-7. doi: 10.5588/ijtld.11.0288.

New treatment

PharmaLundensis has developed a variation of iodinated activated charcoal which may be suitable for the treatment of chronic bronchitis. This product is described in patent application WO2014084763, which was recently granted in Japan. Patent is pending in EU, China and South Korea. Of particular interest is that this application discloses that impregnation with 1.6 % iodine salt provides an equally effective mercury binding as impregnation with 8 % elemental iodine. This means that iodine salt is at least 5-10 times more effective than elemental iodine.

This treatment is at present awaiting results from the new method to manufacture iodinated activated charcoal

D. Flu-induced Respiratory Failure

Every winter, the world is affected by flu epidemics. Often the symptoms are quite mild, but sometimes they become very serious. The Spanish flu caused 50-100 million deaths in 1918-1919 and even the Asian flu (57-58) and the Hong Kong flu (68-70) resulted in millions of dead[1]. Today, the swine flu 2009 spread and caused a great deal of death despite modern care. Influenza viruses can cause such severe airway inflammation that they collapse, which can not be addressed with today's drug. The only possibility is to place the patient in an "artificial lung"[2]. This is an extremely complicated technique, which can only be made available to a handful of patients. A major influenza epidemic of a virus strain that severely worsens lung function would be a nightmare and considered by many experts as one of the greatest threats to the future of humanity.

PharmaLundensis develops a treatment for Flu-induced lung failure. Laboratory experiments will be performed to clarify if pharmacological modification of a specific mechanism can effectively treat this pulmonary disease. An effective drug will be useful to many patients with pulmonary symptoms from the yearly seasonal flu. In addition, the drug will be of great interest to emergency preparedness organizations around the world as protection against future dangerous flu epidemics. Thus, there will be a huge market for an effective product.

1. https://en.wikipedia.org/wiki/Influenza
2. https://en.wikipedia.org/wiki/Extracorporeal_membrane_oxygenation

6. Risks

There are always risks in biotech companies. These include, inter alia, the ability to meet the emerging capital needs of the projects, the effects of the test substance and side effects in clinical trials, permissions from authorities, the company's ability to retain key personnel, existing and future competitors, sustainability of the patents, general business climate, currency risk and political risks. There is no guarantee that the healthcare provider chooses to use EcoFilter® to reduce drug release. Decisions on the use of the system may be delayed, for political, administrative or other reasons. It can not be ruled out that the system works worse than expected or that there are practical problems. It is not certain that patent applications for EcoFilter® will be granted or that granted patents have sufficient commercial strength. The bronchitis product may not be CE certified. It is possible that it is more advantageous to develop the product as a drug or otherwise. It is also not certain that any sales of such a product will generate larger revenues. Furthermore, it is not certain that patent applications will be granted or that granted patents have sufficient commercial strength. Furthermore, it is not certain that the project for the treatment of flu-induced lung failure will be successful, nor that such treatment can be patent-protected or generate significant revenues for the company.

7. Financing

The existing funding is expected to be sufficient for a considerable part of 2018. There is a possibility that the company will receive revenues in 2018, for example from licensing agreements, from the treatment of chronic bronchitis or from the EcoFilter® project. However, it is also possible that a future new share issue may be applicable.

8. General financial information

Audit of auditors
The interim report has not been reviewed by the company's auditor.

Principles for the preparation of the interim report
The interim report has been prepared in accordance with the same accounting principles as in the company's annual accounts for the financial year ended 31st December 2016, that is, in accordance with the Annual Accounts Act and the Swedish Accounting Standards Board, BFNAR 2012:1.

Upcoming financial reports
Report on the fourth quarter 2017: February 15, 2018

Submission of interim report
Lund, November 16, 2017
PharmaLundensis AB (publ)
Board of Directors

Income statement

(SEK)	2017 *Third quarter*	2016 *Third quarter*	2017 *First nine months*	2016 *First nine months*
Net sales	0	0	0	0
Operating expenses				
Other external costs	-1 941 744	-1 528 008	-5 439 904	-4 506 554
Personnel costs	-247 948	-247 948	-744 043	-1 049 844
Depreciations of tangible assets	-102 953	-103 082	-305 498	-306 187
Capitalized development expenditures	882 640	817 573	2 210 152	2 846 622
Operating loss	**-1 410 005**	**-1 061 465**	**-4 279 293**	**-3 015 963**
Result of financial investments				
Interest incomes and similar incomes	-	338	-	375
Interest expenses and similar expenses	-	-448	-342	-1 840
Loss after financial items	**-1 410 005**	**-1 061 575**	**-4 279 635**	**-3 017 428**
Net loss for the period	**-1 410 005**	**-1 061 575**	**-4 279 635**	**-3 017 428**

Balance sheet

(SEK)	Sep 30, 2017	Dec 31, 2016
ASSETS		
Fixed assets		
Intangible assets		
Capitalized expenditure for development and similar	11 518 871	9 308 719
Tangible assets		
Equipment, tools, fixtures and fittings	1 166 437	1 471 935
Financial assets		
Other securities held as fixed assets	1 000	1 000
Total fixed assets	**12 686 308**	**10 781 654**
Current assets		
Current receivables		
Other receivables	266 372	121 164
Prepaid expenses and accrued income	139 518	182 679
Total current receivables	**405 890**	**303 843**
Cash and bank balances	3 406 652	1 451 209
Total current assets	**3 812 542**	**1 755 052**
TOTAL ASSETS	**16 498 850**	**12 536 706**

Balance sheet, cont.

(SEK)	Sep 30, 2017	Dec 31, 2016
EQUITY AND LIABILITIES		
Equity		
Restricted equity		
Share capital	1 014 017	939 821
Fund for development expenditures	5 217 911	3 007 759
	6 231 928	**3 947 580**
Non-restricted equity		
Share premium reserve	50 909 580	42 580 220
Profit or loss brought forward	-37 838 443	-31 689 555
Loss for the period	-4 279 635	-3 938 736
	8 791 502	**6 951 929**
Total equity	**15 023 430**	**10 899 509**
Liabilities		
Current liabilities		
Account payable - trade	607 965	452 941
Other liabilities	16 807	16 780
Accrued expenses and deferred income	850 648	1 167 476
	1 475 420	**1 637 197**
TOTAL EQUITY AND LIABILITIES	**16 498 850**	**12 536 706**
Pledged assets and contingent liabilities		
Pledged assets		
Bank funds	None	50 000
Contingent liabilities	None	None

Changes in equity

2016

(SEK)	Share capital	Fund for development expenditures	Share premium reserve	Profit or loss brought forward	Loss for the year	Total
At beginning of year	939 821		42 580 220	-24 951 581	-3 730 215	14 838 245
Disposition according to the Annual General Meeting				-3 730 215	3 730 215	0
Ongoing new share issue	-64 298		-7 051 408			-7 115 706
New share issues during the year	64 298		7 051 408			7 115 706
Changes in development expenditures		3 007 759		-3 007 759		0
Loss for the year					-3 938 736	-3 938 736
At year-end	**939 821**	**3 007 759**	**42 580 220**	**-31 689 555**	**-3 938 736**	**10 899 509**

2017 (9 month)

(SEK)	Share capita	Fund for development expenditures	Share premium reserve	Profit or loss brought forward	Loss for the period	Total
At beginning of year	939 821	3 007 759	42 580 220	-31 689 555	-3 938 736	10 899 509
Disposition according to the Annual General Meeting				- 3 938 736	3 938 736	0
New share issues during the year	74 196		8 329 360			8 403 556
Changes in development expenditures		2 210 152		-2 210 152		0
Loss for the period					-4 279 635	-4 279 635
At period-end	**1 014 017**	**5 217 911**	**50 909 580**	**-37 838 443**	**-4 279 635**	**15 023 430**

In 2015, following the decision of the Annual General Meeting June 16th 2015, 200,000 warrants were issued to two Board members, which resulted in an increase of the free equity of SEK 40,000. Option rights may be exercised during the period from July 1, 2018 through July 31, 2018 and may maximum lead to approximately 1.1 percent dilution.

In connection with the new share issue, which was registered on June 9th, 2017, 494,642 warrants were issued. Each warrants entitle the holder to subscribe for 1 new share during the period March 1st 2020 - March 31st 2020 for SEK 6. This can lead to a maximum of 2.44% dilution.

Cash flow statement

(SEK)	2017 *Third quarter*	2016 *Third quarter*	2017 *First nine months*	2016 *First nine months*
Operating activities				
Operating loss	-1 410 005	-1 061 465	-4 279 293	-3 015 963
Depreciations	102 953	103 082	305 498	306 187
Interest received	-	338	-	375
Interest paid	-	-448	-342	-1 840
Cash flow from operating activities before working capital changes	**-1 307 052**	**-958 493**	**-3 974 137**	**-2 711 241**
Cash flow from working capital changes				
Increase/decrease in receivables	37 900	231 308	-102 047	16 594
Increase/decrease in current liabilities	93 646	-61 558	-161 777	1 156 942
Change in working capital	**131 546**	**169 750**	**-263 824**	**1 173 536**
Cash flow from operating activities	**-1 175 506**	**-788 743**	**-4 237 961**	**-1 537 705**
Investing activities				
Purchase of tangible assets	-	-25 000	-	-25 000
Purchase of intangible assets	-882 640	-817 573	-2 210 152	-2 846 622
Ash flow from investing activities	**-882 640**	**-842 573**	**-2 210 152**	**-2 871 622**
Financing activities				
New share issue	-		8 403 556	
Subscribed paid capital	-	-	-	5 775 000
Cash flow from financing activities	**0**	**0**	**8 403 556**	**5 775 000**
Cash flow for the period	-2 058 146	-1 631 316	1 955 443	1 365 673
Cash and cash equivalent at the beginning of the period	5 464 798	4 242 327	1 451 209	1 245 338
Cash and cash equivalent at the end of the period	**3 406 652**	**2 611 011**	**3 406 652**	**2 611 011**

PharmaLundensis AB

Telefon: 046 – 13 27 80 | E-post: info@pharmalundensis.se | Hemsida: www.pharmalundensis.se