FOR IMMEDIATE RELEASE **17 July 2014**

PBL AWARDED TWO FURTHER US PATENTS ON SHORT RNAi MOLECULES: US 8,759,102 and US 8,779,236

Plant Bioscience Limited (PBL) is pleased to announce that the United States Patent and Trademark Office (USPTO) has issued US Patent No. 8,759,102 and US Patent No. 8,779,236 with fundamental claims directed to RNAi in cells and organisms to effect gene silencing.

These two new patents granted add to the strength and breadth of PBL's RNAi patent portfolio. The patent family now comprises a total of 9 granted US patents, which cover a wide area of RNAi applications from detection of gene silencing, to methods to silence genes, and compositions and cells containing and producing RNAi molecules.

On 24 June 2014 US Patent No. 8,759,102 was granted with claims to cells comprising **synthetic DNA constructs that express RNAi molecules** to silence target RNA in these cells. Earlier this week (15 July 2014) US Patent No. 8,779,236 was granted with claims to host **cells containing DNA constructs expressing RNAi molecules that silence RNA in a pest, parasite, predator or pathogen**.

The significance of this RNAi patent estate is widely recognised in the AgBiotech and Pharma industries as a critical part for the wide range of applications of interest in the field of RNAi. This is evidenced by the substantial number of licences already granted by PBL for different aspects and applications of PBL's RNAi portfolio. PBL's partners are currently developing products in the area of pharmaceuticals, animal health and agricultural biotechnology.

Dr Jan Chojecki, Managing Director of PBL adds "We are very pleased, that the USPTO has over the past two and a half years recognised Professor Sir David Baulcombe's and Dr Andrew Hamilton's contribution to the field of RNAi and PBL now holds a substantial patent portfolio in the area, covering many aspects and applications of RNAi. Several potential products are currently in clinical trials and product development with our partners. We are looking forward to the market introduction of RNAi based therapeutics and plant health agents which will demonstrate the unique ability of RNAi to improve medicine and agriculture. Furthermore we anticipate partnering with more companies interested in the diverse applications of RNAi."

Dr Lars von Borcke, Business Development Manager of PBL adds "We are continuing with our strategy of broadly licensing our RNAi portfolio. Currently licences are still available for applications in human therapeutics, animal health, plant protection, commercial provision of reagents and diagnostics, and related service activities, and we are looking forward to enter into discussions and agreements on these with new potential partners."

While most of PBL's licences to its RNAi patent portfolio are confidential, PBL has previously announced the partnership with Alnylam Pharmaceuticals (NASDAQ: ALNM), a world leader in the clinical development of RNAi therapeutics (press release) and Dicerna Pharmaceuticals (NASDAQ: DRNA), a second generation RNAi company focused on developing novel therapeutics utilizing its proprietary Dicer Substrate siRNA (DsiRNA) Technology™ and EnCore™ delivery system (press release).

Please click here for a link to the Short RNA section on our website.

For licensing enquiries, please contact Dr Lars von Borcke (lars@pbltechnology.com).

All other enquiries to info@pbltechnology.com.

FOR IMMEDIATE RELEASE **17 July 2014**

About PBL
Plant Bioscience Limited (PBL) www.pbltechnology.com is a technology development and intellectual property management company owned in equal parts by The Sainsbury Laboratory www.tsl.ac.uk , the John Innes Centre www.jic.ac.uk and the Biotechnology and Biological Sciences Research Council www.bbsrc.ac.uk. PBL promotes the development and commercial uptake of academic research results for public use and benefit and is specialised in life sciences, and in particular plant, food and microbial science.

PBL is the owner of the patent rights created by this work of Andrew Hamilton and David Baulcombe.

About The Sainsbury Laboratory
The Sainsbury Laboratory (TSL) www.tsl.ac.uk is a world-leading research centre located in Norwich, UK, focusing on making fundamental discoveries about plants and how they interact with microbes. Professor Sir David Baulcombe is now Regius Professor of Botany and Royal Society Research Professor at The University of Cambridge. Dr Andrew Hamilton is now at The University of Glasgow, in the Division of Cancer Sciences and Molecular Pathology.

About RNAi
The importance of silencing as a scientific discovery was underlined both by the award of a Nobel Prize in 2006 to Andrew Fire and Craig Mello, in recognition of their seminal publication in 1998 on the use of long dsRNA to induce silencing in nematodes, and the Lasker Foundation awarding the 2008 Albert Lasker Basic Research Award jointly to David Baulcombe (whose work demonstrated that short RNA molecules have a broad applicability as markers and inducers of gene silencing in living organisms), jointly with Gary Ruvkun and Victor Ambros (for their combined effort in identifying the first miRNA in nematodes). On issuing the award, the Lasker Foundation noted David Baulcombe's contributions thus: "*For discoveries that revealed an unanticipated world of tiny RNAs that regulate gene function in plants and animals*". In addition, in 2009, Professor Baulcombe was awarded a knighthood "*for services to Plant Science*".

The original patent application that led to the PBL RNAi patent portfolio was filed by PBL in 1999, following Baulcombe and Hamilton's ground-breaking research at The Sainsbury Laboratory in Norwich, UK and published in Science ("A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants", (1999), 286, pp. 950-952). This paper provided the first identification that short RNA molecules are the active agents of silencing, and the patent describes methods and compositions for use of such molecules for inducing silencing in living organisms. The PBL RNAi patent portfolio currently comprises US Patent Nos 6,753,139, 7,704,688, 8,097,710, 8,258,285, 8,263,569 and 8,299,235.

Glossary:

siRNA	short interfering RNA
SRM	short RNA molecule
miRNA	MicroRNA
dsRNA	double stranded RNA
RNAi	RNA interference

US 8,759,102 CLAIMS:

1. A cell comprising at least one synthetic DNA construct that expresses short antisense RNA molecules (SARMs) and short sense RNA molecules (SSRMs), collectively short RNA molecules (SRMs), wherein the SSRMs and SARMs consist of 20-30 nucleotides, and wherein said SARMs are complementary to, and can base pair with, a target RNA in the cell, which target RNA is transcribed from a gene that is silenced when said SRMs are present in the cell, and said SSRMs correspond to the target RNA.

2. The cell of claim 1 wherein said DNA construct is contained in a vector introduced into said cell.

3. The cell of claim 2 wherein said DNA construct is stably maintained by said cell.

4. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 20 nucleotides.

5. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 21 nucleotides.

6. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 22 nucleotides.

7. The cell of claim 1 wherein said gene to be silenced is selected from the group consisting of a gene involved in cancer, apoptosis, cell-cycle regulation, a neurological process and signal transduction.

8. The cell of claim 1 wherein said gene to be silenced is selected from the group consisting of an oncogene, a pocket protein, a transcriptional regulator and a MHC superfamily member gene.

9. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 23 nucleotides.

10. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 24 nucleotides.

11. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 25 nucleotides.

12. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 26 nucleotides.

13. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 27 nucleotides.

14. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 28 nucleotides.

15. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 29 nucleotides.

16. The cell of claim 1 wherein the nucleotide sequences of each SSRM and each SARM consists of 30 nucleotides.

US 8,779,236 CLAIMS:

1. An isolated host cell of a host organism, said host cell modified to contain a DNA construct that expresses short antisense RNA molecules (SARMs) and short sense RNA molecules (SSRMs), collectively short RNA molecules (SRMs), wherein the SSRMs and the SARMs consist of lengths of 20-30 nucleotides; wherein said SARMs are complementary to, and can base pair with, a target RNA, which target RNA is transcribed from a gene that is silenced when said SRMs are present in a cell of a pest, parasite, predator or pathogen of said host organism containing said gene, and said SSRMs correspond to the target RNA; and wherein said gene is endogenous to said pest, parasite, predator or pathogen of said host organism.

2. A host organism comprising the host cell of claim 1 wherein said host organism is a plant and said host cell is a plant cell; and said pest, parasite, predator or pathogen is selected from the group consisting of a plant parasitic nematode, a plant pathogenic virus, a plant pathogenic fungus, and an insect.

3. The host organism of claim 2 which produces SRMs such that any pest, parasite, predator or pathogen that directly feeds off plant cellular contents or extracellular components of said host cell ingest SRMs having sequence homology with genes resident in said pest, parasite, predator or pathogen.

4. The host cell of claim 1 wherein said target gene is not an endogenous gene in said host organism but is endogenous to said pest, parasite, predator or pathogen.

5. The host cell of claim 4 wherein said target gene is an essential gene in said pest, parasite, predator or pathogen.

6. The host cell of claim 4 wherein more than one gene is targeted in said pest, parasite, predator or pathogen.

7. A method to silence a target gene in a pest, parasite, predator or pathogen which method comprises expressing the SRMs in the host cell of claim 1.

8. The host cell of claim 1 wherein each SSRM and each SARM consists of 20 nucleotides.

9. The host cell of claim 1 wherein each SSRM and each SARM consists of 21 nucleotides.

10. The host cell of claim 1 wherein each SSRM and each SARM consists of 22 nucleotides.

11. The host cell of claim 1 wherein each SSRM and each SARM consists of 23 nucleotides.

12. The host cell of claim 1 wherein each SSRM and each SARM consists of 24 nucleotides.

13. The host cell of claim 1 wherein each SSRM and each SARM consists of 25 nucleotides.

14. The host cell of claim 1 wherein each SSRM and each SARM consists of 26 nucleotides.

15. The host cell of claim 1 wherein each SSRM and each SARM consists of 27 nucleotides.

16. The host cell of claim 1 wherein each SSRM and each SARM consists of 28 nucleotides.

17. The host cell of claim 1 wherein each SSRM and each SARM consists of 29 nucleotides.

18. The host cell of claim 1 wherein each SSRM and each SARM consists of 30 nucleotides.

19. A host organism comprising the host cell of claim 1 wherein said host organism is a nematode and said host cell is a nematode cell

Click the links below for PBL's other short RNA patent claims:

ISSUE DATE	ISSUE NUMBER	FIRST CLAIM
8 Jan 13	8,349,607	A method of silencing a target gene in a second cell or a second organism comprising introducing into said second cell or second organism, in which said target gene has not been silenced, either (a) a construct transcribable into short antisense RNA molecules (SARMs) and short sense RNA molecules (SSRMs), collectively short RNA molecules (SRMs), wherein the SSRMs and SARMs consist of 20-30 nucleotides; wherein said SARMs have been identified as present in a first organism wherein the same gene has been silenced and said SARMs are complementary to, and can base pair with, target RNA transcribed from said gene that is silenced in said first organism, and said SSRMs correspond to the target RNA in said first organism; or (b) introducing said SRMs themselves into said second cell or second organism.
30 Oct 12	8,299,235	A composition for introduction into a cell to effect gene silencing, consisting essentially of isolated short antisense RNA molecules (SARMs) and isolated short sense RNA molecules (SSRMs), collectively short RNA molecules (SRMs), wherein the SSRMs and the SARMs consist of 21-30 nucleotides; herein said SARMS are complementary to, and can base pair with, a target RNA, which target RNA is transcribed from a gene that is silenced when said SRMs are present in a cell containing said gene, and said SSRMs correspond to the target RNA; and wherein said gene is endogenous to an organism selected from the group consisting of a plant, a mammal, an avian organism, a reptile, an insect, and a protozoan, or said target RNA is generated by a pathogen.
11 Sep 12	8,263,569	A method of silencing a gene in cells which method comprises introducing into said cells a composition that consists essentially of isolated short antisense RNA molecules (SARMs) and isolated short sense RNA molecules (SSRMs), collectively short RNA molecules (SRMs), wherein the SSRMs and SARMs consist of 20-30 nucleotides; wherein said SARMs are complementary to, and can base pair with, a target RNA, which target RNA is transcribed from a gene that is silenced when said SRMs are present in a cell containing said gene, and said SSRMs correspond to the target RNA; and wherein said gene is endogenous to an organism selected from the group consisting of a plant, a mammal, an avian organism, a reptile, an insect, and a protozoan, or said target RNA is generated by a pathogen, whereby said gene is silenced.
4 Sep 12	8,258,285	A composition for introduction into a cell to effect gene silencing, consisting essentially of isolated short antisense RNA molecules (SARMs) and isolated short sense RNA molecules (SSRMs), collectively short RNA molecules (SRMs), wherein the SSRMs and SARMs are each of a uniform length of 20-24 nucleotides; wherein said SARMs are complementary to and can base pair with a target RNA, which target RNA is transcribed from a gene that is silenced when said SRMs are present in a cell containing said gene, and said SSRMs correspond to the target RNA; wherein said gene is endogenous to an organism selected from the group consisting of a plant, a mammal, an avian organism, a reptile, an insect, and a protozoan, or said target RNA is generated by a pathogen; and wherein if said SARMs and SSRMs consist of 20 nucleotides, said SARMs and SSRMs are unmodified.
17 Jan 12	8,097,710	A method of silencing a gene in cells by post-transcriptional gene silencing (PTGS) which method comprises introducing into said cells a composition that contains short RNA molecules (SRMs), which SRMs are isolated short sense RNA molecules (SSRMs) and isolated short antisense RNA molecules (SARMs) at the same abundance; wherein said SARMs are complementary to a region of a target RNA transcribed from a gene which is silenced when said short RNA molecules are present in cells containing said gene and said SSRMs correspond to said target RNA; and wherein the SSRMs and SARMs consist of 20, 21, 22, 23 or 24 nucleotides, whereby said gene is silenced.
27 Apr 10	7,704,688	A method of detecting gene silencing of a target gene in a mammalian organism or in cellular material of a mammalian organism which method comprises the steps of: detecting in a nucleic acid extract prepared from said organism or in cellular material from said organism the presence as opposed to the absence of short RNA molecules (SRMs) of uniform length which are 20-30 nucleotides in length in said extract, characterizing any SRMs which are present in said extract wherein said characterizing comprises determining sequence identity or similarity with said target gene, wherein the presence of any SRMs having sequence identity or similarity with said target gene indicates silencing of said target gene in the organism or in cellular material from said organism, and confirming that said target gene has been silenced.
22 Jun 04	6,753,139	A method of detecting the silencing of a target gene in a plant, wherein said silencing is initiated by introduction of an exogenous nucleic acid, which method comprises the steps of: (i) obtaining a sample of material from said plant, (ii) producing a nucleic acid extract from said sample, (iii) analyzing said extract such as to determine the presence or absence of short RNA molecules which are 21-25 nucleotides in length (SRMs) in said extract, (iv) characterizing any SRMs which are present in said extract such as to determine sequence identity or similarity with said target gene, and (v) correlating the presence of said SRMs having sequence identity or similarity with said target gene in the extract with the occurrence of gene silencing in said plant.