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Issuer Free Writing Prospectus dated November 20, 2018  
Relating to Prospectus dated November 19, 2018  
Registration No. 333-227974



# Investor Overview

November 2018



## FORWARD-LOOKING STATEMENTS

This investor overview provided by Pulse Biosciences, Inc., contains estimates and forward-looking statements including, among others, statements regarding Pulse Biosciences' future business plans, products, commercial applications, clinical trials, regulatory processes and pathways, markets for its technologies, intellectual property and other future events. You should not place undue reliance on forward-looking statements, as they involve known and unknown risks and uncertainties that are, in some cases, beyond the Company's control and could cause actual results to differ materially from the information expressed or implied. Factors that could materially affect actual results are described in detail in the Company's recent Securities and Exchange Commission filings.

Pulse Biosciences undertakes no obligation to revise or update forward-looking statements to reflect future events or circumstances.

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November 20, 2018

Fellow Stockholders,

From day one our mission at Pulse Biosciences has been to build a viable company that improves and extends the lives of patients through the use of our Nano-Pulse Stimulation™ (NPST™) technology. NPS utilizes non-thermal nanosecond\* duration (from a billionth to a millionth of a second) energy pulses with varying pulse amplitude, pulse duration, pulse rate, and number of pulses in the treatment of tissue. We continue to believe this technology will have applications across multiple medical disciplines and we have made important progress towards our mission. I am pleased to provide you with the following overview of our achievements and plans.

We have advanced our NPS technology through several clinical studies, demonstrating excellent safety and efficacy in difficult-to-treat skin lesions, including Seborrheic Keratosis\* and Sebaceous Hyperplasia\*. In parallel with our clinical successes, we have developed and introduced into the clinic our current generation NPS technology platform, the CellFX™ System. Our proprietary CellFX System will be our first commercial system, designed for beneficial and cost-effective patient outcomes, physician and clinic ease-of-use, volume manufacturing, and with underlying technology that supports a networked pay-per-click business model. The pay-per-click business model should allow us to directly align the value we deliver to the patient and physician for each unique indication. On the strength of our clinical data, the introduction of our proprietary CellFX System, and a growing pipeline of potential indications in difficult-to-treat skin lesions, we are planning for a commercial launch in aesthetic dermatology in 2019, and believe it represents a significant near-term opportunity for our company.

In addition to aesthetic dermatology, we continue to invest in the area of oncology and believe our CellFX System may play a role in the field of cancer immunotherapy\*. We have ongoing pre-clinical programs in this area and have also commenced our human Basal Cell Carcinoma\* biomarker study, marking our first step in understanding the potential of our CellFX System in this significant skin cancer opportunity.

All of us at Pulse Biosciences remain confident in our ability to achieve our mission. In the accompanying update you will find further detail regarding our progress and plans to deliver on this mission. In addition, you will find information regarding our recently announced rights offering. We believe this rights offering is an efficient and effective way for the company to raise additional capital while allowing all of our current stockholders to participate and maintain their ownership stake.

Thank you for your continued support of Pulse Biosciences!

Best Regards,

A handwritten signature in black ink, appearing to read 'D. Uecker'.

Darrin R. Uecker  
Director, President, Chief Executive Officer and Stockholder

\*as defined in the glossary at the end of the Overview

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Pulse Biosciences is a medical therapy company bringing to market our proprietary CellFX™ Nano-Pulse Stimulation™ (NPS™) System. Our mission is to build a viable company that delivers novel, proprietary, and differentiated products that have the potential to significantly improve and extend the lives of patients in the markets we serve. To achieve this mission, we intend to:

- *Demonstrate the unique benefits of our proprietary CellFX System and its unique mechanism of action across a number of compelling indications.* The CellFX System is the only tunable nanosecond\* pulsed energy system designed for use in human medicine that we are aware of. The proprietary CellFX System allows for the adjustment of four key pulsing parameters: pulse duration, pulse amplitude, pulse frequency, and the number of pulses, depending on the tissue and desired treatment outcome. We have conducted or are conducting several clinical studies, including a skin dose ranging and safety study, a study in Seborrheic Keratosis (SK), Sebaceous Hyperplasia (SH), Basal Cell Carcinoma (BCC), and we just initiated a study in warts. We plan to initiate an additional study in acne during 2018. We expect to conduct clinical studies on an ongoing basis to continue to demonstrate the value of our CellFX System across a growing list of valuable indications; and
- *Commercialize our proprietary CellFX System and applications for its use across a broad array of clinical indications.* In early Q1 2019 we plan to submit a 510(k) to the U.S. Food and Drug Administration (FDA) for clearance to market and sell for the specific indications of SK and SH in aesthetic dermatology. Based on a successful regulatory filing and timing of a clearance we plan to launch the CellFX System in aesthetic dermatology market in Q4 2019. As additional clinical data becomes available, we expect to expand the indications in aesthetic dermatology. We also believe the CellFX System will prove to be a valuable instrument in other medical disciplines, such as oncology, and we plan to commercially pursue indications in those disciplines as we develop the clinical evidence.

To date, substantially all of our resources have been dedicated to the research and development of our NPS technology platform, and we have not generated revenue from the sale of our products. Revenue from our commercial products and applications will commence after we obtain the necessary regulatory and marketing clearance and introduce our products.

We have incurred significant operating losses since our inception and have an accumulated deficit of approximately \$66.8 million as of September 30, 2018. The process of developing and commercializing our CellFX System and NPS applications requires significant research and development, preclinical testing and clinical trials, manufacturing operations and arrangements as well as regulatory and marketing clearance. These activities, together with our general and administrative expenses, are expected to result in operating losses until the commercialization of our CellFX System and NPS applications generate sufficient revenue to cover our expenses. We expect that losses will fluctuate from quarter to quarter and that such fluctuations may be substantial. Achieving profitability depends upon our ability to successfully complete the development of our products, obtain required regulatory clearance and successfully manufacture, market and sell our NPS applications and products.

## Our Technology

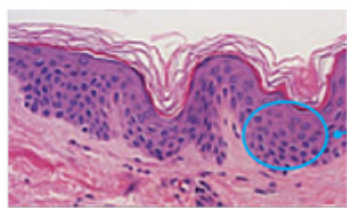
Nano-Pulse Stimulation delivered by our proprietary CellFX System is our differentiated platform that delivers ultrafast energy pulses, with pulse durations from billionths up to a millionth of a second, to targeted tissue. Our NPS energy pulses enter cells and we believe alter the function of the internal cellular organelles, including the mitochondria and endoplasmic reticulum, without disrupting the integrity of the outer cell membrane or extracellular tissue, leading to regulated cell death\* (RCD\*).

RCD\* is a process exhibited by cells in the human body when they undergo stress and are unable to restore cellular homeostasis. In the case of cancer cells this RCD\* process may result in immunogenic cell death (ICD\*) that stimulates the immune system to mount a systemic immune response against antigens\*, or markers, in those cancer cells. Our pre-clinical studies suggest that our CellFX System may stimulate RCD\* which in cancerous cells, may lead to ICD\*.

Our proprietary CellFX System's unique non-toxic and non-thermal mechanism of action that we believe initiates RCD\* is a biophysical mechanism brought about by the tunable speed and amplitude of our NPS pulses interacting with the physical structure of cells. While our CellFX System delivers pulses that directly affect the internal organelles of cells, they have no functional effect on acellular tissue, such as collagen, a protein that supports tissue structure and healing. In short, with our proprietary CellFX System, we can deliver a unique cell-focused effect delivered to the internal structures of treated cells that we believe leads to RCD\* while preserving surrounding acellular tissue, a combination that may potentially lead to highly differentiated treatment applications.

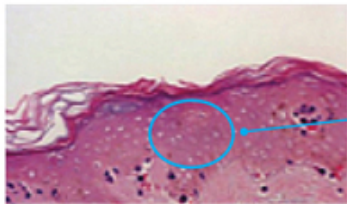
We have clinically demonstrated (Figure 1) the ability of our CellFX System to initiate RCD\* without disrupting the integrity of the outer cell membrane in a human skin study. Histology shows that viable cells treated with NPS become non-viable while remaining intact and then are eliminated through the body's normal processes.

Figure 1 - Demonstrated Mechanism of NPS Treatment



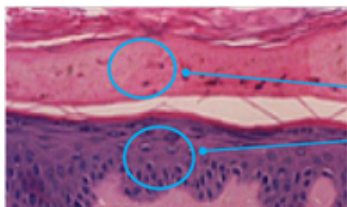
### **Healthy Skin**

- Healthy epidermal cells with dark nuclei



### **One (1) day post-NPS treatment**

- Cells in treated epidermis are nonviable (ghost cells)
- Cell membranes and surrounding acellular tissue are intact
- No indication of thermal damage



### **Seven (7) days post-NPS treatment**

- Treated epidermal layer is detaching
- Healthy epidermis is emerging below
- No inflammation in the dermal foundation of the skin

## Our CellFX System

We have developed and plan to commercialize our current generation NPS platform, the CellFX™ System. The CellFX System (Figure 2) includes a multi-use handpiece and an initial family of five (5) single-patient use dermatology treatment tips. The system is designed for use in many treatment settings, including a physician's office or clinic, an outpatient surgery center or a hospital. The system is a mobile cart-based system that can easily be transported from room to room and is setup and ready for treatments in a matter of minutes.

The treatment tips enable treatment of a variety of sizes, initially from 1.5mm to 10.0mm square, and wirelessly connect to our CellFX System when they are plugged into the handpiece. This enables the use of automated treatment settings based on the treatment tip being utilized.

The system was engineered for volume manufacturing and the use of contract manufacturing partners to ensure our ability to meet anticipated demand while effectively managing underlying system costs.

In addition, the CellFX System includes the underlying technology to support a networked per-click revenue model. The per-click revenue model will be used to charge on a per-lesion, or lesion treatment basis, as opposed to a per-treatment tip, or per-procedure, basis. This aligns the incentives of the payer, physician, and Pulse Biosciences, especially in a cash paying procedure setting where the patient is paying out-of-pocket for the treatment. This also allows us to use a value-based pricing model, adjusting price based on the value the system is delivering for each specific indication.

Our CellFX System has been successfully used in our clinical studies.



Figure 2 – The CellFX System



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## Initial Commercial Opportunity – Aesthetic Dermatology

### Overview

Based on our early clinical data demonstrating the unique, non-thermal, cell targeting mechanism of action, we believe there is a significant opportunity for our CellFX System in aesthetic dermatology in the United States. According to the 2017 Consumer Survey by the American Society for Dermatologic Surgery (ASDS) the number of consumers considering a cash-pay cosmetic procedure has more than doubled, from 30% in 2013 to 70% in 2017. The survey also highlighted that consumers ranked their dermatologist as the #1 influencer of aesthetic procedure decisions. As a result, to further explore our opportunity in aesthetic

dermatology we have worked closely with top key opinion leaders (KOLs) in the aesthetic dermatology field to identify those procedures in which our CellFX System would provide a unique value proposition.

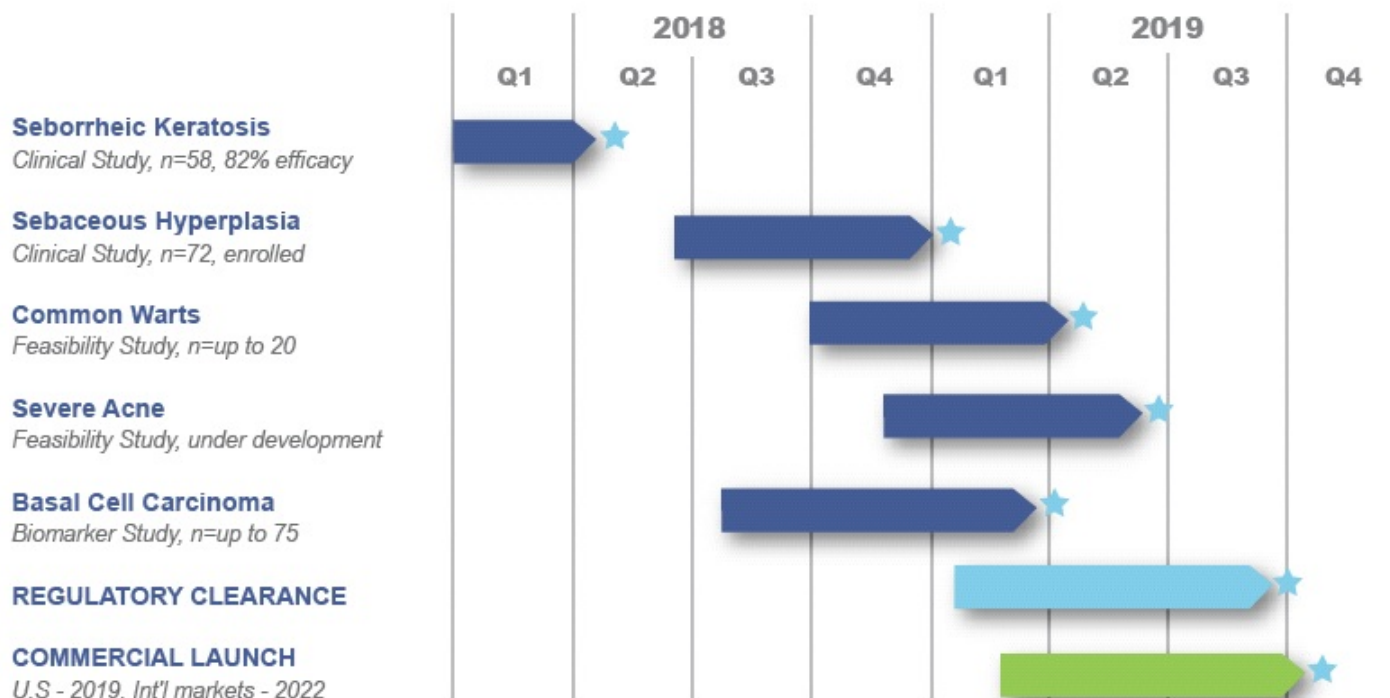
We plan to launch our CellFX System in the United States during 2019 in key metropolitan markets with high concentrations of dermatologists and aesthetic procedure specialists, which allows access to major markets with an efficient direct sales force. We intend to scale our sales and support infrastructure commensurate with the scale of our installed customer base. We plan to pursue a CE mark with the intent of expanding to international markets after successfully developing a market for our CellFX System in the United States.

### Commercialization Strategy

We believe there are four elements of our commercial strategy that will contribute to our success in the aesthetic dermatology market.

- **Key Opinion Leaders (KOLs):** We believe our close collaboration with key opinion leaders in dermatology which has guided our mechanism of action studies and clinical study priorities will yield early recognition of the CellFX System from the scientific podium and in peer reviewed journals. We work with key opinion leaders who demand sound science, solid clinical studies, and their own positive clinical experience with our CellFX System before commercial introduction.
- **Early CellFX Introduction:** We believe that our planned clinical studies including the top 40 key opinion leaders in aesthetic medicine will increase the number of proven applications that are treatable with the CellFX System at launch. We believe that our early adopter strategy will drive both system sales and system utilization for the next wave of adopters in the early launch phase later in 2019. We expect that this strategy will allow us to efficiently and effectively maximize our success in this market with a relatively concentrated sales and marketing investment.
- **Scale Appropriate Sales and Marketing:** We plan to scale our clinical, marketing, and sales infrastructure investment along with the rate of utilization for each installed system. We believe that early launch physician and patient satisfaction can create high leverage advocacy for the next wave of adopters and drives utilization of our CellFX System.
- **Per-Click Revenue Model:** We expect our “per-click” business model to provide a recurring revenue stream for each installed system and believe that with each new clinical application as demonstrated in clinical trials will increase the usage per installed system. We believe that this business model scales and builds value for all stakeholders. We plan to build out our sales, marketing, and training team in a controlled manner to set the stage for a commercial launch, with the first revenue units projected for late 2019.

Pulse Biosciences has and is conducting clinical studies in key application areas.

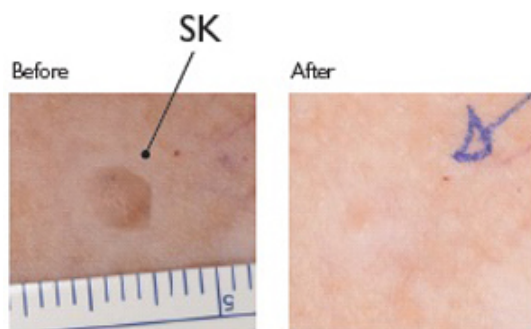


CLINICAL STUDIES

Seborrheic Keratosis\*

Seborrheic Keratosis (“SK”) (Figure 3) is one of the most common non-cancerous skin growths in older adults. SK usually appear as a brown, black or light tan growth on the face, chest, shoulders or back and has a waxy, scaly, slightly elevated appearance. SK are normally painless, and patients often seek to have them removed if they become irritated by clothing or for cosmetic reasons.

Figure 3 - NPS Treated Seborrheic Keratosis



Cleared SK at 106-day follow-up

Results from our clinical study indicate that a single treatment from our CellFX System is more effective than a recently approved topical agent, which showed a 51% efficacy rate, usually after multiple treatments. We believe that the results of this clinical study pave the way for us to explore commercial opportunities for the CellFX System in other similar common lesions that present in the epidermis.



## Prevalence

SK affects approximately 83 million patients in the United States (J Clin Aesthet Dermatol. 2017; 10(3):16–25) and based on a 2018 Clinician Survey conducted by SERMO, sponsored by Pulse Biosciences, clinicians in our target market indicated that they see 52 patients per week on average with SK; however only a third of these patients receive treatment, which we believe is largely due to inferior efficacy and cosmetic outcomes of existing procedures, such as cryoablation.

## NPS Seborrheic Keratosis Clinical Study

Patients: 58 (3 treated lesions per patient)

Study Centers: 4 (United States only)

### Study results

After a single NPS treatment, **82%** of the 174 SKs treated in the study were **rated as clear or mostly clear** by clinical investigators. Patients in the study rated 78% of treatment outcomes as satisfied or mostly satisfied.

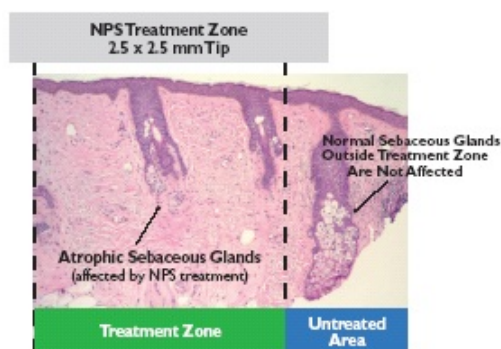
Zero device or procedure-related adverse events were reported.

### Sebaceous Hyperplasia\*

Sebaceous Hyperplasia (“SH”) is a common, benign condition of sebaceous glands in adults of middle age or older. SH occurs when the sebaceous glands become enlarged, creating small, shiny, yellowish lesions or bumps, usually 2-4 millimeters in diameter and typically on the face.

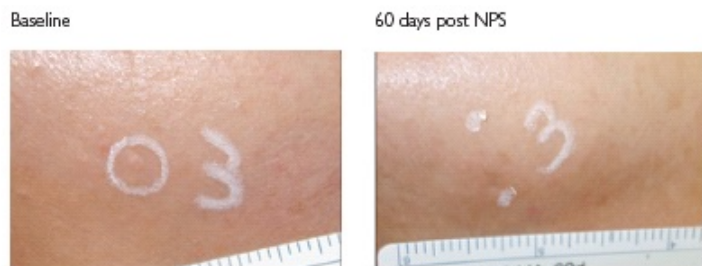
Results from our research have demonstrated that NPS has a unique ability to penetrate into the dermis and target cellular structures, such as the sebaceous gland, without damaging the surrounding dermis, making it a potentially unique and highly effective treatment modality for targeting SH lesions and similar targets residing deeper within the dermis of the skin. Our histological review of treated tissue has shown the unique ability of the CellFX System to treat and eliminate the sebaceous gland while sparing surrounding acellular structures (Figure 4).

Figure 4 - Histology of NPS Treated Sebaceous Glands



Our SH study has completed enrollment and treatments of 72 patients. Based on preliminary 60-day follow-up results from the first 35% of treated lesions, over 95% of treated SH lesions have been reported as clear or mostly clear by investigators (Figure 5).

Figure 5 - NPS Treated Sebaceous Hyperplasia Lesions



### **Prevalence**

Sebaceous Hyperplasia affects an estimated 4.3 million patients in the United States based on a 2018 Clinician Survey conducted by SERMO, sponsored by Pulse Biosciences. Clinicians in our target market indicated that they see 31 patients per week on average with SH; however only approximately 20% of these patients receive treatment for SH, which we believe is due to a lack of a standard of care and poor efficacy and cosmetic outcomes for thermal based treatment modalities that may be utilized.

### **NPS Sebaceous Hyperplasia Clinical Study**

Patients: 72 (up to 4 treated lesions per patient)

Study Centers: 5 (United States only)

Treatments: Up to 2 NPS treatments per lesion.

### **Interim Study results**

After NPS treatment, based on data from the first 79 treated lesions, **more than 95%** of the SH lesions treated in the study were **rated as clear or mostly clear** by clinical investigators. Approximately 7% of treated lesions received a second treatment during the course of the study.

Zero device or procedure-related adverse events reported to date.

### **Feasibility Clinical Studies**

Based on the results from our SK data, and the interim SH data showing the ability of NPS to treat lesions in the epidermis while sparing the dermis, we recently initiated a feasibility study in the treatment of cutaneous warts and plan to commence a feasibility study in the treatment of moderate to severe acne.

## **Cutaneous Warts**

### **Prevalence**

Approximately 22 million patients in the United States (prevalence 7% of the population; Medscape; June 2018; US Population 325.7 million; US Census Bureau)

### **NPS Cutaneous Warts Feasibility Study**

Patients: Up to 20

Study Centers: Two (2) – Including Scripps Health

### **Moderate to Severe Acne**

Early results in our SH study garnered significant interest from our key opinion leaders around other conditions involving sebaceous glands, notably acne. The sebaceous gland plays an integral role in the development of acne and our ability to treat the sebaceous gland as evidenced in our SH study gives us confidence to evaluate NPS in this application of a sizeable commercial opportunity.

### **Immuno-oncology - Nano-Pulse Stimulation Initiated Immunogenic Cell Death**

During August 2018 we commenced a clinical study to evaluate the CellFX System and NPS in Basal Cell Carcinoma, or BCC\*, the most prevalent form of skin cancer. We believe BCC represents a bridge between our developments in dermatology and those in oncology. This is our first NPS human study in cancer and it will allow us to look at both the ability of NPS to treat BCC lesion cells and the immune response changes as a result of the NPS treatment. This is not a therapeutic endpoint study, but it is an important first step that enables us to move quickly to demonstrate safety and NPS effect in treating skin cancer and sets us up for a follow-on study aimed at a therapeutic endpoint. We expect to complete enrollment, patient treatments and data collection during the first quarter of 2019.

### **Regulatory**

The FDA regulates the medical device market to ensure the safety and efficacy of these products. The FDA has three different pathways for a medical device to gain approval for commercialization: pre-market approval (PMA), De-Novo, or 510(k).

Based on our previous conversations with the FDA and knowledge gained from those interactions, we plan to utilize the 510(k) path for specific indications in aesthetic dermatology and are targeting a submission in the first quarter of 2019. We expect that this submission will include data from our SK and SH clinical studies. We believe the 510(k) is the appropriate path for clearance of these indications and look forward to the submission and to working with the FDA.

## Intellectual Property

We maintain a portfolio of intellectual property surrounding our CellFX NPS system. As a medical technology company our current patents and ongoing intellectual property development are, and will continue to be, a priority for our business. We believe our intellectual property is an important competitive advantage for us. We also rely on trade secrets, know-how, continuing technological innovations and licensing opportunities to further develop, maintain and strengthen our competitive position. We actively protect our intellectual property through a combination of patent registrations, trademarks, copyright protections, confidentiality agreements with our employees, consultants and other parties, and access control to sensitive information.

We own or have a license to 84 issued patents worldwide and have 84 patent applications pending worldwide, with the earliest expiration of a United States issued patent, in this case a licensed patent, in 2020 and the latest in 2035. As we have over the last several years, we are filing and plan to continue to file new patent applications to protect our systems, algorithms, applicators, methods, and designs of our technologies and products as they evolve. Medical technologies such as ours may be utilized in many different applications and incorporate several patentable features, and our strategy will be to always strive to protect our products and technologies with multiple patents directed to the variety of features and applications, in order to establish a strong defense against competitors and such that an expiration of a single patent does not lessen our overall comprehensive coverage. We believe our current CellFX System is protected by several issued patents and is also covered in multiple pending applications we are pursuing.

**CellFX™ System** – Pulse Biosciences' proprietary, patent protected NPS delivery system comprised of a tunable NPS pulse generator, hand piece and applicator tips of varying configurations.

**Nano-Pulse Stimulation™ (NPST™)** – Pulse Biosciences' non-thermal cell focused technology utilizing ultrafast (billionth of a second), energy pulses with unique pulse amplitude, pulse duration, pulse frequency and number of pulses to alter the function of internal cell structures and initiate regulated cell death, or immunogenic cell death in the case of cancer cells.

**Nanosecond** – one billionth (1/1,000,000,000th) of a second

**Antigens** – a substance such as a chemical, bacteria or virus that causes the body to make an immune response against that substance.

**Basal Cell Carcinoma (BCC)** - abnormal, uncontrolled growth or lesion that arise in the skin's basal cells, which line the deepest layer of the epidermis (the outermost layer of the skin). BCCs are often caused by sun exposure and present as open sores, red patches, pink growths, shiny bumps, or scars. BCCs rarely metastasize, however, require medical attention.

**Immunogenic Cell Death (ICD)** - a form of RCD\* that is sufficient to activate an adaptive immune response specific for cellular or viral antigens expressed by dying cells.

**Cancer Immunotherapy** – a treatment therapy that uses the body's own immune system to help fight cancer.

**Regulated Cell Death (RCD)** - a mechanism by which the cell activates its own machinery to self-destruct. RCD\* is important for the maintenance of tissue homeostasis.

**Sebaceous Hyperplasia (SH)** - small (2-4mm) shiny pale-yellow or flesh-colored bumps on the skin, often on the face caused when sebaceous glands become enlarged with trapped sebum (oils excreted by the sebaceous gland).

**Seborrheic Keratosis (SK)** - a common non-cancerous skin growths that usually develop in older adults. SKs may present as waxy brown, black or tan growths with a slightly elevated appearance that often appear on the face, chest, shoulders and back.

Pulse Biosciences has filed a registration statement (including the Prospectus) with the Securities and Exchange Commission (the "SEC") for the rights offering to which this communication relates. Before you invest, you should read the Prospectus in that registration statement and other documents Pulse Biosciences has filed with the SEC for more complete information about Pulse Biosciences and the rights offering. You may get these documents for free by visiting EDGAR on the SEC web site at [www.sec.gov](http://www.sec.gov). Alternatively, a copy of the Prospectus may be obtained from Broadridge Corporate Issuer Solutions, Inc., the Company's information and subscription agent for the rights offering, by calling (888) 789-8409 (toll-free) or by emailing [shareholder@broadridge.com](mailto:shareholder@broadridge.com).



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