



## Executive Summary for TS-CCSC (Tumor Specific Cell Cycle Synchronous Chemotherapy)

**Overview:** While the goal of chemotherapeutic development is to make drugs that are specific to cancer, NexGen's TS-CCSC Protocols make cancers specific to existing S-Phase cytotoxic drugs. The TS-CCSC protocols use only existing FDA approved drugs, including many generics, allowing for a fairly immediate large step forward in best standard of care and a large reduction in cancer healthcare costs.

**The Problem:** Best in class S-Phase cytotoxics (e.g. gemcitabine, irinotecan) can kill 100% of cells that are in the S-Phase of the cell cycle. However, less than a third of cancer cells are in the S-Phase during chemotherapy.

**The Opportunity:** Boosting the number of cancer cells in the S-Phase from less than a third to an eventual goal of 100% would provide a market transforming technology and a major advance in the treatment of cancer. FDA approved drugs to do this already exist for many cancers, with some drugs being repurposed from other areas of medicine.

**The Product:** TS - CCSC protocols modulate tumor specific mutations and characteristics to achieve tumor specific S-Phase enrichment and synchronization relative to successive administrations of S-phase cytotoxic chemotherapeutics, while simultaneously inhibiting tumor regrowth between administrations of S-Phase cytotoxic. The TS-CCSC Protocol approach is a 3 step process that is repeated in cycles:

### 0) Distributed Cancer Cells



**Example - S-Phase Cytotoxic and Prostate Cancer:** A Cornell Medical School study found that around half of prostate cancers are driven by an estrogen activated cell surface receptor (fusion mutation). Under a TS-CCSC protocol, after an initial administration of an S-Phase cytotoxic to depopulate the tumor, 1) a GnRH antagonist and aromatase inhibitor would be used to zero out indigenous estrogen levels for 4 weeks to aggregate the cancer cells in the G1 Phase, 2) exogenous estrogen would then be administered to flush the cancer cells into the S-Phase and 3) an S-Phase cytotoxic would be administered to kill the cancer cells. Alternatively, if the prostate cancer was testosterone dependent, the aromatase inhibitor would be deleted from step 1 and testosterone would be substituted for estrogen in step 2. The approach effectively makes the tumor specific to a non tumor specific S-Phase cytotoxic.

**Overcoming Prior Art Failures:** The enormous therapeutic potential of CCSC is commonly acknowledged, however prior art attempts at CCSC failed because of inadequate aggregation periods and lack of targeted aggregation. Our patents overcome these reasons for failure.

**Primary Markets:** The 3 issued US patents cover TS - CCSC for endocrine dependent (ED) cancers, cancers driven by HER2 overexpression, and cancers driven by HER1 (aka EGFR) overexpression. Estimates of the prevalence of these mutations vary widely and do not typically specify the exact nature of the mutation (e.g. overexpression or inappropriate expression), making accurate projections difficult, however using prevalence alone indicates ~ 900,000 new prospective US patients annually. Conservatively assuming only 25% of the prospective patients are subsequently characterized as ideal responders would translate into 225,000 US patients annually.

Cancer	New Cases	Deaths	Prevalence			TS-CCSC Prospects			CCSC Total
			HER1	HER2	ED	HER1	HER2	ED	
Lung	219,440	159,390	55%	30%		120,692	65,832		186,524
Breast	194,280	40,610	15%	20%	60%	29,142	38,856	116,568	184,566
Prostate	192,280	27,360	60%		70%	115,368		134,596	249,964
Colon/Rect.	146,970	49,920	50%			73,485			73,485
Bladder	70,980	14,330	40%			28,392			28,392
Renal	57,760	12,980	70%			40,432			40,432
Uterine	53,430	27,310	50%		30%	26,715		16,029	42,744
Pancreatic	42,470	35,240	40%			16,988			16,988
Oral/Pharynx	35,720	7,600	80%			28,576			28,576
Brain/Nerve	22,070	12,920	45%			9,932			9,932
Ovary	21,550	14,600	5%		80%	1,078		17,240	18,318
Esophagus	16,470	14,530	75%			12,353			12,353
Other	405,930	145,550							
<b>Total</b>	<b>1,479,350</b>	<b>562,340</b>				<b>503,152</b>	<b>104,688</b>	<b>284,433</b>	<b>892,273</b>

**Value Proposition:** The value proposition for the 225,000 ideal responders would be Best Standard of Care at a fraction of the cost of expensive proprietary drug regimens.

**Market Potential:** A \$ 50,000 annual regimen price for ideal responders translates into \$ 11 Bil. in revenue.

**Business Model:** The proposed “TS-CCSC Chemotherapy Centers” service model would allow participating oncologists to make more money, reduce overall cancer treatment costs, and provide funding for ongoing TS-CCSC development into new cancers. The business model effectively usurps money from expensive proprietary big pharma drug regimens and as such the cancers initially targeted would be those where TS-CCSC can displace expensive proprietary drug regimens. Publication and promotion of TS-CCSC clinical results, as well as patient recruitment, will be handled by TS-CCSC Chemotherapy Centers, with participating oncologist services built into the regimen price

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