Opportunity Assessment of Novel Peptide Antagonist cJun

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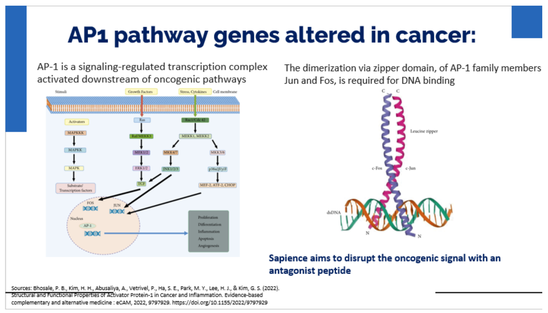
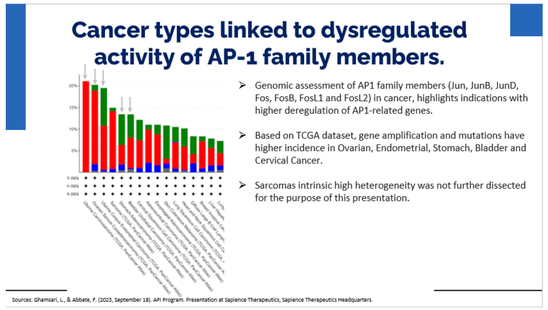
ABSTRACT

Sapience Therapeutics, Inc. has developed a novel peptide antagonist (JunAP) that targets the AP-1 transcription factor complex, which plays a crucial role in oncogenesis and immune suppression. An analysis of The Cancer Genome Atlas (TCGA) data found higher incidence of AP-1 gene alterations in ovarian, endometrial, stomach, bladder and cervical cancers. This research used a comprehensive three-pronged approach to inform cJun's clinical development strategy. The opportunity assessment encompassed population analysis, competitive landscape evaluation, and revenue potential estimation across the relevant indications. The population analysis utilized SEER data to characterize the U.S. patient population. Assessment of ongoing trials identified obstacles and openings for cJun's in the cancer drug landscape. A revenue forecast model provided indication-specific sales projections. Together, this opportunity assessment supports advancing cJun for bladder and endometrial cancers. Notably, the analysis uncovered cJun's potential in HPV-driven malignancies, an unexpected opportunity for significant patient benefit. The integrated analysis has strategically informed the indication prioritization and clinical advancement of this highly innovative AP-1-targeting peptide therapeutic.

INTRODUCTION





Objectives:

1) Analyze patient population data including incidence and mortality across 5 cancer types
2) Review currently approved and developmental therapies to reveal limitations and openings for the cJun antagonist
3) Develop revenue forecast models to predict market potential of cJun antagonist over 10-year period
4) Synthesize findings regarding optimal target indications from these analyses to inform strategic clinical advancement

APPROACH

Selection of Indications for Treatment with cJun Antagonist Peptide

- Following detailed discussions with Sapience's translational medical team and an assessment of prevalence rates and potential therapeutic benefit, five cancer indications were selected for treatment with the cJun antagonist peptide: bladder, endometrial, gastric, cervical and ovarian.
- Indications were further narrowed to stage of disease chosen based on prognosis outcomes with current available lines of therapy within each indication.

Population Analysis

- Prevalence, incidence, annual growth, and percentage of cancers diagnosed in the advanced stages were assessed for each cancer population.

Competitive Landscape Analysis

- Therapies available for each cancer type were assessed based on their therapeutic category and mechanism of operation.
- Competitive risk of prospective therapeutics targeting the cJun pathway were evaluated.

Revenue Projection Model

- Revenue projections were generated for individual cancer types, taking into consideration population analysis.

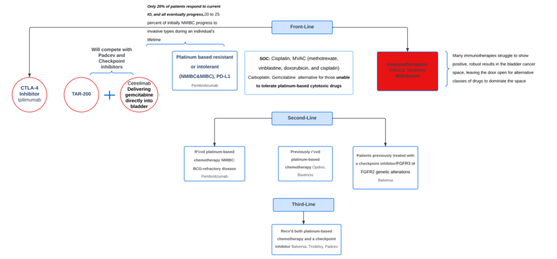
FINDINGS

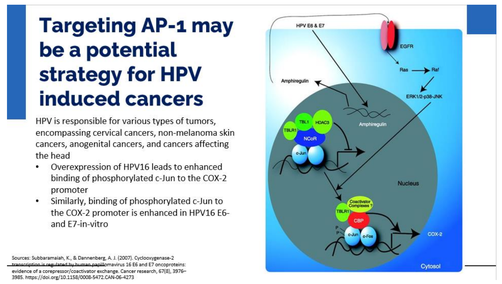
	Prevalence	Est Annual Pop.	Est. Incidence Growth	Qualitative evidence of AP-1 Complex Dysregulation	Potential US Market	Projected US CAGR	Development Pipeline	Expected Market Impacts to Sapience	Clinical Trial Feasibility	ALL
Bladder	725,549	82,290	2.58%	++	$396.29M-$3.5B	24.2%	Multiple PD1/PDL1 Checkpoint Inhibitors (~20% RR, followed by progression); Lack of pipeline development in MIBC	Minimal Impacts	Several competing trials and challenges with enrollment	
Endometrial	769,342	59,580	1.19%	+++	$1.6B-$3.3B	7.1%	Multiple PD1/PDL1 Checkpoint Inhibitors. Promising pipeline agents have high toxicity profile	Minimal Impacts	Low % suspension due to enrollment	
Gastric	127,211	26,500	2.03%	+	$398M-$1.79B	16.2%	Various PD-1 inhibitors; Focus on HER2; Limited targeted therapies (locoregional & HER-2 negative) ; 1 promising pipeline drugs targeting nine MOA (Claudin 18)	Minimal Impacts	Low suspension rate, but Large # of competing trials beyond 2026	
Cervical	296,981	13,960	.78%	+++	$306.7 M-$1.5B	17.6%	PD-1/PDL 1 & PARP inhibitors expected to dominate market	Minimal Impacts	High suspension rate due to inclusion restrictions	
Ovarian	236,511	19,710	-.22%	+	$1.1B-$3.3B	11.9%	Robust pipeline include novel MOA, i.e., Paprya PIK3CA novel inhibitor, targeting high unmet need	Negative	Very low suspension rate due to enrollment	

This rating system employs a color-coded scale to indicate level of favorability.

highest level · mid range favorability · 2nd best · least favorable rating

Current and Pipeline Treatments for Muscle Invasive Bladder Cancer (MIBC)





CONCLUSIONS & RECOMMENDATIONS

This analysis identified muscle invasive bladder and endometrial cancer as optimal initial indications for Sapience's AP-1 antagonist based on high recurrence rates and substantial unmet need for second line therapies. Notably, the research also revealed opportunities to target virally-mediated tumors by disrupting AP-1 signaling. HPV triggers AP-1 to induce overexpression of the tumor-promoting COX-2 enzyme, presenting a prospect for cervical and other HPV-positive cancers lacking treatment options.

Given the central role of AP-1 dysregulation across viral and non-viral malignancies, it is recommended Sapience pursue: 1) Muscle invasive bladder cancer as the lead indication; 2) Endometrial cancer as the secondary indication; 3) Further research into cervical and other HPV-cancers.

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