CellCentric is a clinical stage biotechnology company with a deep foundation in epigenetic research.

Developing CCS1477, a first-in-class cancer drug targeting p300/CBP, to address major patient unmet needs.
Pioneering for patients

CellCentric

First-in-class p300/CBP bromodomain inhibitor

For patients with few alternatives:
- late stage, drug resistant prostate cancer (mCRPC)
- relapsed/refractory multiple myeloma, AML, lymphomas
- tumours with specific mutations (bladder, lung)

80,000+
Men with prostate cancer
could ultimately benefit from
CCS1477 annually

20,000+
Patients with blood cancers
multiple myeloma, AML,
lymphomas

50+
Epigenetic-related targets
Investigated over time by the
CellCentric team

CCS1477
Drug prioritised, advanced
First-in-class p300/CBP bromo-
domain inhibitor
## CCS1477, first-in-class p300/CBP inhibitor

**Addressing Patient Needs**

- CCS1477 is a new cancer drug in development to treat major patient populations for whom there are few alternatives:
  - late stage, drug resistant prostate cancer
  - certain relapsed/refractory blood cancers (AML, MM, NHL)
  - patients with tumours with p300 or CBP mutations

**Target → Action**

- CCS1477 inhibits p300/CBP. These twin proteins regulate oncogenes found to be critical in tumour development, but so far have been undruggable. This includes the down regulation of c-MYC, IRF4 and transcription factors such as AR.

  - The link between p300/CBP inhibition and clinical utility is very clear (e.g. downgrading AR and AR variants for treating late stage prostate cancer).

**Specificity and Differentiation**

- There are different ways to inhibit p300/CBP. **CCS1477 targets the bromodomain pocket.** This allows potency and specificity, whilst minimising off target effects, compared to drugging p300/CBP’s HAT catalytic domain or CH1 domain.

  - CCS1477 is also differentiated from drugs targeting bromodomains on other proteins (e.g. BET inhibitors), in being much less broad acting on gene regulation.

**Clinical Application**

- CCS1477 is in patients well ahead of comparable competition.

  - It is a small molecule, formulated as a capsule taken orally. It is relatively inexpensive to manufacture and develop.

  - It can be used after and in combination with existing drugs, building and extending existing oncology commercial franchises.

  - CCS1477 is endorsed and being used by key figures; Johann de Bono, Karen Knudsen, Andy Davis.
CCS1477 in the clinic

- Company originally spun out of the University of Cambridge, with Azim Surani CBE FRS
- Investigated over 50 epigenetic-related targets before focusing on twin histone acetyltransferases, p300 and CBP
- Have developed a highly specific, potent inhibitor, formulated as an oral capsule. **First-in-class**, in the clinic

Drug resistant, late stage prostate cancer

+ abiraterone
+ enzalutamide

Multiple Myeloma, NHL

Acute Myeloid Leukaemia

Tumours with specific genetic drivers
p300 and CBP are twin (paralogue) proteins that act directly and indirectly as activators of genes associated with cancer cell growth.

Three pockets of p300 and CBP can be targeted with small molecule inhibitors. The amino acid sequences are highly conserved between the two paralogue proteins.

p300/CBP inhibition causes tumour stasis and regression in models of prostate cancer (mCRPC), as those of haem malignancies incl. multiple myeloma and AML.

Certain tumours (lung, bladder) have high frequencies of LoF mutations in either p300 or CBP. These can be particularly sensitive to inhibitors that bind to both proteins.
• **CCS1477 is first in its class**, the first small molecule bromodomain inhibitor of p300/CBP to be used in patients.

• In prostate cancer, CCS1477, unlike other agents, down-regulates not just the androgen receptor (AR), but also AR splice variants. These are important in the innate or acquired resistance to existing treatments (e.g. abiraterone, enzalutamide).

• There are other drugs that target bromodomains (BET inhibitors). CCS1477 is highly specific for p300/CBP and thus has a different profile from them. CCS1477 retains activity in cancer cell lines that have been made resistant to BET inhibitors (JQ1, OTX-15, iBET-151).

• CCS1477 has an unusual duration of effect in pre-clinical models. Tumour stasis is sustained far beyond cessation of drug administration.

• This prolonged anti-tumour effect has not been reported with inhibitors of the HAT catalytic site, or with BET inhibitors.

• CCS1477 also seems to be effective whilst impacting fewer genes compared to HAT inhibitors and other bromodomain inhibitors. Thus it should have a cleaner effect.

• In breadth-of-efficacy cancer cell panel testing, CCS1477 has a very specific effect on clusters of cancer types, rather than being generally cytotoxic like a BET inhibitor.

• Unlike many other cancer agents in development, CCS1477 has the potential to be used as a monotherapy for multiple applications, not just in combination with existing agents.
Sustained tumour block following drug dosing cessation in three different pre-clinical models

- Not caused by residual drug or active metabolites
- Dose proportional effects

Prostate cancer (22Rv1)

Acute Myeloid Leukaemia (MOLM16)

Multiple myeloma (OPM2)
Drug resistant (inherent or acquired) late stage prostate cancer (mCRPC) is driven by the over expression of the androgen receptor (AR), mutated (AR-mut) and truncated forms of AR (AR-SV), as well as c-Myc.

CCS1477, inhibits the expression and function of AR, AR-mut, AR-SV and c-Myc.
Multiple myeloma cell lines, as well as those of AML and lymphomas, are highly sensitive to CCS1477.
CCS1477 in multiple myeloma model

• CCS1477 causes dose-dependent anti-tumour efficacy, including regression, in OPM-2 model of multiple myeloma
• Efficacy sustained post drug cessation (also seen in models of AML and castrate-resistant prostate cancer)
• Tumour treatment with CCS1477 associated with reduction in c-Myc and IRF4
Superior pre-clinical efficacy of CCS1477 over current therapies, and combination benefit

OPM-2 tumour bearing NOD / SCID model; CCS1477 and/or standard of care agents dosed by oral gavage, once daily
As clinical trials of CCS1477 expand, so does CellCentric’s core team and network of key consultants.
after, or in combination with 2nd generation anti-hormonal drugs for mCRPC

**Clinical positioning**

**PROSTATE CANCER**

<table>
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<tr>
<th>Drug</th>
<th>Non-metastatic, castrate resistant</th>
<th>Metastatic castrate sensitive</th>
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<td>Zytiga Abiraterone</td>
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<td>Xtandi Enzalutamide</td>
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<tr>
<td>Nubeqa Daralutamide</td>
<td>Approved 2019</td>
<td>Phase III</td>
<td>NA</td>
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CCS1477 for tumours resistant (inherent or acquired) to 2nd generation anti-hormonal drugs

**HAEMATOLGICAL MALIGNANCIES**

Relapsed/refractory disease
after, or in combination with agents such as pomalidomide

**TUMOURS WITH SPECIFIC MUTATIONS**

Tumours with loss of function p300 or CBP mutations
high prevalence in bladder and small cell lung cancers
AR+ or c-Myc dependent tumours

CCS1477 use moving earlier in disease progression over time?
Deep scientific foundation, epigenetics
- CellCentric was co-founded with one of the pioneers of epigenetics, Prof Azim Surani FRS CBE
- Collaborated with over 25 leading international labs

Opportunity triage
- Investigated >50 epigenetic-related targets
- Arginine methyl transferase programme bought by Takeda
- CellCentric now focused on acetyltransferases p300/CBP

p300 and CBP
- Gene expression co-activator proteins associated with cancer
- Blocking the twin proteins causes profound, sustained tumour growth inhibition

CCS1477
- First-in-class specific, potent small molecule inhibitor
- Potential for targeted, large cancer patient groups
- New Drug on the Horizon at AACR, Chicago 2019

Now in patients
- Late stage prostate cancer trial ongoing; patients resistant to current treatments (initiated at the Royal Marsden Hospital)
- Clinical testing for the treatment of blood cancers now begun, with patients with specific tumour drivers to follow

Strong, long term financial support
- CellCentric's lead investor is Boston based Morningside
- Committed to the long term development of CCS1477
Company leadership

**Will West**  CEO  ex-P&G Healthcare. Chair of John Innes Centre. BiolIndustry Association Board

**Thea Stanway**  Finance Director  ex-PwC

**Neil Pegg**  Research Director  ex-Glaxo, OSI. Co-developed PI3K inhibitors at Piramed

**Tomasz Knurowski**  CMO  TMC Pharma. Ex-Allergan, Simbec-Orion

**Karen Clegg**  Dir. Clinical Operations  ex-AZ, also Kesios biotech

**Nigel Brooks**  Dir. Translational Science  ex-AZ, prostate cancer translational lead, Manchester Cancer Research Centre