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

For patients with few alternatives:

• late stage, drug resistant prostate cancer (mCRPC)
• blood cancers, incl. relapsed/refractory multiple myeloma, AML, lymphomas
• tumours with specific mutations (bladder, lung)

First-in-class p300/CBP inhibitor

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 proven 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.
Company at a glance...

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 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)
- Testing for the treatment of blood cancers following, as well as specific cancers with p300 or CBP mutations

Strong, long term financial support
- CellCentric’s lead investor is Boston based Morningside
- Committed to the long term development of CCS1477
p300 and CBP are twin (paralogue) proteins that act directly and indirectly as activators of genes associated with cancer cell growth.

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

Certain tumours (lung, bladder) have mutations in either p300 or CBP. These can be particularly sensitive to inhibitors that bind to both proteins.

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.
• **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)**

**Multiple myeloma (OPM2)**

**Acute Myeloid Leukaemia (MOLM16)**
CCS1477 knocks down key drivers of mCRPC

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.
From mechanism of action through to specific clinical application:

- **Monotherapy**
  - + Abiraterone
  - + Enzalutamide

- **MM, NHL**
  - + Pomalidomide

- **AML**

- Other tumours, such as AR-dependent breast cancer
Clinical operations

- **Prof Johann de Bono** (Royal Marsden Hospital) is the Chief Investigator for the prostate programme
- **Prof Andy Davies** heads the haematological malignancy programme
- Clinical sites throughout the UK and expanding
- Long term collaboration with **Prof Karen Knudsen**, AACI President elect and Director of the SKCC, Philadelphia, from where US clinical operations will expand
- CellCentric also collaborates with Profs **Leif Bergsagel** (Mayo Clinic, Phoenix), **Laura Pasqualucci** (SKMCC, New York), **Pete Nelson** (Fred Hutchinson, Seattle)
Company leadership

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

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

Thea Stanway  Finance Director
ex-PwC

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

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

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