Corporate Research

FluoGuide

Initiation of coverage | Healthcare | Denmark | 30 November 2020

The cutting edge of fluorescence-guided surgery

FG001 is the sole clinical stage asset of FluoGuide A/S, in development for fluorescence-guided cancer surgery, with the aim to improve surgical outcomes and eliminate residual cancer cells in the resection cavity. In our view, FG001 has the potential to deliver all the key performance objectives of fluorescence-guided surgery across a broad spectrum of cancer types, and, although it is still early, if successful, we see blockbuster potential for FG001.

FG001 addresses high recurrence rates despite surgical removal of cancer

FG001 is being developed by Copenhagen-based FluoGuide A/S, founded in 2018. FG001 is a uPAR-targeted fluorescent imaging agent intended for real-time surgical use to improve surgical outcomes as well as for photodynamic therapy to kill residual cancer cells in the vicinity of the resected tumour, thereby increasing the curative potential of cancer surgery. FG001 is initially being developed for glioblastoma, an aggressive brain cancer and orphan disease that has a dismal prognosis. In preclinical models, FG001 enabled identification and isolation of sub-millimetre lesions at a distance from the primary tumour site.

A relatively streamlined regulatory pathway to approval

FluoGuide has begun enrolling patients for its phase 1/2 trial of FG001 in glioblastoma, with the first data readout expected during 2020. We believe that FG001 will be able to secure orphan designation from the FDA and EMA, and we note that contrast agents have an easier path to market than typical pharmaceuticals, and the bar in glioblastoma in particular is low.

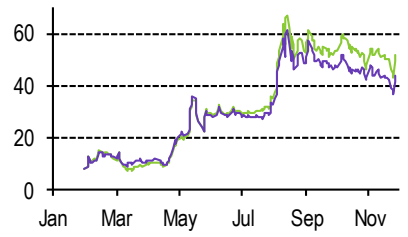
Solid market potential and substantial upside potential with near-term triggers

We arrive at a risk-adjusted valuation range of DKK 42-57 p.s., based on peak market penetration of 40-70% for various cancer types, +/-5%, and a US price of USD 10,000 per procedure (EU: 65% of US), implying 2034 peak sales of DKK 572-730m, risk-adjusted (DKK 17.9-22.9bn de-risked). We believe FG001 has the potential to turn FluoGuide into a profitable biotechnology company.

Key Data (2020E)

Price (DKK)	52.00
Reuters	FLUO.TE
Bloomberg	FLUO SS
Market cap (DKKm)	548
Market cap (USDm)	88
Market cap (EURm)	74
Net debt (DKKm)	(18)
Net gearing	(293%)
Net debt/EBITDA (x)	0.9
Shares fully dil. (m)	10.5
Avg daily turnover (m)	0.0
Free float	66%

Share Price (12M)



Absolute (green) / Relative to Denmark (purple).

Marketing communication commissioned by:
FluoGuide

Financials (DKK)

Year end: Dec	2018	2019	2020E	2021E	2022E
Revenues (m)	0	0	1	0	0
Adj. EBIT	(0)	(11)	(21)	(38)	(51)
Pre-tax profit (m)	(0)	(12)	(21)	(38)	(51)
EPS	(0.01)	(1.49)	(1.65)	(2.73)	(3.17)
Adj. EPS	(0.01)	(1.49)	(1.65)	(2.73)	(3.17)
DPS	0.00	0.00	0.00	0.00	0.00
Revenue growth (%)	n.m.	n.m.	n.m.	(100.0)	n.m.
Adj. EBIT growth (%)	n.m.	n.m.	n.m.	n.m.	n.m.
Adj. EPS growth (%)	n.m.	n.m.	n.m.	n.m.	n.m.
Adj. EBIT margin (%)	n.m.	n.m.	n.m.	n.m.	n.m.
ROE (%)	n.m.	n.m.	n.m.	n.m.	n.m.
ROCE (%)	n.m.	n.m.	n.m.	n.m.	n.m.
PER (x)			n.m.	n.m.	n.m.
Free cash flow yield (%)			(0.5)	(4.5)	(5.3)
Dividend yield (%)			0.0	0.0	0.0
P/BV (x)			90.70	13.46	75.61
EV/Sales (x)			0.00	0.00	0.00
EV/Adj. EBITDA (x)	0.0	0.0	0.0	0.0	0.0
EV/Adj. EBIT (x)	0.0	0.0	0.0	0.0	0.0
Operating cash flow/EV (%)			n.a.	n.a.	n.a.
Net debt/Adj. EBITDA (x)	(0.00)	(0.00)	0.85	1.69	0.58

Source for all data on this page: SEB (estimates) and Millistream/Thomson Reuters (prices)

Contents

Page

Case summary

FluoGuide is a medical innovator in fluorescence-guided surgical tools
FluoGuide is developing a cancer-selective fluorescent contrast agent, FG001, for real-time surgical guidance to enhance the ability to surgically remove tumours and to destroy residual cancer cells in the resection cavity with photodynamic therapy, with the aim to improve surgical efficacy and safety outcomes. Surgery is a mainstay of cancer therapy, and in many cases represents the only option with curative potential. Nevertheless, recurrence rates are high, even for many early stage cancers, which can be traced to the presence of residual cancer cells that seed new tumour growth, often with greater malignancy. FluoGuide recently initiated enrolment in a phase 1/2 trial in patients with high-grade glioma, a group of highly aggressive brain cancers with some of the poorest rates of survival amongst all cancers. Data from human cancer xenograft models indicate that FG001 binds cancer cells with high selectivity and specificity, increasing the rate of gross resection with margins negative for residual cancer tissue, and enabling identification and surgical removal of distant metastatic tumours that could not be identified with the naked eye.

FG001 targets an attractive niche in a rapidly growing market
FG001 is targeting the fluorescence-guided surgery market, and in particular the near-infrared imaging segment, which has been forecasted to grow at a 15% CAGR to USD 822m through 2023. FluoGuide is initially targeting a rare cancer, opening the door to a potential Orphan Drug Designation, which would solidly position FluoGuide in another of what we consider one of the most attractive niches in the pharmaceutical sector – a USD 136bn market as of 2019, forecasted to grow at a 12.2% CAGR – and which should facilitate premium pricing, in addition to other benefits.

Attractive GBM market potential, further growth prospects
Glioblastoma is a highly aggressive brain cancer that is generally considered incurable. Surgery is the most efficacious available therapy. An approval for glioblastoma would demonstrate the utility of FG001 and support development of the clinical program in other indications, the crown jewel of which is breast cancer, a large population with a high rate of surgical resection, and for which fluorescence-guided surgery is not yet in routine use. We also note that management has stated that it plans to develop two or three contrast agents targeting uPAR, the same cancer-targeting mechanism as FG001.

An unmet need for discriminating guided surgery imaging agents
Currently approved imaging agents have limited utility for fluorescence-guided cancer surgery, because they are unable to deliver any of a combination of key performance objectives, including broad cancer specificity and selectivity; including with respect to tumour cell heterogeneity; suitability for real-time tumour visualization during surgery, including at the microscopic level; compatibility with intraoperative surgical imaging systems; safety; and selective tumour toxicity, e.g. via photodynamic therapy. We believe that the design of FG001 endows it with the potential to meet all of these performance objectives, and hence secure routine use in surgery for a broad range of cancer types.

Assuming that FG001 can demonstrate superiority on certain secondary endpoints over standard of care and obtain regulatory approvals in 2024-27 (depending on indication and geography), we model peak market share across the US and EU of 70% for glioblastoma and grade 3 glioma, and 40% peak share in each of resectable breast and resectable lung cancer, all by 2034, when patents and/or a potential orphan designation would expire. Assuming that FG001 is priced at USD 10,000 in the US, and 65% of that in the EU, we forecast peak sales in the range of DKK 706-815m for glioblastoma, and DKK 17,884-22,885m across all indications, on a fully de-risked basis.

Management with deep experience in the field & drug/device development

We appreciate the depth of experience of FluoGuide's management team, both in terms of previous drug/device development, as well as within the field itself. We highlight CEO Morten Albrechtsen's prior experience from various positions at Nycomed Pharma (now Takeda Pharmaceutical), Nanovi and Boehringer Ingelheim, in addition to being a seasoned entrepreneur. We value CSO Prof. Andreas Kjaer's experience as Chief Physician at the Rigshospitalet, the National University Hospital of Denmark, and note that he has also developed several other tracers that have reached first-in-human clinical use.

Sufficient funds to take FG001 through phase 3 for Glioblastoma

With DKK 18m in cash on-hand, we believe that management has sufficient funds to take FG001 through phase 3 for glioblastoma, although we also believe that, in order to maximize the commercial potential of FG001 by expanding the number of targeted indications, FluoGuide will likely need to take in additional capital. However, given the multi-blockbuster potential of these indications and upside from the current share price levels, we would view this as a highly positive development and an offensive, rather than defensive action.

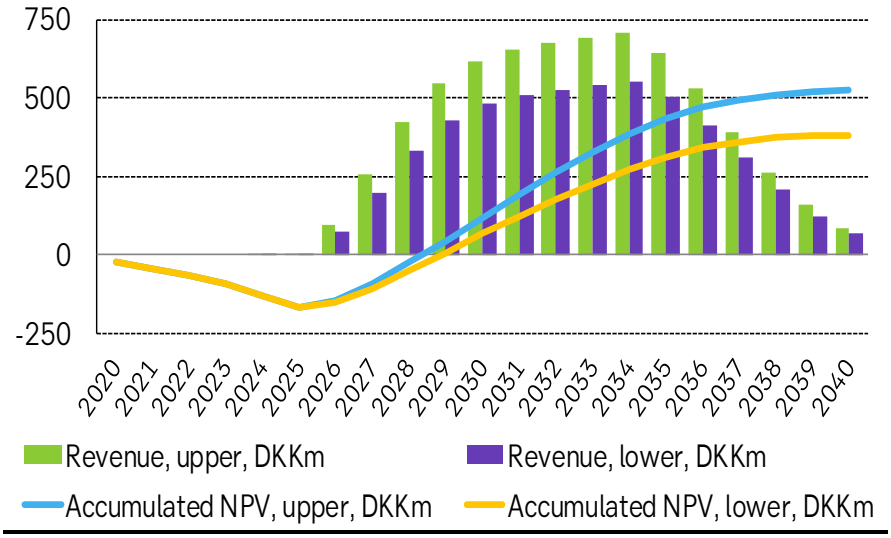
Development and regulatory risk-adjustment

FluoGuide has demonstrated FG001's utility in human cancer xenograft models across a range of cancer subtypes, including glioblastoma, pancreatic cancer, and head and neck cancer, with encouraging performance and safety/tolerability. Still as a phase 1 program, that is about to produce its first clinical data, it is still fairly early, so we assume a probability of approval ranging from 5% for glioblastoma, to 3% for resectable breast cancer, and, because it has not yet been demonstrated that FG001 can cross an intact blood-brain barrier, 2% for grade 3 glioma. That said, we note that the fluorescent tracer backbone, indocyanine green, is already approved and in wide use in the US and EU.

Valuation range DKK 42-57

Our valuation of FluoGuide is based upon a risk-adjusted net present value (rNPV) of FG001 for glioblastoma, grade 3 glioma, resectable lung cancer, and resectable breast cancer, plus cash, for an equity value that we estimate to be in the range of DKK 42-57 per share. We currently do not attribute any value to additional indications that FluoGuide is pursuing, such as colorectal cancer and pancreatic cancer, but as data accumulates, we expect these opportunities to add to the value of FG001.

Valuation summary: net present value of FG001



Source: SEB

Our valuation range is particularly sensitive to our assumptions for market penetration and probability of approval, *P*(approval). The upper and lower ends of the range are based on an interval of +/-5% peak market penetration from the midpoint (see assumptions for details), which varies by cancer type.

Per share equity value sensitivity to peak market penetration and *P*(approval)

DKK

Change in P(approval) for all indications (in pp)	Change in peak penetration for all indications (in pp)						
	-15.0%	-10.0%	-5.0%	0.0%	5.0%	10.0%	15.0%
-2.0%	0	3	6	9	12	14	18
-1.0%	13	19	24	29	34	40	46
0.0%	26	33	42	50	57	65	72
1.0%	39	49	59	69	79	89	102
2.0%	51	64	76	88	104	116	129
3.0%	64	78	93	111	126	141	156
4.0%	76	93	113	131	148	166	183

Source: SEB

We see substantial upside to our valuation if and when FG001 is launched in the US and EU, beginning in 2024. Our fully de-risked valuation range (100% probability of approval across all four indications) is DKK 1,754-2,248 per share.

Extensive scope for de-risking newsflow, with imminent triggers

We expect the most prominent newsflow to relate to patient safety, real-time tumour contrast enhancement during surgery, and surgical outcomes from the phase 1/2 trial, and we note that, given that we have yet to see clinical data, the scope for de-risking on safety data and real-time tumour contrast enhancement is substantial. We expect initial safety data to be announced this month.

Catalyst calendar

Timing	Event type	Details
2020-Q4	Trial readout	Ph1 result of first dose escalation readout (safety)
2021	Clinical trial milestone	Ph1/2 result of subsequent dose escalation groups (PoP)
2021-mid	Trial readout	Ph1 topline
2021-H2	Trial readout	Ph 2 efficacy data
2022-H1	Clinical trial milestone	Ph2b/3 trial initiation
2021	Pipeline milestone	Decision on number of uPAR-targeted products (2-3 expected)
2023+	Pivotal trial readout	Ph2b/3 topline
2023+	Regulatory milestone	Regulatory filing
2023+	Regulatory milestone	Potential approval

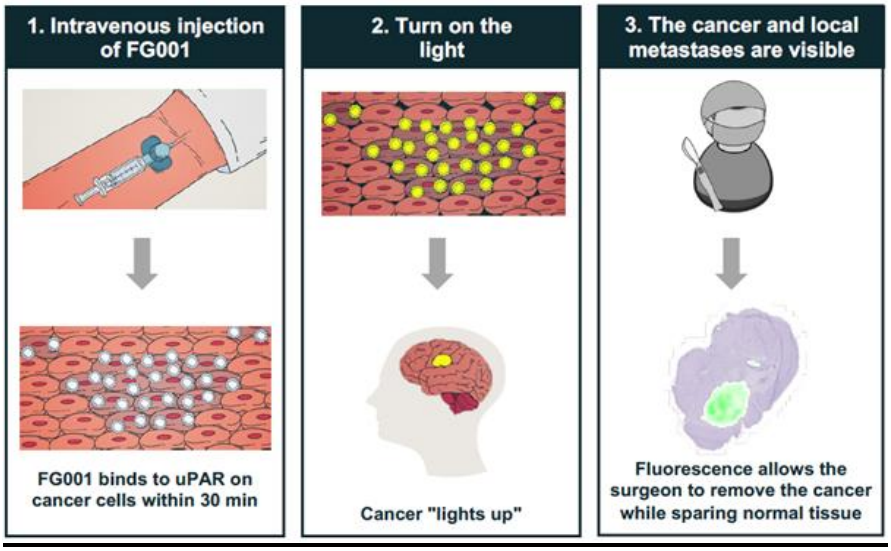
Source: SEB, FluoGuide

Main risks

In our view, the main risks to the case include (1) a potential inability to translate promising pre-clinical findings to the clinical setting, and we note that there is an incomplete overlap in xenografted tissue between FG001 fluorescence and the uPAR protein that it targets; (2) potential proteolysis of the peptidyl linker in human serum; (3) the relatively high price we assume, compared to the that of currently marketed contrast agents; and (4) competition, particularly outside glioblastoma, which appears to be increasing.

FluoGuide: company overview

FluoGuide's lead product is FG001, for use in fluorescence-guided surgical imaging



Source: FluoGuide, SEB

FluoGuide develops surgical solutions that are expected to reduce suffering for the patient, increase the likelihood of cure as well as reduce costs for the health care system. The lead candidate, FG001, is a uPAR targeted guidance of cancer surgery, which has shown excellent pre-clinical results for glioblastoma and has a direct and short path to market with the potential to expand to other indications (e.g. breast cancer, lung cancer, colorectal cancer, head and neck cancer, and pancreatic cancer), according to company information.

Company history

FluoGuide was founded and incorporated in 2018 by Professor Andreas Kjaer (MD, PhD, DMSc and MBA) following years of extensive research within molecular imaging with PET, PET/MRI, and optical imaging, as well as targeted radionuclide therapies (theranostics) in cancer via his positions at the University of Copenhagen and as chief physician at Rigshospitalet, the National University Hospital of Denmark. Prior to founding FluoGuide, Professor Kjaer and his research group received the prestigious Grand Solutions grant from the Innovation Fund Denmark for the FluoGuide project, with the objective to expand the pipeline for fluorophore-based products. In May 2019, FluoGuide was listed on the Spotlight Stock Market.

Management

Morten Albrechtsen, CEO holds an MD and B.B.A. and is a seasoned entrepreneur with broad experience across several different therapeutic areas including both drugs and devices. Prior to joining FluoGuide, Dr Albrechtsen held various positions in Nycomed Pharma (now Takeda Pharmaceuticals Ltd.), Nanovi, Boehringer Ingelheim GmbH, and Enkam.

Henrik Moltke, CFO is Henrik Moltke, holds an MSc (Econ) in strategy and international economics and has more than 30 years of experience from life sciences and health care sectors, with roles such as CFO and Senior Vice President. The primary focus of his career has been venture financing, including IPOs and follow on capital increases in the public markets, investor relations, business development, finance planning and strategic development. Zoetis (acquired Scandinavian Micro Biodevices- SMB), Astion Pharma, NeuroSearch.

Andreas Kjaer, CSO is an MD, PhD, DMSc and professor at the University of Copenhagen and chief physician at the Rigshospitalet, the National University Hospital of Denmark. His research is focused on molecular imaging with PET, PET/MRI, and optical imaging in cancer and cardiovascular disease. Dr Kjaer has developed several new tracers that have reached first-in-human clinical use and has published more than 400 peer reviewed articles. Dr Kjaer also holds an MBA from Copenhagen Business School (CBS).

Grethe Nörskov Rasmussen, CDO holds an M.Sc and PhD in Biochemistry from the Danish Technical University. Prior to joining FluoGuide, Dr Nörskov Rasmussen held various positions in Ascendis Pharma A/S, Maxygen Inc. and Novo Nordisk A/S.

Board of Directors

Arne Ferstad, Chairman of the Board is CEO and Director of Ankor Consultants Ltd. Previous experience includes various positions in Baxter and Pharmacia Corporation. Mr Ferstad holds a Finance/Marketing degree from Marked-foringskolen in Oslo and studied Management at INSEAD/Cedep in France.

Shomit Ghose, Member of the Board is currently Managing Director and General Partner at ONSET Ventures, a Silicon Valley based venture fund. He has served on multiple boards within ONSET's portfolio, and previously served as Chief Executive Officer of Truviso, where he also sat on the Board. Mr Ghose holds a degree in Computer Science from the University of California Berkeley.

Micaela Sjökvist, Member of the Board currently holds the position as Head of Investor Relations at Securitas AB. Prior to joining Securitas, Ms Sjökvist had various roles at Grayling and Telia Sonera AB. Ms Sjökvist holds a B.Sc in Economics and Business Administration from Uppsala University.

Peter Mørch Eriksen, Member of the Board is currently serving as the CEO of BioPorto A/S. Prior to joining BioPorto A/S, Mr Mörch Eriksen was the CEO of Sense A/S and held various positions in Medtronic in both the US and Denmark. Mr Mørch Eriksen has an accounting background supplemented with courses in management.

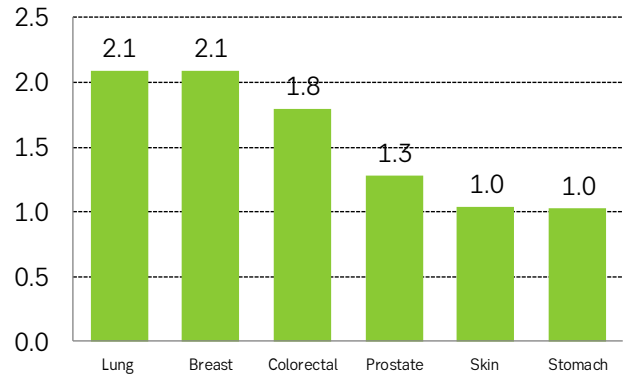
Andreas Kjaer, Member of the Board currently serves as CSO and Head of the Scientific Advisory Board at FluoGuide.

Fluorescence-guided surgery

Surgery: a cornerstone of cancer therapy

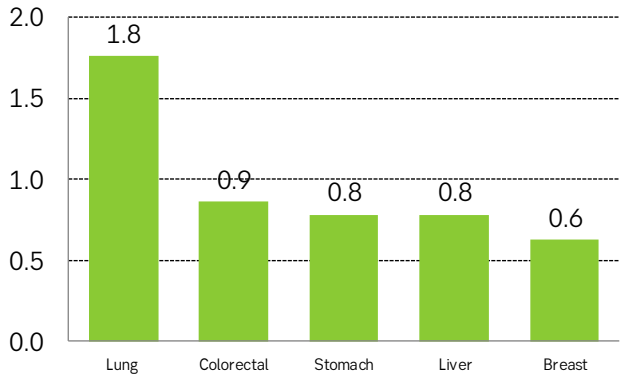
According to data from the World Health Organisation (WHO), cancer is the second leading cause of death globally and was responsible for an estimated 9.6m deaths in 2018. Approximately one out of six deaths globally are due to cancer. The most common cancers include lung cancer, breast cancer, and colorectal cancer. The most common causes of cancer deaths are cancers of lung, colorectal, and stomach.

Most common cancers (in millions)



Source: WHO, SEB

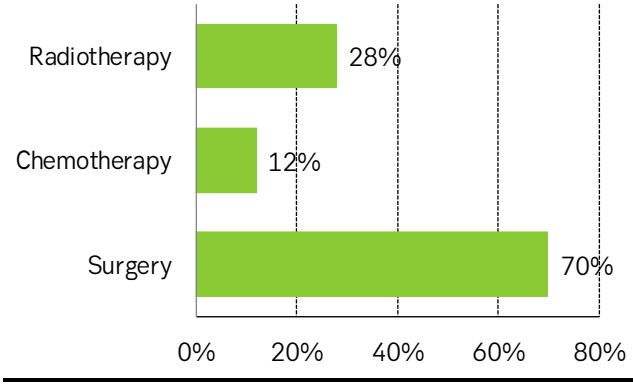
Most common cause of cancer deaths (in millions)



Source: WHO, SEB

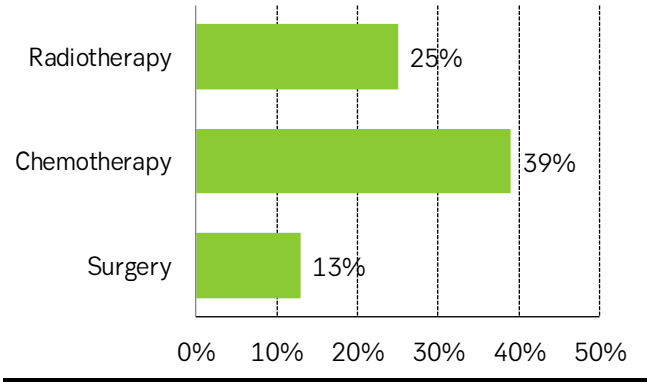
The cornerstones of today's cancer treatments are surgery, radiation therapy, and pharmacological therapy (e.g. chemotherapy and immunotherapy), alone or in combination. According to the NHS in the UK, c. 70% of all cancer patients in stage 1 (the earliest disease stage) receive surgery compared twith only c. 13% for those patients in the latest disease stage (stage 4).

Typical treatments for stage 1 patients (all cancers)



Source: NHS, SEB

Typical treatments for stage 4 patients (all cancers)



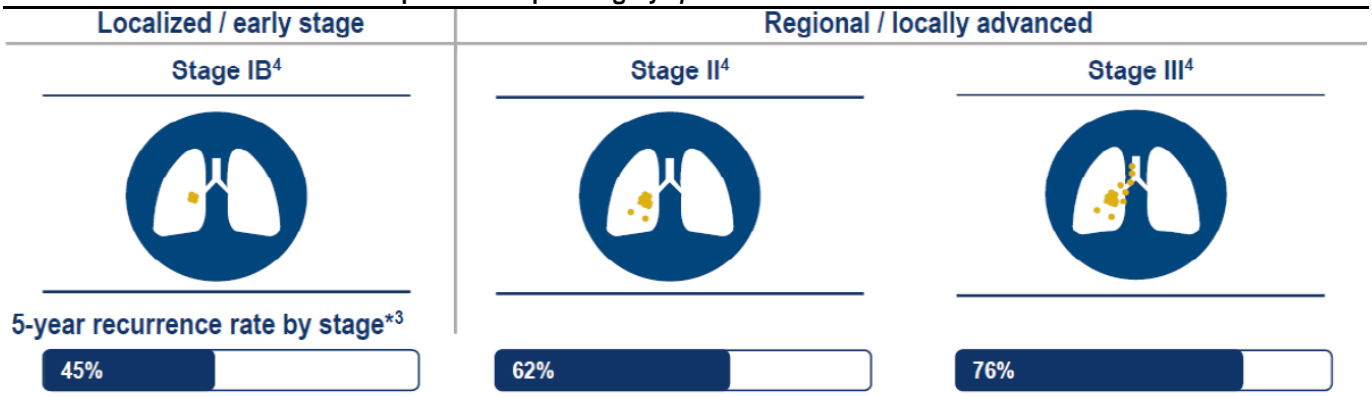
Source: NHS, SEB

Limitations of surgery

Surgery without image guidance is limited by the ability of the surgeon to discriminate tumour from healthy tissue, which is biologically constrained to macroscopic lesions, and by palpation, which cannot detect single cells or clusters of small numbers of cells. In some cases, surgery is curative, although this tends to decrease as cancers become more advanced, and in some cases, surgery is the only option that can improve outcomes. Still, the mortality rates in cancers such as GBM, TNBC, and advanced lung cancer leave much to be desired, even after therapy, with recurrence rates that can reach nearly 100%.

Meanwhile, even early stage cancers often have high recurrence rates, despite surgical resection and adjuvant chemotherapy, as exemplified, in the chart below, by non-small cell lung cancer (NSCLC) across many large randomised clinical trials.

Recurrence rate of 45-76% in NSCLC patients despite surgery +/- chemo



Source: Pignon et al., 2018. J Clin Oncol 26:3552-3559 via Herbst et al., 2020. ASCO Meeting oral abstract, SEB

The main cause of this therapeutic deficiency is residual tumour cells, which seed recurrent tumours. However, another important factor behind the poor outcomes is the detrimental effect of overzealous removal of healthy tissue in an effort to remove residual cancer. A number of technologies have been applied to this problem, with conventional methodologies including various imaging techniques, functional assessment in awake patients, as well as adjuvant pharmacological therapies (like chemotherapy).

Conventional imaging techniques, like CT and MRI, suffer from poor tissue contrast, unsatisfactory spatial resolution, and insufficient sensitivity to detect small lesions. They are often too cumbersome or dangerous to be positioned in an operating theatre and in many cases, they lack real-time application, limiting their utility in the surgical setting. Waking functional assessment, such as electrode monitoring of speech or motor signal function, is used to define tumour margins, but is limited to specific, eloquent brain areas, and cannot provide the resolution to detect residual cancer cell. Adjuvant therapies, e.g. chemotherapy, are limited by cancer resistance mechanisms.

Fluorescence-guided surgery (FGS) has the potential to enable real-time macro and microscopic identification of cancer cells, and, through photodynamic therapy, to ablate residual tumour cells and small clusters.

FGS agent performance objectives

At a fundamental level, imaging agents for FGS need to produce superior survival outcomes, a requirement that is ultimately a function of the ability to safely identify and destroy tumour cells. This is determined by the pharmacokinetic and pharmacodynamic characteristics of the chemical, and the extent to which those characteristics facilitate surgical precision.

1. Sensitivity and specificity

If the purpose of therapeutic cancer surgery is to remove malignant tissue while sparing healthy tissue, then it is essential to be able to discriminate tumours from normal tissue, with high specificity and selectivity. A contrast agent that facilitates this must, therefore, specifically accumulate in the target tissue, with no or limited nonspecific binding in healthy tissue. The quantification of this is described as the tumour-to-background ratio (TBR).

In order to be able to accumulate in the tumour, an imaging agent must be able to reach, recognise, and adhere to it, and for unbound agent to be removed more quickly from the body. The agent's ability to do so depends on parameters that include

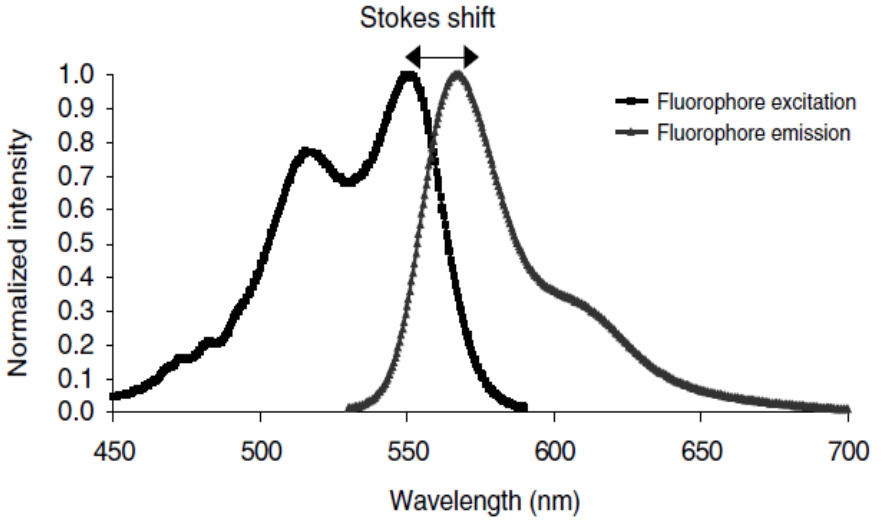
- **Bioavailability**: the agent must be able to be taken up and to reach its target in the body.
- **Target selection**: the agent must be able to bind the tumour cells/tissues and avoid binding healthy cells/tissues (i.e. the receptor or other target with which it interacts), meaning that the target should be a tumour-specific biomarker.
- **Target affinity**: the agent must bind its target sufficiently stably to remain on the tumour long enough for surgical resection.
- **Circulating half-life**: the unbound agent should be eliminated relatively quickly from the body so as to ensure sufficient contrast between healthy and diseased tissue, but if it is eliminated too quickly, the contrast enhancement will be limited.

Antibodies meet the first three conditions, but tend to fail on the fourth, due to their long circulating half-lives, typically of a week or more.

2. Visualisability

Given the importance of visual inspection in surgery, the ability to visualize the contrast agent is also essential (palpation seems less practical for the microscopic surgical scale), and for this, contrast, spatial resolution, and image depth are key. Given these performance objectives, it was perhaps inevitable that fluorescent probes would become a popular surgical tool.

Illustration of a stokes shift: larger shifts give a lower signal-to-background ratio

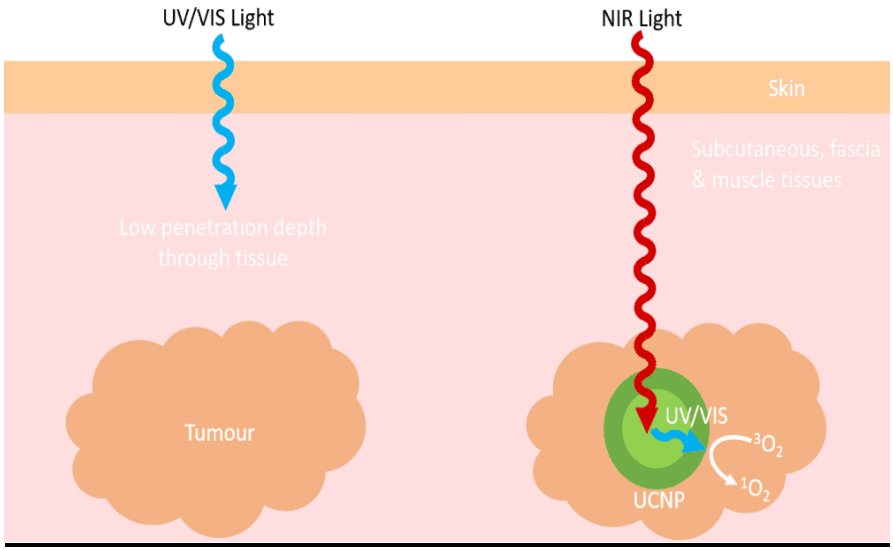


Source: Ghoushchi, 2015. DOI: 10.13140/RG.2.2.33261.38884

Fluorescent molecules have various properties that render them more or less suitable probes, chief among them that good probes have a large extinction coefficient[1] with large Stokes shift[2], large quantum yield[3], and high photobleaching[4] threshold. Good probes are bright, do not scatter much light (and hence have lower background noise), and stay bright for a long time.

[1] the strength with which a substance absorbs light at a given wavelength
[2] The difference between the wavelength of light absorbed and that emitted by a substance
[3] The ratio of photons emitted by a substance to photons absorbed by it
[4] Loss of fluorescence capacity, due to photon-induced chemical damage

Near-infrared light penetrates tissue better than UV/visible light



Source: https://www.edinst.com/blog/jacs-publication-ucnp/

In addition, probes that absorb light at longer wavelengths, i.e. in the near-infrared range (NIR) as opposed to the visible range, have better tissue penetration (up to 1 cm[5]). This is useful because tumours are resected as a mass of tissue, leaving a cavity surrounded by healthy tissue, but if parts of the tumour have migrated a short distance away, they will be below the surface, so probes that fluoresce despite being below the surface of the tissue will be easier to identify. This is in part because many biological substances are endogenous chromophores – they autofluoresce – within the visible range, but not the NIR, so fluorophores that emit in the NIR result in less scattering from the excitation source, resulting in a higher tumour-to-background ratio. Formally speaking, this is because scattering intensity is proportional to the inverse fourth power of the wavelength[6].

3. Heterogeneous presence of the target on the tumour cell surface

Unfortunately, biology puts a variety of constraints on what the ideal approach to FGS can look like. As any pathologist can tell you, there is no such thing as a ubiquitously expressed gene, and cancer cell populations are intrinsically heterogeneous; the more advanced the cancer, the greater the heterogeneity. One strategy to overcome cancer marker heterogeneity is to combine probes that have distinct targets, but this increases the probability that other performance objectives will be compromised.

In most solid tumours, it is the tumour margins that are most important, as those are the cells invading and migrating around local tissue, and hence the region giving rise to residual cancer cells that seed recurrent tumours.

4. Safety

Safety is always a critical performance objective in medicine. For FGS, a fluorescent contrast agent would be chemically inert (at least in the absence of excitation) and have a short circulating half-life with non-toxic metabolites. One shortcut to develop a novel fluorescent contrast agent is to modify a fluorescent probe whose safety is already clinically established.

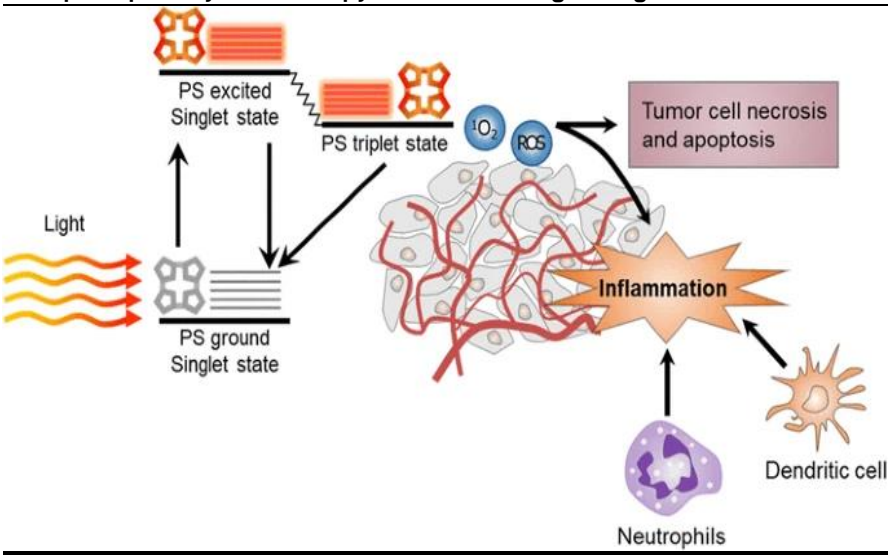
[5] He et al. 2017. Mol Imaging 16:1-15
[6] He et al. 2017. Mol Imaging 16:1-15

5. Compatibility with intraoperative imaging systems
The ability to execute precise, specific, and radical tumour resection is limited with the naked eye and palpation alone, so imaging modalities that demarcate malignant margins and metastatic tissue are routinely used peri and intraoperatively[7].

Because fluorescent probes are typically best visualised under conditions of low ambient light, or, in the case of NIR probes, are invisible to the eye, intraoperative fluorescence imaging systems must be used that perform the fluorophore excitation and emission detection and relay it via an image to the surgeon.

6. Selective tumour toxicity
Although not a requirement for FGS, strictly speaking, if the goal of tumour resection is curative, and residual cancer cells are the cause of tumour recurrence, then a contrast agent that is able to selectively ablate cancer cells should also be considered a performance objective. The use of light to induce direct cancer cell killing and indirect killing by immune recruitment is called photodynamic therapy (PDT).

Principle of photodynamic therapy: cancer cell killing with light



Source: Hwang et al., 2018. J Pharm Investigation 48:143-51

Photodynamic therapy (PDT)

PDT generates a cytotoxic singlet oxygen through interactions between optical light and a photosensitiser in the presence of oxygen[8]. Briefly, fluorophore excitation results in the generation of oxygen free radicals (ROS) that damage nearby cells' mitochondria, triggering cell death, as well as inflammation, which recruits the immune system to assist in tumour killing[9]. Because the target to which the photosensitiser binds should have been selected from its tumour specificity, only tumour cells will be nearby, so the cytotoxicity will be limited to the tumour cells. Most photosensitisers can be employed as contrast agents, enabling combination of FGS and PDT via a single agent, and potentially improving survival and other outcomes, including functional recovery, and the limitation of functional deficits.

[7] He et al. 2017. Mol Imaging 16:1-15
[8] He et al. 2017. Mol Imaging 16:1-15
[9] Hwang et al., 2018. J Pharm Investigation 48:143-51

A study in contrasts: ICG vs. 5-ALA

Comparison of the pros and cons of ICG and 5-ALA

Indocyanine green (ICG)	5-aminolevulinic acid (5-ALA)
Pros	
Selectively accumulates in and around tumours	Natural metabolite of haemoglobin metabolic pathway (i.e. safe)
Absorption and emission within the NIR	Blood-brain barrier penetration
Binds serum proteins, behaving as a macromolecule with larger hydrodynamic diameter and increased fluorescence intensity, leading to better retention and detection of cancerous tissues	Induces synthesis and accumulation of fluorescent molecule in cancer cells, as a function of lower levels of ferrochelatase enzyme compared to healthy tissue
Widely tested in many cancer types and approved for use in humans	Widely tested in many cancer types and approved for use for glioma resection in humans
Cons	
Lacks tumour specificity	Lacks tumour specificity
Unsuitable for photodynamic therapy	Unsuitable for photodynamic therapy
Susceptible to photobleaching	Susceptible to photobleaching
Uncertain suitability for brain tumours	Not suitable for low-grade gliomas
Low quantum yield	Emission in visible, not near-infrared, range
Unstable in aqueous solution	low intensity at tumour margins
Short circulation time (t1/2 = 2.5-3 min), limiting the number of molecules delivered to the tumour, and hence to lower contrast enhancement	

Source: He et al. 2017. Mol Imaging 16:1-15; Alston et al., 2019. Biomed Opt Express 10(5):2478-92

Two widely used fluorescent contrast agents are indocyanine green (ICG) and 5-aminolevulinic acid (5-ALA). ICG is the most widely used contrast agent in surgical navigation, and labels tumours by virtue of the "enhanced permeability and retention effect", whereby larger molecules are taken up by cancer cells to a greater extent than by healthy cells. However, the effect, at least as it pertains to ICG, is not a feature of a variety of tumours. Lee and colleagues[10] have suggested that high dose ICG may be able to cross the blood-brain barrier in the tumour vicinity due to enhanced permeability, but ICG is not by itself an ideal probe for brain tumour imaging.

5-ALA was approved by the EMA in 2007 and by the FDA in 2017 and is widely used for FGS in surgical resection of glioblastoma. It is a biproduct of haemoglobin biosynthesis that is metabolised to a fluorescent molecule. 5-ALA is thought to accumulate preferentially in glioblastoma cells due to lower levels of ferrochelatases in this cell type, as well as increased active transport by ABCB6. However, because 5-ALA and its metabolite are also produced in healthy tissue, as well as the fact that neither molecule is bound to a fixed cell and so can diffuse away from the tumour, 5-ALA's utility is limited for imaging of tumour margins.

Challenges in bringing agents to market

There are a number of challenges to bringing novel surgical contrast agents to market, including in the US, because surgical guidance is highly decentralised, and inter-specialty communication is limited. While this has enabled development and widespread commercialisation of fluorescence-guided surgical systems, the barriers to bringing new contrast agents to market have been higher. There are several reasons for this[11], including:

- An over-reliance on preclinical tumour models that were selected because they give a strong signal (i.e. the bar for choosing suitable clinical candidates is too low).
- Variability in target validation and clinical data reporting.
- Inherent difficulty of running surgical trials due to variation in surgeons' skill, institutional norms, and pathology processing.
- Lack of standardisation in pre and clinical data analyses.
- Suboptimal regulatory processes.

[10] Cho et al., 2019. Front Surg 6(11)
[11] Pogue et al., 2018. J Biomed Optics 23(10)

These challenges are a double-edged sword, because, although it is harder to bring new agents to market, there are fewer competitors than might otherwise have been the case, particularly of those that have more widespread potential.

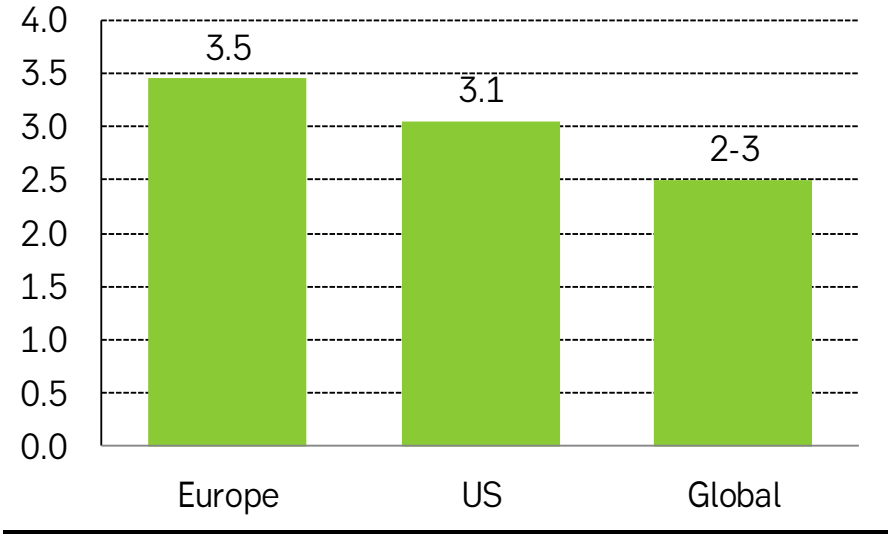
Therapeutic areas

High-grade glioma: low-hanging fruit

Epidemiology

FluoGuide's initial target indication is high-grade glioma, including glioblastoma. Globally, there are an estimated 240,000 new glioblastoma cases each year. According to the SEER database, the incidence rate for glioblastoma is 3.19 per 100,000 population in the US, 3.35 across the EU5, and an estimated 2-3 per 100,000 globally. Accordingly, approximately 27,000 patients are diagnosed with glioblastoma each year across the US and EU. Glioblastoma is a rare disease in both markets, qualifying drugs for Orphan Drug Designation; moreover, because of the high unmet need, products targeting it are more likely to qualify for e.g. Priority Review, Breakthrough Therapy Designation, or Accelerated Approval.

Glioblastoma incidence (per 100,000)



Source: National Cancer Institute SEER Database, SEB

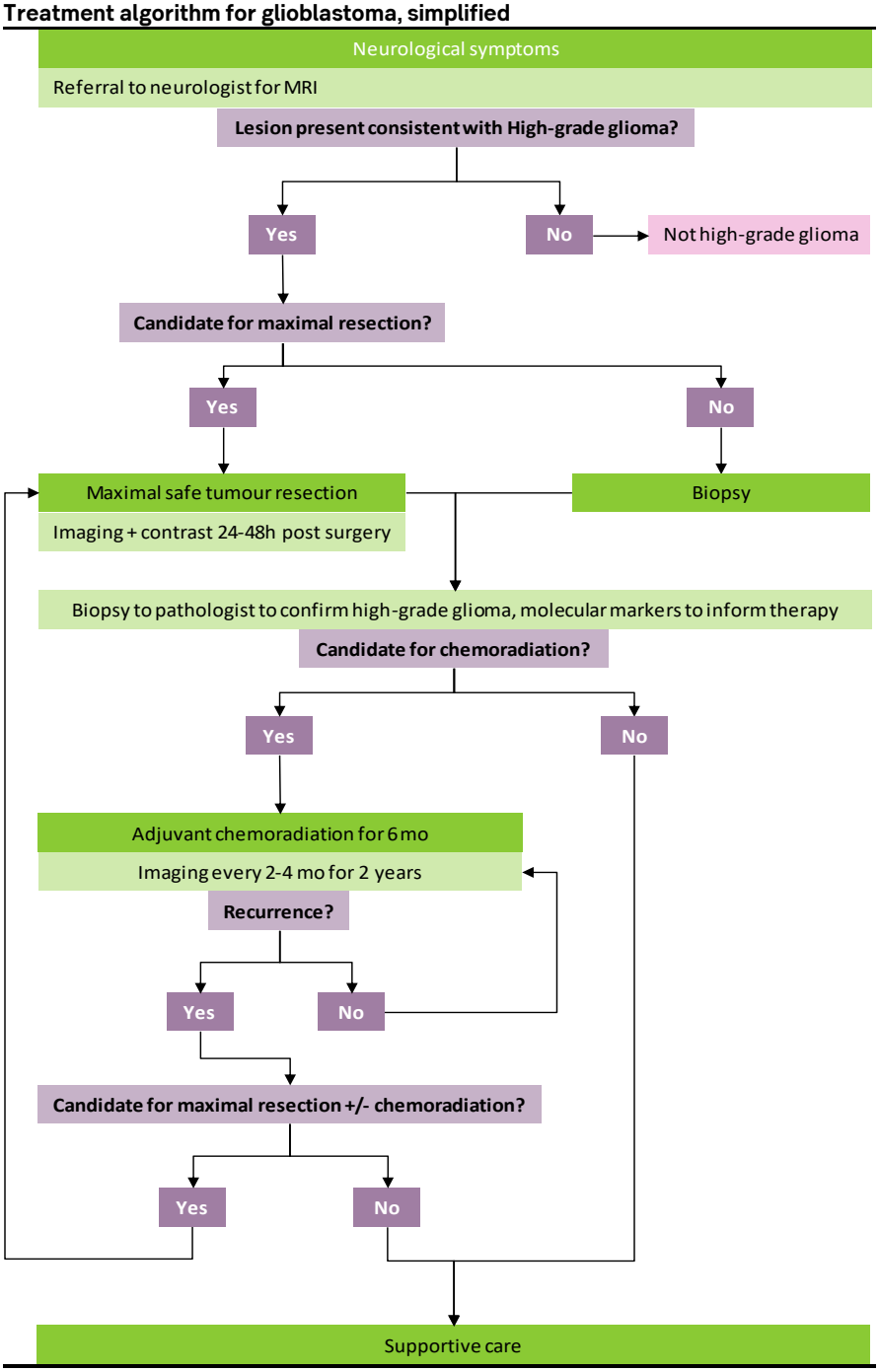
Treatment algorithm for high-grade glioma, including glioblastoma

Suspicion of high-grade glioma is raised by neurological symptoms and brain scan suggestive of high-grade glioma. Guidelines for the US (NCCN) and Europe (ESMO) call for evaluation and treatment planning by a multidisciplinary team, including a neurosurgeon, medical oncologist and radiation oncologist, and, preferably, an expert neuropathologist and neuroradiologist.

Maximal safe tumour resection is recommended for patients with good performance status, as measured by Karnofsky performance status (KPS), and overall health, depending on the patient's age, the feasibility of decreasing the tumour mass effect (which negatively impacts neurological function), and overall resectability (number and location of lesions and time since last surgery, if applicable). Open or stereotactic biopsy may also be undertaken to confirm diagnosis and inform therapeutic decisions if maximal resection is not possible.

Following surgery, tissue samples are sent for pathology testing, including staging and analysis of genetic and epigenetic markers. In Europe, where 5-ALA has been on the market longer than the US, an increased complete resection rate and improvement in the progression-free survival (PFS) is noted when 5-ALA is used. In the US, essentially all patients are biopsied to confirm diagnosis and inform potential therapeutic decisions, but in Europe, patients over 75 are less likely to be biopsied, reflecting a higher threshold for therapeutic intervention, although biopsy is also recommended in ESMO guidelines.

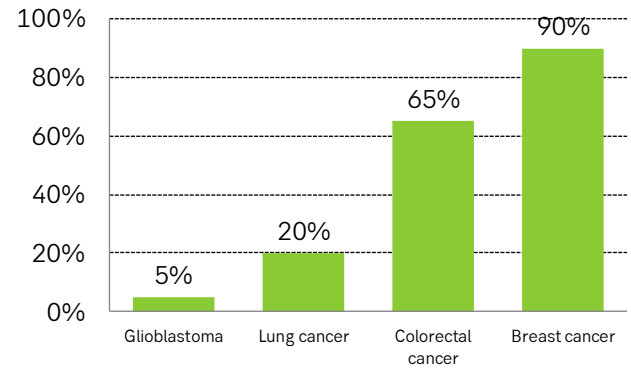
Treatment algorithm for glioblastoma, simplified



Source: SEB, NCCN guidelines, ESMO guidelines

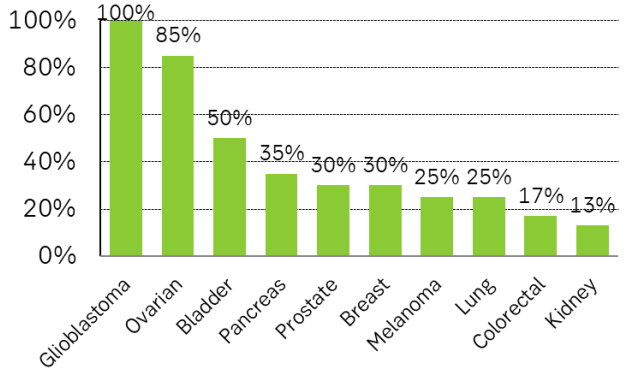
Carmustine-containing wafers may be implanted into the resection cavity following maximal resection, which has been shown to marginally improve median survival compared with radiotherapy alone. MRI (or CT, if MRI is infeasible) of the patient is supposed to be conducted within 24-48 hours after surgery, with and without contrast. Adjuvant chemoradiation[12] is standard of care. As follow-up care, patients should receive brain MRI 2-6 weeks after radiation therapy has ended. If results are stable, this should be repeated every 2-4 months for 2-3 years. Although recurrence is common, metastasis is rare, so surgery and chemoradiation is typically repeated in patients with good performance status.

Five-year survival rates selected cancers



Source: FluoGuide, SEB

Recurrence rate selected cancers



Source: FluoGuide, SEB

Clinical course and prognosis

Glioblastoma has one of the lowest five-year survival rates in oncology and limited improvements in survival has been achieved in the last decade with local recurrence in nearly 100% of the cases, according to company data. For Glioblastoma, the five-year survival rate is c. 5% compared with e.g. lung cancer (c. 20%), colorectal cancer (65%) and breast cancer (90%).

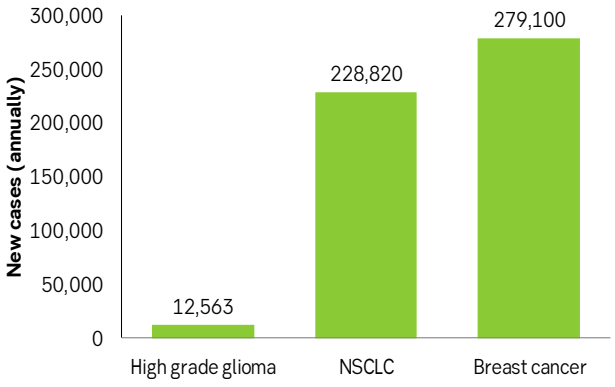
Overall survival in high grade glioma

	Median overall survival (mOS), years
Grade 4 (Glioblastoma)	1.25
Grade 3	
Anaplastic astrocytoma	3.5
Anaplastic oligodendroglioma	10

Source: Current ESMO guidelines for high-grade glioma (2014 edition)

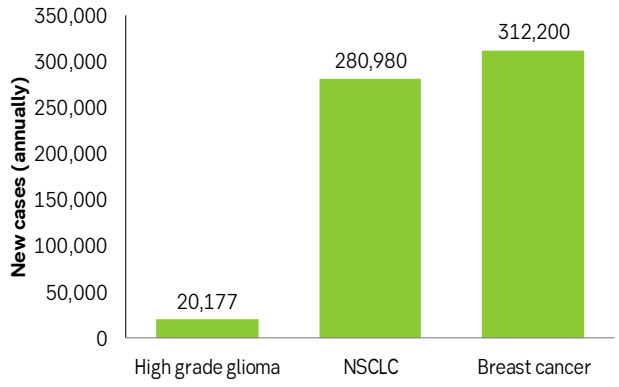
[12] Temozolomide (or bendamustine if patient has a methylated MGMT promoter) with fractionated external beam radiation therapy

Targeted patient population, US



Source: NCCN, SEER

Targeted patient population, EU



Source: Globocan 2020 report

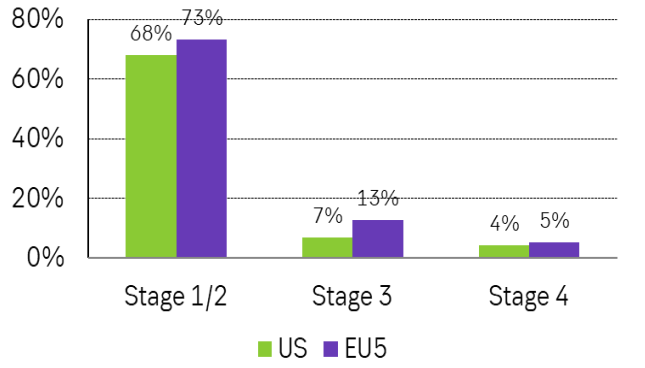
Adjacent opportunities

Beyond glioblastoma and grade III glioma, we believe FluoGuide is targeting breast cancer and lung cancer as second indications, with proof-of-concept studies being likely up and running in 2021. Because breast cancer and lung cancer are among the most common cancer types in the world, this would increase the patient population massively.

Breast cancer

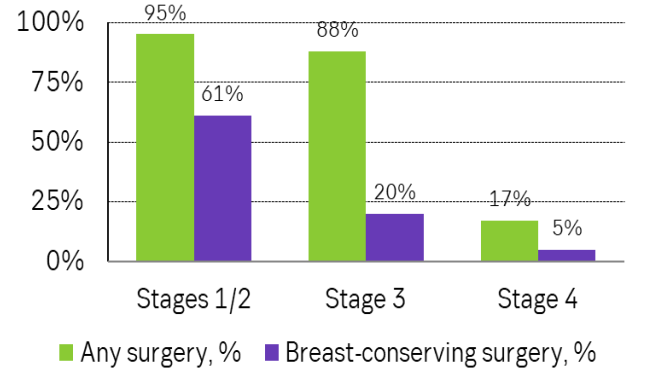
The American Cancer Society estimates that c. 279,100 individuals will be diagnosed with and 42,690 will die from breast cancer in the US in 2020. In Europe, 522,513 individuals were diagnosed with breast cancer in 2018 whereas 137,707 died from the disease (Globocan, 2018). Breast cancer can be divided into a variety of different subtypes depending on the aetiology, clinical presentation, including size, location, and number of lesions, molecular characteristics, and treatment response.

Share of total BC incidence by stage



Source: US National Cancer Database, Walters et al., 2013. BJC 108:1195; Grosclaude et al., 2001. Breast Cancer Res Treat 70(2):137-43; Minicozzi et al., 2012. Tumori 98(2):204-9; Baeyens-Fernandez et al., 2018. BMC Cancer 18(1):781; Katalinic et al., 2020. Int J Cancer 147(3):709-18

Rate of surgical resection by breast cancer stage



Source: SEB; Cancer Treatment & Survivorship Facts & Figures, 2019-2021

Surgery in earlier stages is more likely to be curative than at more advanced stages, and as the number drugs targeting specific subtypes of cancer, and particularly advanced cancer, has increased, the rate of resection in late stage cancer has declined. Although the vast majority of breast cancer patients undergoes surgery, several distinct procedures exist, including mastectomy (total removal of the mammary gland and nipple), as well as breast-conserving surgery, which is a group of surgery types that vary by degree of breast conservation. It is possible that FGS would be found more appropriate for some types of breast cancer surgery than others. It is also possible that the confidence obtained with FGS may improve the proportion of breast surgeries that can be performed as breast-conserving surgeries. A key obstacle to breast cancer market penetration for FluoGuide is that FGS is not yet an established therapeutic modality, so the equipment required for FGS is not currently available in most operating theatres.

Lung cancer

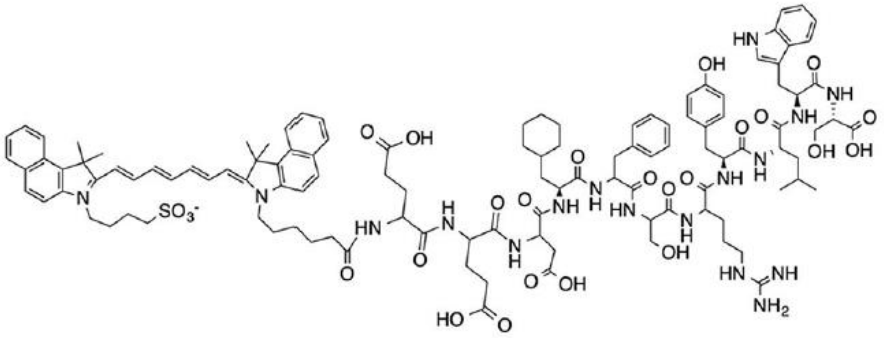
Lung cancer arises from the cells of the respiratory epithelium and is broadly divided into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), accounting for 15% and 85% of the annual new cases, respectively. NCCN estimates that c. 229,000 individuals will be diagnosed with non-small cell lung cancer in the US in 2020, and Globocan estimates the incidence of lung cancer in Europe at c. 470,000 cases (Globocan, 2018). Lung cancer incidence in the US has been declining since the early 1980s (Howlader et al., 2010). The death rate in lung cancer is high, with 5-year overall survival of only 20%.

Surgery, radiotherapy, and systematic therapy are the most common treatment options in NSCLC and can be used either alone or in combination. The goal of surgery in stage I or II disease is curative (Howington J. et al., 2013). In the UK, 10.6% of NSCLC patients were treated with surgery[13], but the figure is 25% in the US[14].

[13] Riaz et al., 2012. Thorax 67:811-814
[14] Dransfield et al., 2006. Clin Lung Cancer 7(4):268-72

FG001

FG001: an ICG-conjugated uPAR agonist

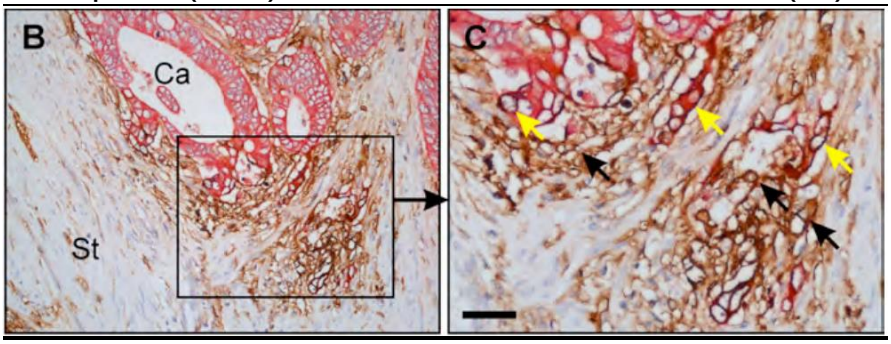


ICG-Glu^{1}-Glu^{2}-Asp^{3}-Cha^{4}-Phe^{5}-(D)ser^{6}-(D)arg^{7}-Tyr^{8}-Leu^{9}-Trp^{10}-Ser^{11}

Source: Juhl et al., 2016. PLOS One DOI:10.1371/journal.pone.0147428

FluoGuide's lead product, FG001, is an indocyanine green-conjugated uPAR agonist (AE105), designed to more effectively label tumour margins and hence drive better fluorescence-guided surgical outcomes by facilitating complete resection, as well as elimination of residual cancer cells using photodynamic therapy.

uPAR expression (brown) at the tumour-stromal interface of colon cancer (red)



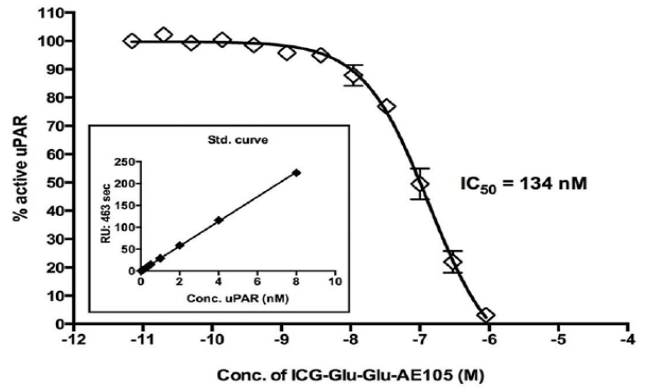
Source: Kriegbaum et al., 2011. Curr Drug Targets 12:1711-28

uPAR marks the tumour-stromal interface

uPAR is the urokinase type plasminogen activator receptor (gene name *PLAUR*), which plays a role in normal tissue homeostasis, particularly in the vasculature and on white blood cells, where it is mostly present at low or undetectable levels, but sharply upregulated in activated cells, such as macrophages and vascular cells participating in angiogenesis. The lung has some of the highest baseline levels of uPAR. uPAR is also constitutively upregulated in and around many cancer cell types, especially carcinomas, particularly at the tumour-stromal interface[15], i.e. the tumour margins. This is interesting from a surgical perspective, because it is the margins that give rise to the great majority of recurrences; indeed, it makes it an interesting candidate for PDT, because a retrospective analysis reported that 77% of glioblastoma recurrences occur within 20mm of the site of the original tumour mass[16]. This marginal expression of uPAR is particularly notable in colorectal, gastric, and mammary carcinomas. In glioblastoma and squamous cell carcinoma of the skin, uPAR is highly expressed throughout the tumour.

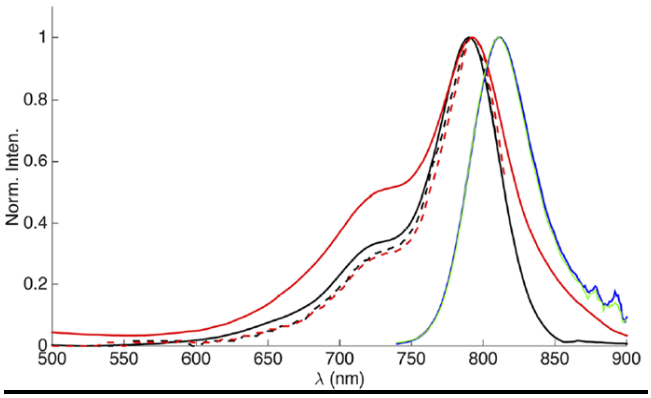
[15] Kriegbaum et al., 2011. Curr Drug Targets 12:1711-28
[16] Sherriff et al., 2013. Br J Radiol https://doi.org/10.1259/bjr.20120414

FG001 is a potent uPAR agonist



Source: Juhl et al., 2016. PLOS One DOI:10.1371/journal.pone.0147428

FG001 (red) emits in the NIR, similarly to ICG itself (black)

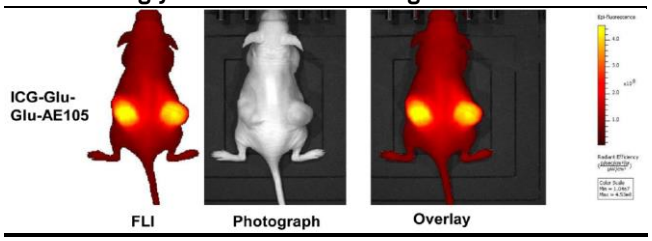


Source: Juhl et al., 2016. PLOS One DOI:10.1371/journal.pone.0147428

FG001: a novel contrast agent localising to the tumour-stromal interface

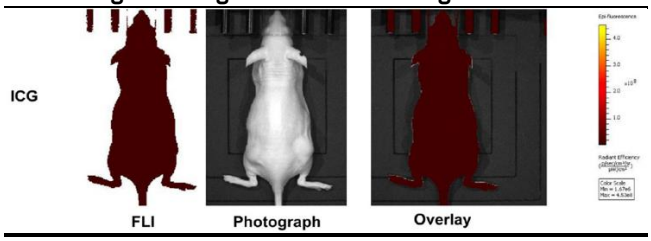
By conjugating ICG to uPAR agonist AE105, FluoGuide has synthesised a novel contrast agent with fairly high affinity (IC50=134nm) for uPAR, and a similar, if slightly broader, near-infrared range emission profile to unconjugated ICG.

FG001 strongly localises to GBM xenograft in nude mouse



Source: Juhl et al., 2016. PLOS One DOI:10.1371/journal.pone.0147428

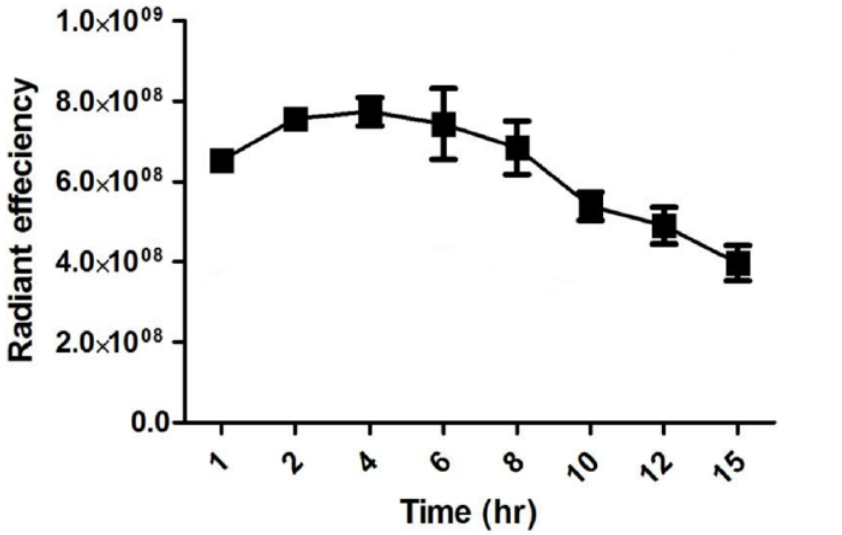
ICG alone gave no signal in the GBM xenograft model



Source: Juhl et al., 2016. PLOS One DOI:10.1371/journal.pone.0147428

Cells from a human glioblastoma cell line engrafted into the flanks of nude mice to form xenografts were readily macroscopically identified following administration of FG001, but not following administration of unconjugated ICG. This also demonstrated the first evidence of tissue penetrance by FG001 fluorescent emissions.

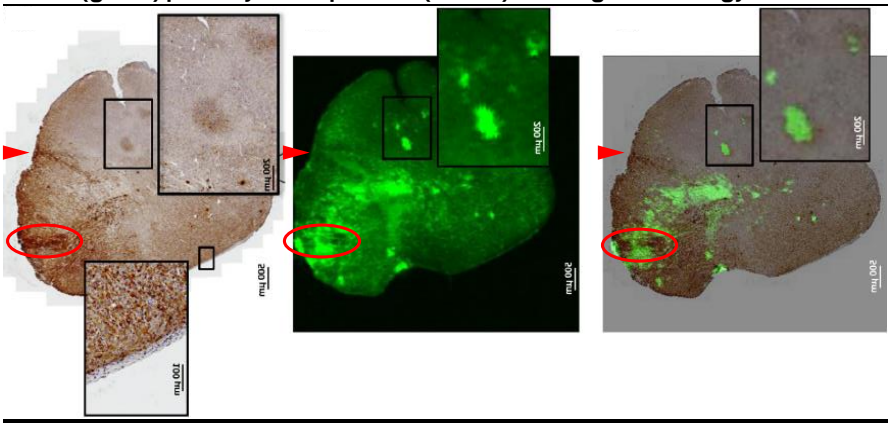
Single administration of FG001 offers a surgical window of 7 hours or more



Source: modified for simplicity from Juhl et al., 2016. PLOS One DOI:10.1371/journal.pone.0147428

Importantly, a single administration of FG001 opens a nearly 8-hour surgical window, which is sufficient for most brain tumour resections.

FG001 (green) partially overlaps uPAR (brown) in xenograft histology sections



Source: SEB; Juhl et al., 2016. PLOS One DOI:10.1371/journal.pone.0147428

Histological analysis of the dissected xenografts show substantial FG001 labelling of uPAR, although the observation of islands of non-FG001 labelled uPAR (red arrowhead and part of encircled area in the images above) is somewhat incongruous with the overall data. There are a number of potential explanations for this, any or all of which could apply, including:

- Non-specific binding of the anti-uPAR antibody used in the staining.
- Other factors affecting the quality of staining.
- FG001 might be unable to bind all forms of uPAR; this itself could be due to various factors, e.g.
    - Human uPAR from xenografts could be inactivated by surrounding mouse tissue.
    - The uPAR detected might be present only in intracellular compartments in the non-FG001-labelled islands.
    - FG001 might be inactivated, by some factor, e.g. proteases, in those or adjacent tissue regions, limiting access.

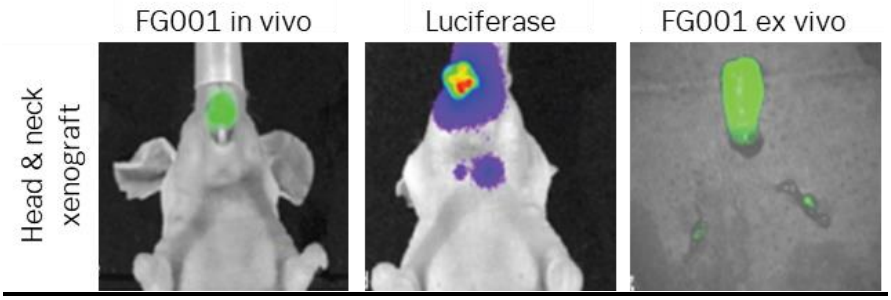
Whether this finding is of significance for the biologically more relevant setting of the clinic can only be resolved there, and FluoGuide should soon have that data from its ongoing study, although as we describe below, it does not appear to have been a limiting factor in other xenograft models. In the meantime, the data provides proof of principle that FG001 is able to label uPAR-expressing human cancer cells in a highly specific manner.

FG001 improves the ability to identify metastases in xenograft models

FG001 has been tested in xenograft models of pancreatic cancer and head and neck cancer, in which it has enabled identification of metastases that were not identified by white light surgery. An advantage of these studies compared with the clinical setting is that the cancer cell lines used could be engineered prior to xenografting in order to produce a highly sensitive bioluminescent marker (luciferase), such that these cells were detectable by means other than FG001, enabling estimation of FG001's sensitivity as a cancer cell imaging agent.

Importantly, all foci detected by the naked eye were also detected with the fluorescent signal, but FG001 was also able to detect foci that were undetectable to the naked eye. In pancreatic xenografts[17], whereas 29 (67%) of a total of 43 positive metastases were identified by white light surgery, a further 6 (81% total) were identified by FG001, with lesions of as little as 1mm detectable with the tracer. These 43 lesions were present across 8 animals, with the 6 lesions identified with FG001 found across 4 of them, which is to say that metastases were identified by FG001 alone, not white light surgery, in half the animals. We note that the study design is susceptible to issues of bias, as the surgeon operated first under white light, and FGS used only after the surgeon concluded that all metastases had been identified.

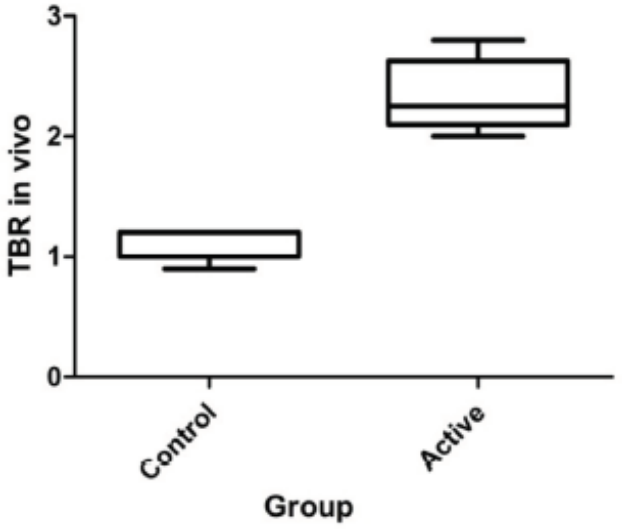
FG001 can detect submillimetre metastases across a variety of cancer types



Source: Christensen et al., 2017. Oncotarget 8(9):15407-19

Another study employed a mouse xenograft model of head and neck cancer, in which FG001 enabled identification of sub-millimetre metastases in the lymph nodes by NIR, which were not visible by white light.

FG001 tumour-to-background ratio in head and neck xenograft model



Source: Christensen et al., 2017. Oncotarget 8(9):15407-19

[17] Juhl et al., 2019. Oncotarget 10(59):6308-16

Promising tumour-to-background ratio, but models easier than real world

FG001 resulted in a TBR of 3.5x in both glioblastoma and pancreatic cancer xenograft models, and 2.4x in head and neck cancer xenograft models. A major limitation of these xenograft studies is that the xenografted tumours all originate from the same clone, so they are less heterogeneous than would typically be the case in a real-world or spontaneous case. This has been demonstrated in a study of 5-ALA in lung cancer models, in which mouse xenograft models had a TBR of 3-fold higher than in spontaneous lung cancer canine models, which more closely resemble real-world lung cancer in humans[18].

FG001 appears to have performance benchmarks superior to those of 5-ALA

	FG001	Gliolan (5-ALA)
Manufacturer	FluoGuide A/S	SBI Holdings, Inc.
Marketing status	Development (Ph 1/2)	Approved in >30 countries, incl. US, EU
Light	NIR	Visible
Tissue penetrance	10-20mm	1-2mm
Fluorescence intensity	High	Low
Photobleaching	Slow	Fast
Tumour-specificity	High; cell-bound	Moderate; free floating
Time from administration to use	0.5-1 hour	6-24 hour

Source: adapted from FluoGuide

Overall favourable profile of FG001 vs. 5-ALA, but it is still early days

We conclude that FG001 has an attractive overall profile, improving on the profile of unmodified ICG, and comparing favourably to 5-ALA, with greater tissue penetrance and potentially higher TBR, due to its emission in the NIR range. With respect to 5-ALA, its weak fluorescence is correlated with infiltrating tumour and medium tumour cell density, so whether FG001 continues to show high fluorescence intensity in a clinical setting, particularly given the fact that spontaneously occurring tumours display more heterogeneity than xenografts, remains to be seen. Although we have not seen data on FG001 with respect to photobleaching, FluoGuide argues that it is relatively slow compared with 5-ALA, although this may be offset by the fact that visible light does not penetrate tissue as deeply[19].

Photodynamic therapy is key, but we have no data yet

Given the high recurrence rate in cancers of all stages, and the frequent proximity of the site of recurrence to the original tumour, the ability to ablate isolated residual cancer cells or cell clusters is a key potential driver for FG001, but FluoGuide has yet to conduct these experiments. The main risks to success (i.e. improved outcomes) are limitations of FG001 tissue penetrance in human tissue and unanticipated safety issues.

[18] Predina et al., 2019. Sci Rep 9:7629
[19] Hadjipanayis et al., 2015. Neurosurg 77(5):663-73

Clinical development path and timeline

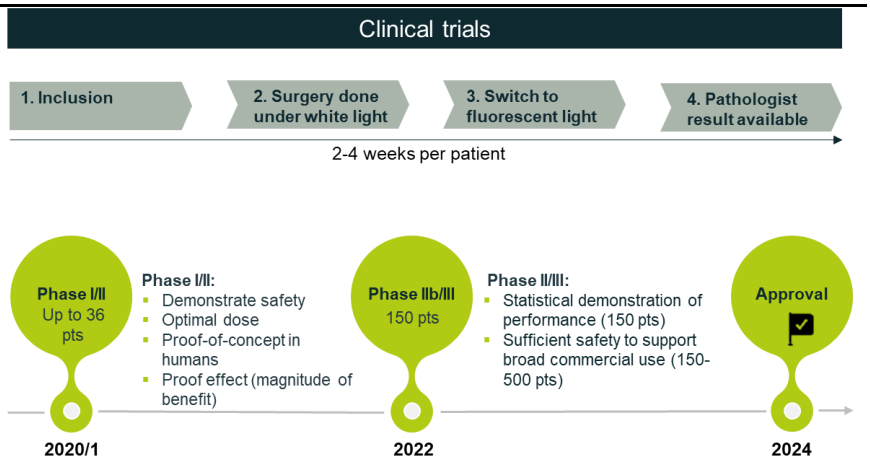
FG001 – a direct and short path to market

Classified as an imaging agent within medicinal product regulation

Glioblastoma qualifies for orphan drug designation

Clinical studies are straightforward and require few patients

- **Clear endpoint**: Positive predictive value (relative # cancer biopsies light up validated by pathologist)
- **No/small placebo arm**: Fewer patients needed
- **Short time frame**: Enrollment to surgery
- **Single blind**: Initial results known after the first few patients
- **No competition for patients:** Treatment can be done in addition to other treatments

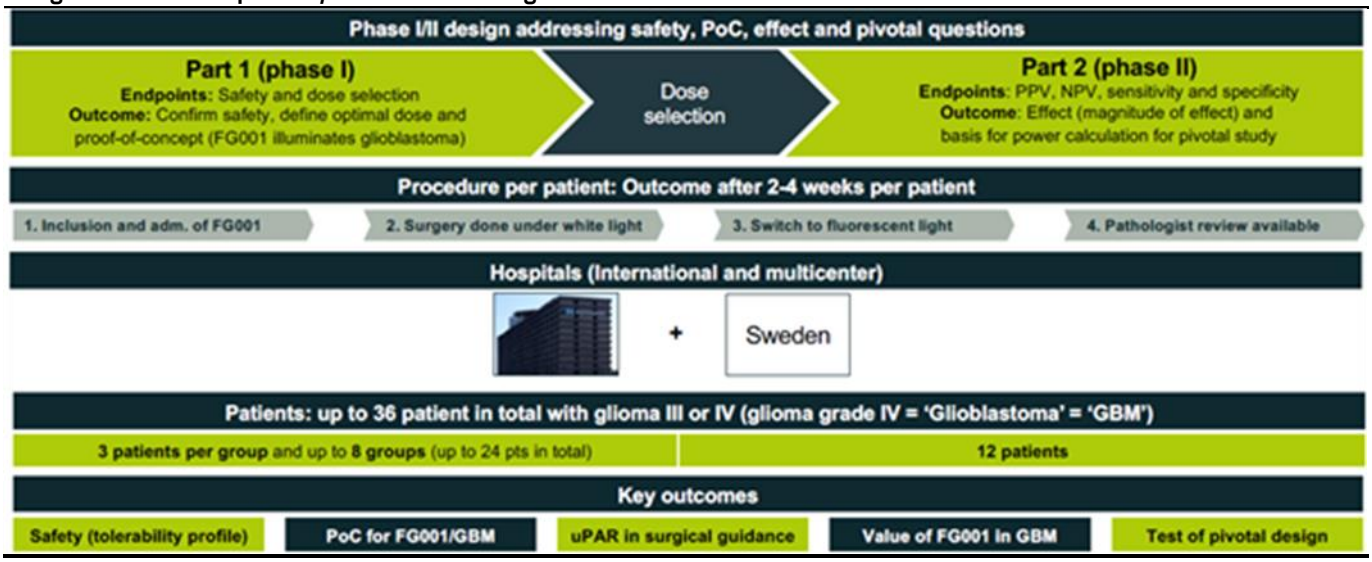


Source: FluoGuide, SEB

Phase 1/2 trial underway for high grade glioma

FluoGuide initiated a phase 1/2 clinical trial for FG001 on 9 November, for patients with high grade glioma (anaplastic, or grade 3, glioma, and glioblastoma, a.k.a. grade 4 glioma). Glioblastoma is a logical first indication to choose, because of the high level of uPAR expression throughout the tumour, as well as the fact that there is a defined regulatory pathway to approval, based on the approval of 5-ALA.

Design of FluoGuide's phase 1/2 trial of FG001 in glioblastoma



Source: FluoGuide

The phase 1/2 trial consists of two parts: a dose-escalation (8 x 3 patients) part to establish safety and proof-of-concept, and an efficacy part (12 patients), to be conducted at the optimal dose from the first part. FluoGuide has stated that it will enrol a maximum of 36 patients into its trial, depending on how well tolerated FG001 is at the various doses[20]. The second, efficacy part is intended to provide an estimate of the benefit of FG001, in order to motivate pricing, as well as to calculate how the confirmatory/pivotal trial will need to be powered[21].

Phase 1/2 catalyst calendar

Timing	Event type	Details
2020-Q4	Trial readout	Ph1 result of first dose escalation readout (safety)
2021	Clinical trial milestone	Ph1/2 result of subsequent dose escalation groups (PoP)
2021-mid	Trial readout	Ph1 topline
2021-H2	Trial readout	Ph 2 efficacy data

Source: SEB, FluoGuide

Benchmarking proof-of-concept trial outcomes against 5-ALA trials

Efficacy in the phase 1/2 will be probed with standard FGS endpoints, including positive predictive value (PPV), negative predictive value (NPV), sensitivity, and specificity. Across a number of clinical trials, 5-ALA has produced the following outcomes in glioblastoma[22]:

- 75-95% sensitivity has been reported, with most reports above 90%.
- 53-96% specificity, with most studies in the 80% decile.
- PPV performance of 88-100%.
- NPV performance of 22-91% is the most widely varying, with a median NPV of around 60%.

These findings indicate that the biggest room for improvement is with respect to false negative fluorescence. However, the diffuse, low-density nature of infiltrative growth makes false negatives inherently more likely (hence the rationale to complement FGS with PDT). Still, this is perhaps where NIR fluorescence will give FG001 the edge.

[20] https://fluoguide.com/first-patient-enrolled-in-the-phase-i-ii-clinical-trial-testing-fg001-in-patients-with-high-grade-glioma/
[21] FluoGuide Q3 report.
[22] Hadjipanayis et al., 2015. Neurosurg 77(5):663-73

Summary of phase 3 randomised clinical trial of 5-ALA vs. white light only

	5-ALA	White light only
No. pts	139	131
Baseline characteristics		
Age ≤55y	32%	33%
Karnofsky performance scale <80, %	20%	24%
Tumour near eloquent brain regions, %	47%	41%
National Institutes of Health Stroke Score (NIHSS), median (range)	1 (0-10)	1 (0-8)
Pathological analysis, % pts		
Oligoastrocytoma (grade III)	0%	1%
Oligodendroglioma (grade III)	0%	2%
Anaplastic astrocytoma (grade III)	2%	2%
Astroblastoma (grade III)	1%	0%
Gliosarcoma (grade IV)	6%	6%
Giant-cell glioblastoma (grade IV)	4%	2%
Glioblastoma multiforme (grade IV)	88%	88%
Missing data	0%	1%
Efficacy outcomes		
Complete resection, % pts	65.0%	35.9%
Median tumour volume, cubic cm	0.0	0.7
Median survival, mo	15.2 (n.s.)	13.5
mPFS, mo	5.1	3.6
6mo PFS, %	41.0%	21.1%
Adverse Events (AEs)		
Deterioration in NIHSS		
at 48 hours	*26.2%*	*14.5%*
at 7 days	*20.5% (n.s.)*	*10.7%*
at 6 weeks	*17.1% (n.s.)*	*11.3%*
at 3 months	*19.6% (n.s.)*	*18.6%*
30-day mortality rate	4.0%	2.0%
Frequent early severe AEs, % pts		
Hemiparesis	3.0%	2.0%
Aphasia	2.0%	0.0%
Convulsions	2.0%	1.0%
Epidural haematoma	1.0%	1.0%

Source: Stummer et al., 2006. Lancet Oncol 7(5):392-401

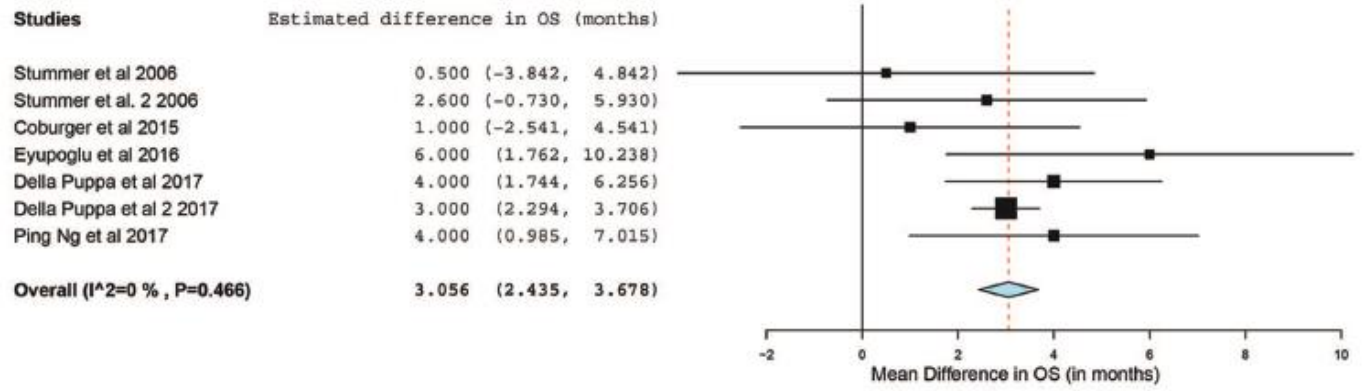
Phase 2b/3 pivotal trial

As stated in regulatory filings, following the presumptive success of the present study, FluoGuide intends to initiate a pivotal phase 2b/3 trial in 2022 (assuming all 8 cohorts in the phase 1/2 trial be enrolled), pitting FG001 head-to-head against 5-ALA with the aim to show (1) non-inferiority (the bar for regulatory approval) on the primary endpoint, which is likely to be sensitivity or positive predictive value, and (2) superiority on the secondary endpoints, likely specificity or negative predictive value. A successful outcome should enable regulatory filings and approval in 2023-24. We believe management will conduct an extension to the study or a separate study to demonstrate the value of features like photodynamic therapy. In parallel, management aims to establish a prioritised pipeline of uPAR-targeted products, to prepare clinical studies for other indications for FG001 (e.g. breast, lung cancer), as well as to prepare commercial scale manufacturing of FG001.

Benchmarking potential phase 2b/3 outcomes against 5-ALA trials[23]

In addition to comparing sensitivity, specificity, PPV, and NPV, previous studies of 5-ALA offer other important performance benchmarks, including complete resection of contrast-enhancing tumour, with reports of 63-89% of patients using 5-ALA, including the results of a controlled trial, which reported 65% vs. 36% complete resection in the control group. 5-ALA has had a mixed track record in studies comparing progression-free and overall survival between 5-ALA and white-light surgery alone[24]. A meta-analysis of various trials found no significant OS difference across published studies, although there was a consistent trend toward benefit. Measurement of survival outcomes is confounded by many factors, including choice of and responsiveness to subsequent adjuvant therapy and differences in skill level from one surgeon to another.

Overall survival difference of 5-ALA vs. white light surgery



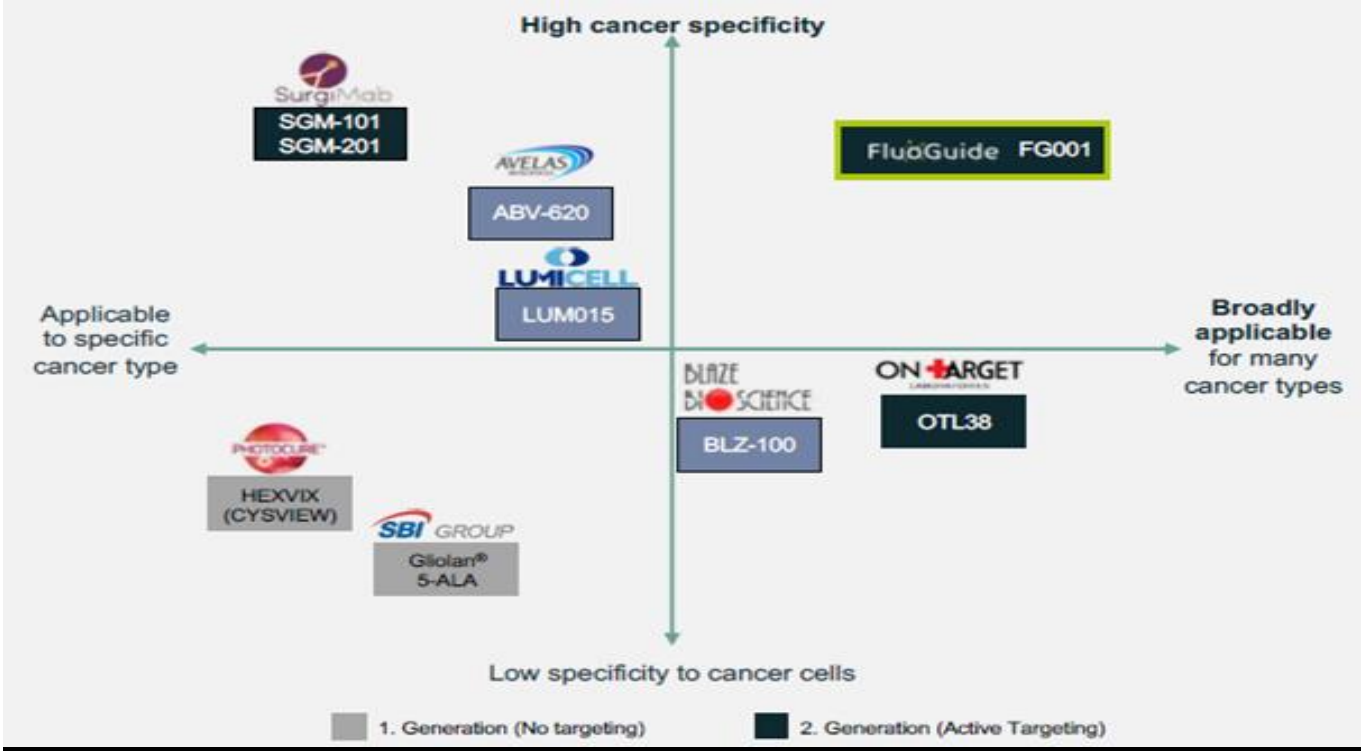
Source: Gandhi et al., 2019. Front Oncol 9:620

[23] Hadjipanayis et al., 2015. Neurosurg 77(5):663-73
[24] Gandhi et al., 2019. Front Oncol 9:620

Beyond 5-ALA: competitive overview

We note a variety of different intelligent surgical targeting products, other than 5-ALA, currently under preclinical/clinical development or having already been regulatory approved and currently are available in the market.

Competitor overview



Source: FluoFuide

- **SGM-101 and SGM-201 from SurgiMab**. SurgiMab focuses on developing injectable fluorescent conjugates to be used during Fluorescence-Guided Surgery (FGS). Its lead candidate, SGM-101 is currently in Phase III, for colorectal cancer, with preliminary clinical data expected in 2021. According to company data, SGM-101 is a tumour-specific antibody conjugated to a near-infrared fluorochrome which selectively binds to a specific marker (CEA) which is overexpressed in gastrointestinal and other tumours (e.g. pancreas, lung and gastric cancer). SGM-201 use the same technology, albeit with a different marker (AMHR-II) and is currently in pre-clinical stage for ovarian cancers.

SurgiMab pipeline

	Surgery	Preclinical	Phase I	Phase II	Phase III
SGM-101	Colorectal cancer				
	Pancreas cancer				
	Lung cancer				
	Gastric cancer				
	Digestive cancer screening				
SGM-201	Ovarian cancers				

Source: SurgiMab, SEB

- **Pegloprastide (AVB-620) from Avelas Biosciences.** Avelas Biosciences lead product candidate Pegloprastide (AVB-620) is based on the science of activatable cell-penetrating peptides and is intended to be used as a fluorescent marker to cancer cells to assist surgeons, in real-time, to identify cancerous tissue. According to company data, Pegloprastide recently completed a successful phase II/III pivotal for fluorescent detection of cancer during breast cancer surgery, showing that the use of Pegloprastide during surgery correctly identified cancer in up to 75% of patients who would have otherwise been candidates for a repeat (re-excision) surgery. Pegloprastide's overall accuracy in detecting true positives/true negatives was c. 81%.

Avelas Biosciences pipeline

	Surgery	Preclinical	Phase I	Phase II	Phase III
Pegloprastide	Breast cancer				
	Ovarian cancer				
	Colorectal cancer				
	Melanoma				
	Head and neck cancer				
	Sarcoma				

Source: Avelas Biosciences, SEB

- **LUM015 from Lumicell** is designed to enable surgeons to see residual cancer cells in the cavity walls in real-time during surgery according to company data. LUM015 consists of three main components, including a onco-fluorescent agent that targets the tumour and is designed to fluoresce near cancer cells when activated by proteases, a hand-held lightweight single-cell resolution imaging device and a software solution which produces real-time images indicating the location of residual cancer. LUM015 has completed a phase I safety study and a phase II feasibility study for breast cancer surgery. In total, LUM015 is currently being investigated in seven different cancer types.

Lumicell pipeline

	Surgery	Preclinical	Phase I	Phase II	Phase III
LUM015	Breast cancer				
	Prostate cancer				
	Brain cancer				
	Gastrointenstinal cancers				
	Peritoneal Surface Malignancies				
	Pancreatic cancer				
	Sarcoma				

Source: Lumicell, SEB

- **HEXVIX (CYSVIEW in the US) from Photocure** is selectively taken up by cancer cells in the bladder, causing them to generate a bright pink/red glow during cystoscopy with a blue light enabled cystoscope. In turn, this is intended to allow for earlier and better detection as well as more complete removal of tumours. Hexvix/Cysview is regulatory cleared in Europe and the US and generated revenues of NOK 213m in FY 2019.

- **BLZ-100 from Blaze Bioscience** is described as a tumour paint product candidate and is being developed for cancer surgery in multiple solid tumour types. BLZ-100 is administered intravenously and circulates in the body and lights up cancer cells, according to company data. BLZ-100 consists of a peptide and a fluorescent dye which binds and internalise into cancer cells, emitting light in the near-infrared range. BLZ-100 has demonstrated clinical proof of concept in four phase I studies for brain, breast, and skin cancers. Pre-clinical utility of BLZ-100 has been shown across prostate, lung, colorectal and other solid tumour cancers according to company data. BLZ-100 is currently being evaluated in a Phase II/III study for paediatric central nervous system (CNS) tumours and was granted Fast Track Designation by the FDA in April 2020.

- **Pafolacianine (OTL-38) from On Target Laboratories**. On Target's fluorescent markers consists of a near-infrared dye and a targeting molecule or ligand that binds to receptors typically overexpressed on cancer cells, according to company data. On Target's lead candidate Pafolacianine targets folate receptors commonly found on many cancers, including ovarian and lung cancer and is currently investigated in two phase III studies for these indications. On Target is also investigating its OTL78 compound, a PSMA-targeted fluorescent marker, for intraoperative imaging in prostate cancer in a phase I/IIa study.

On Target Laboratories pipeline

	Surgery	Preclinical	Phase I	Phase II	Phase III
Pafolacianine	Ovarian cancer Lung cancer				
OTL78	Prostate cancer				

Source: On Target Laboratories, SEB

Intellectual property rights

FG001 patent

Product	Patent number	Application	Validity	Filed	Expiration
FG001	WO/2016/041558A1	Perioperative optical imaging of invasive cancer	US, EU	2014	2034

Source: FluoGuide, SEB

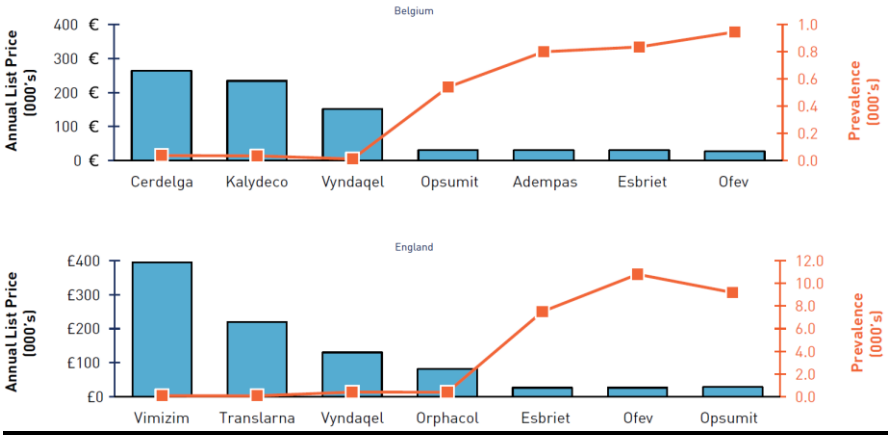
FluoGuide owns a patent family which protects FG001 and that has been issued in the US and Europe. The patents do not expire until 2034, providing a long period of protection from generic competition.

Orphan drug designation

In addition, we believe it may be possible for FluoGuide to secure orphan drug designation for FG001. Although no approved contrast agent has orphan designation, Ascelia Pharma's contrast agent, Mangoral, has obtained orphan designation and is currently in phase 3, and Life Molecular Imaging obtained EU orphan designation for Florbetaben.

Historically, two major obstacles discouraged the development of drugs to treat rare diseases: (1) the high development costs of bringing a new drug to the market; and (2) the limited revenue potential of the small number of patients. In order to address this public health need, the US Congress passed the Orphan Drug Act in 1983, providing incentives associated with the orphan drug designation to make sure orphan drug development is financially viable. A rare disease is defined by the Act as any disorder or condition which affects fewer than 200,000 persons in the US. Similar legislation was adopted in Japan in 1993 and in the EU in 2000, and the statutes specify a prevalence rate ceiling that implies a maximum prevalence of 50,000 and 256,000 patients, respectively. Over 500 orphan drugs and biologic products have been developed and marketed in the US since the Act was implemented, compared with 38 in all years prior to 1983.

Orphan drugs command premium pricing



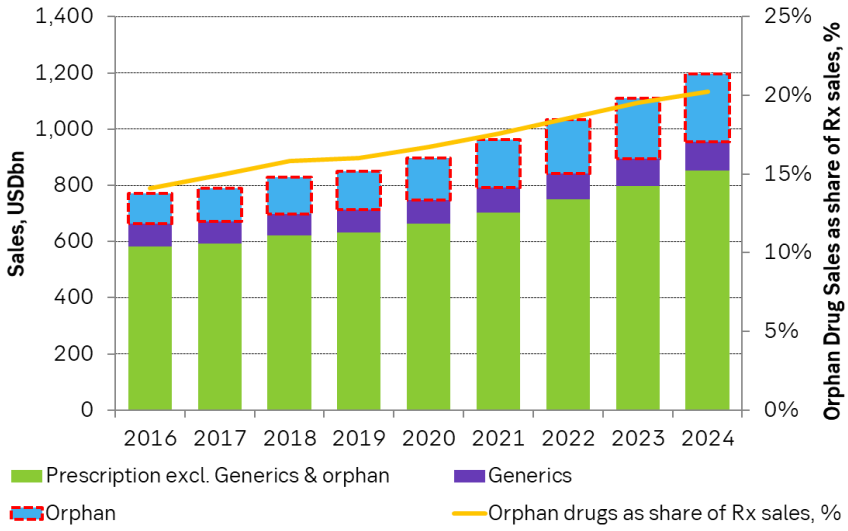
Source: Cockerill et al., 2017. Health Advances White paper

Benefits of Orphan Drug Designation

- Premium drug pricing.
- Market exclusivity: seven years of marketing exclusivity from the date of approval in the US and 10 years in the EU.

- Reduced R&D costs in the US via:
    - 50% tax credit on R&D costs.
    - R&D grants for Phase I to Phase III clinical trials.
    - Waived user fees.
- Reduced R&D costs in the EU via EMA protocol assistance at a reduced charge.
    - Administrative and procedural assistance at a reduced fee for small and medium-sized enterprises.
    - Provide funding for the European Commission and other sources, such as Horizon 2020 and e-rare.

Orphan drug sales projection



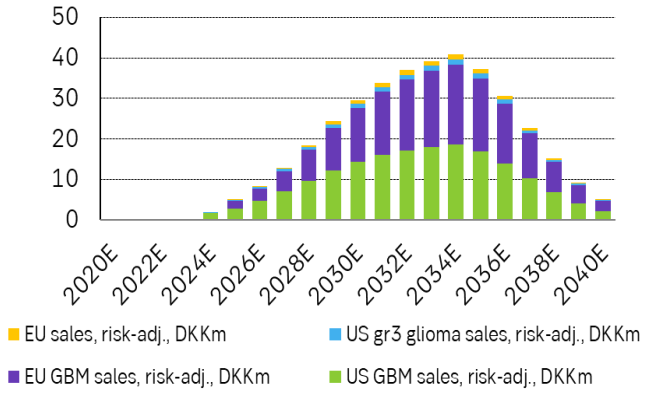
Source: 2019 EvaluatePharma Orphan Drug Report; SEB

Market size and sales projections for orphan drugs

The total global market for orphan drugs is estimated at USD 136bn in 2019 and projected to grow to USD 242bn by 2024 (CAGR of 12.2%), according to EvaluatePharma. This is more than double the rate predicted for conventional drugs. Although the subject of drug prices has garnered significant US media attention in recent years, we believe that even if some mechanism to limit pricing were to be taken seriously as part of a political platform, the current state of US politics renders it unlikely to pass over the medium-term. We note that several of the bestselling orphan drugs are within oncology.

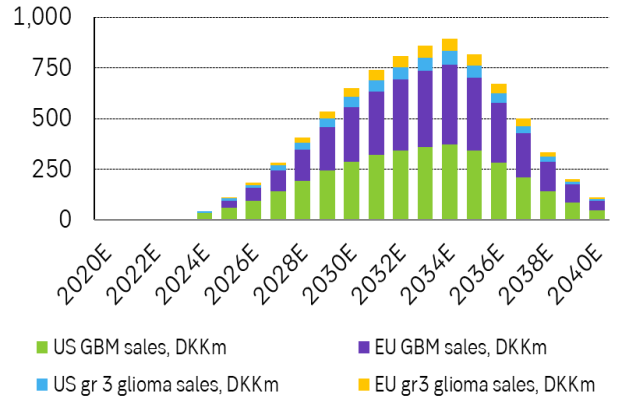
Market potential and forecasts

FG001 sales for high-grade glioma, risk-adj.



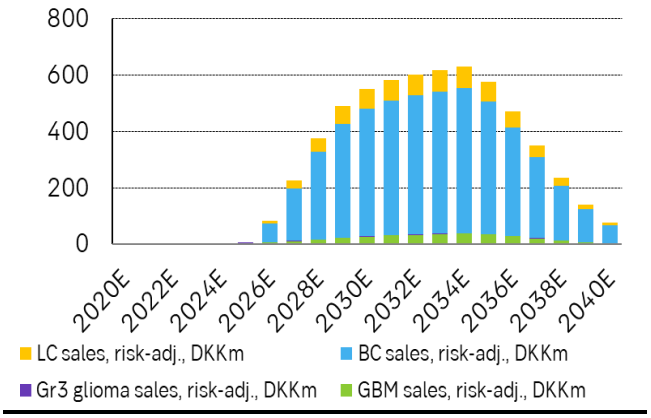
Source: SEB

FG001 sales for high-grade glioma, de-risked



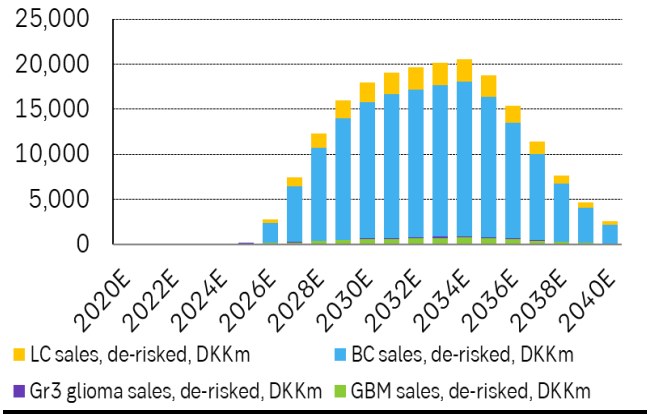
Source: SEB

FG001 sales by cancer type, risk-adj.



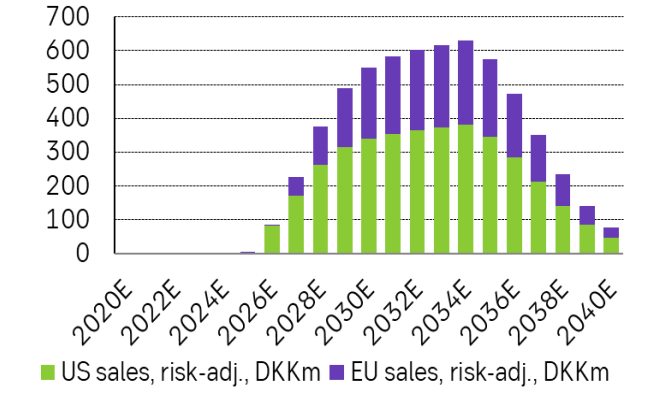
Source: SEB

FG001 sales by cancer type, de-risked



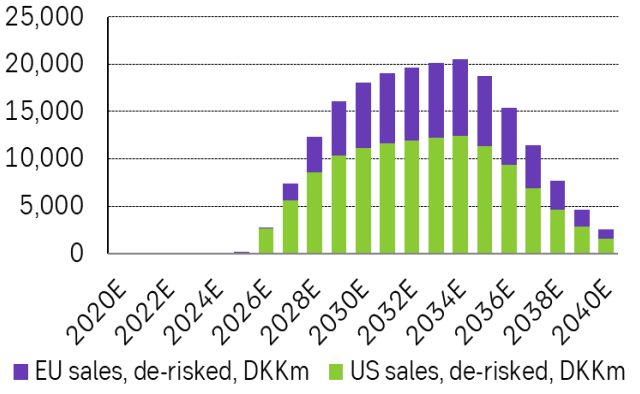
Source: SEB

FG001 sales by region, risk-adj.



Source: SEB

FG001 sales by region, de-risked



Source: SEB

FG001 sales forecast by region and cancer type, risk-adj. and de-risked, 2020-2034

(DKKm)	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E
US sales, de-risked	0	0	0	0	40	68	2,642	5,599	8,531	10,253	11,073	11,515	11,825	12,093	12,349
EU sales, de-risked	0	0	0	0	0	43	73	1,763	3,707	5,639	6,782	7,337	7,640	7,853	8,036
US sales, risk-adj.	0	0	0	0	2	3	85	178	272	327	353	368	378	386	395
EU sales, risk-adj.	0	0	0	0	0	2	3	56	118	179	215	233	243	250	256
GBM, de-risked	0	0	0	0	34	95	155	241	344	453	550	628	686	729	761
Gr3 glioma, de-risked	0	0	0	0	6	16	26	41	58	76	93	106	115	122	128
BC, de-risked	0	0	0	0	0	0	2,161	6,116	10,258	13,351	14,978	15,772	16,250	16,627	16,976
LC, de-risked	0	0	0	0	0	0	372	965	1,578	2,012	2,235	2,345	2,414	2,469	2,520
Total, de-risked	0	0	0	0	40	111	2,714	7,362	12,239	15,891	17,855	18,852	19,465	19,946	20,385
GBM, risk-adj.	0	0	0	0	2	5	8	12	17	23	28	31	34	36	38
Gr3 glioma, risk-adj.	0	0	0	0	0	0	1	1	1	2	2	2	2	2	3
BC, risk-adj.	0	0	0	0	0	0	65	183	308	401	449	473	487	499	509
LC, risk-adj.	0	0	0	0	0	0	15	39	63	80	89	94	97	99	101
Total, risk-adj.	0	0	0	0	2	5	88	235	389	505	568	601	621	636	651

Source: SEB

Risk-adj. peak sales sensitivity to peak market penetration and price

DKKm		Price in the EU (top)/US (bottom)						
		1,625	3,250	4,875	6,500	8,125	9,750	11,375
		2,500	5,000	7,500	10,000	12,500	15,000	17,500
Change in peak penetration for all indications (in percentage points)	-15.0%	103	207	310	413	517	620	723
	-10.0%	123	246	369	492	615	739	862
	-5.0%	143	286	429	572	714	857	1000
	0.0%	163	325	488	651	813	976	1139
	5.0%	182	365	547	730	912	1095	1277
	10.0%	202	405	607	809	1011	1214	1416
	15.0%	222	444	666	888	1110	1332	1554

Source: SEB

Risk-adj. peak sales sensitivity to peak market penetration and *P*(approval)

DKKm		Change in peak penetration for all indications (in pp)						
		-15.0%	-10.0%	-5.0%	0.0%	5.0%	10.0%	15.0%
Change in P(approval) for all indications (in pp)	-2.0%	156	185	214	243	272	301	330
	-1.0%	284	339	393	447	501	555	609
	0.0%	413	492	572	651	730	809	888
	1.0%	542	646	750	855	959	1063	1167
	2.0%	671	800	929	1058	1188	1317	1446
	3.0%	800	954	1108	1262	1416	1571	1725
	4.0%	929	1108	1287	1466	1645	1824	2004

Source: SEB

Growth drivers and risks

Drivers

Industry shift to near-infrared imaging
According to a report by Markets and Markets, the NIR imaging market is set to expand at a CAGR of 15% in 2017-2023, from USD 416m to USD 822m, driven by indocyanine green vascular imaging, and with North America the major revenue generating region throughout the forecast period. Major imaging systems manufacturers include Medtronic and Stryker.

Superior product attributes and outcomes
As described above, and although it has yet to be clinically demonstrated, we see several reasons to think that FG001 could be superior to 5-ALA, including that it targets uPAR, which should render it more tumour or tumour margin-specific, and that it uses NIR emission rather than visible light emission, increasing the tumour-to-background ratio, as well as deeper tissue penetration, which opens the door to photodynamic therapy, potentially enabling more straightforward demonstration of survival benefit.

Risks

Reimbursement challenges: price pressure from cheaper alternatives
The ability to secure premium pricing is key to FG001's market potential. We see three principle factors which will determine the rate of reimbursement: (1) orphan drug status; (2) a demonstration of superior outcomes in FGS vs. 5-ALA; and (3) successful demonstration of its utility for photodynamic therapy. We addressed the importance of orphan drug designation above. Demonstrating superiority over 5-ALA is essential, because 5-ALA is sold for around USD 2,500 in the US and EUR 1,000 in Europe, whereas we believe that FluoGuide intends to seek more premium pricing, of around USD 10,000, for FG001, and payers will balk at paying up without a clear benefit. While this, together with orphan designation, may be sufficient for reimbursement for high-grade glioma, it may be more challenging in the far larger (non-orphan) breast and lung cancer markets; however, if FG001 proves amenable for use in photodynamic therapy, we believe reimbursement would be far easier, given that USD 10,000 is similar to the cost *per month* of targeted pharmaceuticals.

Imaging systems are not in routine use for resection of all types of cancer
Although already widely used for Glioblastoma and certain other cancers, FGS is not yet in routine use in breast cancer surgery. This means that a rollout of FG001 as a contrast agent in breast cancer surgery would require simultaneous rollout of compatible imaging equipment. Three prerequisites for successful adoption are that it should meaningfully improve outcomes without disrupting normal workflow, and do so on a cost-neutral basis (at least in terms of the overall economic burden). In our view, FGS with FG001 has that potential, because it is intended for real-time operative imaging and could limit time in the operating room by facilitating discrimination between normal and malignant tissue, as well as potentially reducing the need for subsequent therapy.

Cost drivers

Manufacturing strategy
FG001 is a peptide-conjugated fluorophore, but small enough to qualify comfortably as a small molecule. Accordingly, we assume operating manufacturing costs to be relatively low. FluoGuide has contracted a CDMO to manufacture FG001. This has the advantage of keeping capex low but increases COGS. Therefore, we assume a 90% gross margin.

Go-to-market strategy
Management has stated that it plans to take FG001 to market directly for glioblastoma, given that it only needs a small sales force of about 10 sales reps in the US for this orphan disease. Management has stated that it intends to explore distribution agreements for the other indications, but as we do not know the terms of such agreements, nor whether they will be realised, we have assumed that FluoGuide will market FG001 itself for all indications, on which basis we assume SG&A costs of 25% of sales.

R&D: maximising the uPAR opportunity
FG001 is something of a pipeline-in-a-product, given that it has the potential to target a variety of cancers, and we note that management has expressed the desire to develop several uPAR-targeting agents. Therefore, we have assumed costs to fund expansion of the clinical program beyond glioblastoma, as well as for photodynamic therapy.

Forecast assumptions

List of forecast assumptions

	Glioblastoma		Grade III glioma		Breast, resectable		Lung, resectable	
	US	EU	US	EU	US	EU	US	EU
No. pts	10,470	16,814	2,094	3,363	279,100	312,200	228,820	280,980
Popn. g rate, %	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Share of pts w. uPAR	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Share of pts on surgery	58.0%	50.0%	42.5%	40.0%	87.0%	81.0%	25.0%	14.0%
Avg. no. procedures	1.2	1.2	1.2	1.2	1.2	1.2	1.03	1.03
Launch year	2024	2025	2024	2025	2026	2027	2026	2027
Peak year	2034	2034	2034	2034	2034	2034	2034	2034
Peak penetration, %	70%	70%	70%	70%	40%	40%	40%	40%
P approval	5%	5%	2%	2%	3%	3%	4%	4%
	USD	USD	USD	USD	USD	USD	USD	USD
Price	10,000	6,500	10,000	6,500	10,000	6,500	10,000	6,500
Price CAGR	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
USDDKK	6.2000							

Source: SEB

Number of patients

Glioblastoma, a.k.a. grade 4 glioma

We base our patient population for Glioblastoma in the US on the review of Quinn T. Ostrom and colleagues of the descriptive epidemiology of primary brain and central nervous system (CNS) tumours in the US population for the diagnosis years 2006-2010. According to the analysis, the incidence rate per 100,000 was 3.19 and by applying this to the current US population, the annual diagnosed Glioblastoma patients are 10,470, we estimate. For Europe, we have used an incidence rate in 100,00 of 3.65, derived from incidence rates in England (4.60), France (4.01), Spain (2.99) and Germany (3.46). The incidence rates in France, Germany and Spain are derived from incidences in 2017 (Research and Markets, 2020), and the incidence rate in England is based on glioblastoma in England between 2007-2011 (Public Health England, 2016).

Grade 3 glioma

Given that 5-ALA is used in patients with grade III Glioma, and that surgery is a primary treatment modality, we argue that those patients are likely to benefit from FluoGuide's FG001. According to Rasmussen and colleagues, which reviewed grades and types of gliomas in the DNOR database in the period 2009-2014, the grade III glioma share was 14% of the total glioma population (n=1,930) and 20% of the glioblastoma population. By following that logic, we arrive at a total number of grade III glioma patients of 7,461 in the US and Europe (Rasmussen et al., 2017).

Breast cancer

According to the NCCN, 279,100 individuals will be diagnosed with breast cancer in the US in 2020. For Europe, we have used incidence rates for Central and Eastern Europe, Northern Europe, Southern Europe and Western Europe according to International Agency for Research on Cancer (WHO). Based on data from Globocan, 2018, we note that new cases in breast cancer were 522,513, which yields an implied incidence rate in 100,000 of 70. By applying this to our population for Europe, which is the EU, we estimate new cases of 312,200 per year.

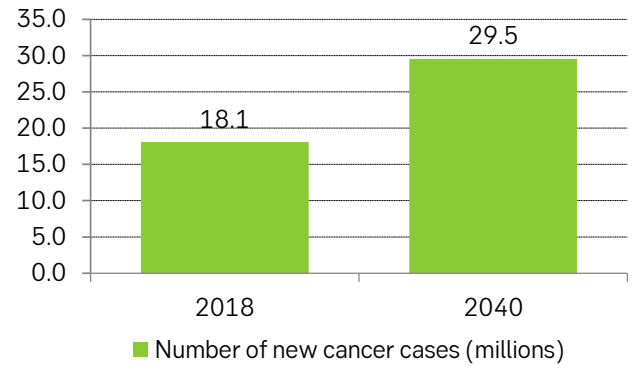
Lung cancer

For lung cancer, NCCN estimates that 228,820 new cases will occur in the US in 2020. For Europe, our incidence rate of 63 in 100,000 is again based on data from Globocan, 2018 and derived in the same way as for breast cancer, implying 280,980 new cases.

Patient population growth rate

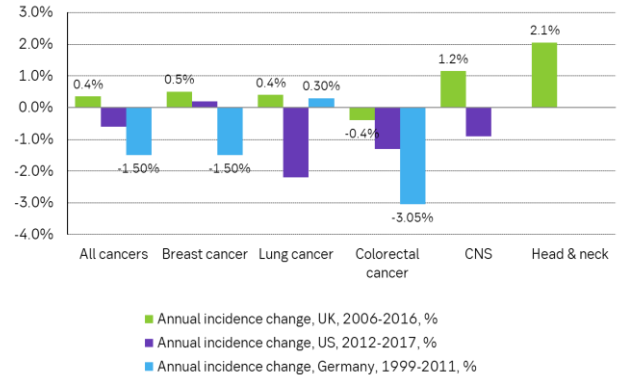
We have left the patient population growth rate at 0%, reflecting the balance of several trends. Firstly, long-term growth expectations for the general population in Europe and the US have slowed to less than 1% according to government census forecasts. Secondly, although worldwide cancer incidence is increasing, it is relatively stable or declining in Europe and the US.

Cancer incidence worldwide is increasing...



Source: WHO IARC, SEB

...but US and EU cancer incidence rate trends largely flat



Source: SEER;CancerResearch UK; Quante et al., 2016. Cancer Med 5(9):2649-56; SEB

Thirdly, as more targeted pharmaceuticals come to market, the need for surgery may be decreasing for some cancers, but it is difficult to find data on trends in surgical resection rates. Two studies that did report rates over time, for head and neck cancer[25] and NSCLC[26] showed modest declines in the rate of resection. Resection rates could start to increase, however, if photodynamic therapy following FGS proves successful at improving outcomes.

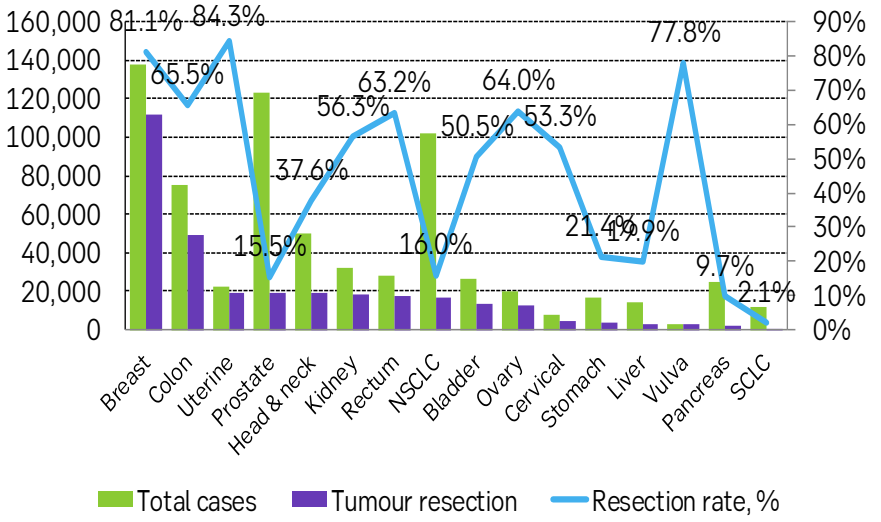
Treatment algorithm

uPAR

uPAR appears to be broadly expressed in high-grade glioma, lung cancer (particularly the tumour margins, at least in NSCLC), and in the stroma around breast cancer tumours, based on histological analysis[27]. The published literature is limited to only a small number of tumour samples, so given that it was unclear how closely associated uPAR is with these tumours, we contacted researchers at a glioblastoma biobank in Uppsala, who told us that 23 of the 24 glioblastoma samples they have express *PLAUR*, the gene encoding uPAR. With such a high frequency of expression (>95%), we think FG001 could be used without testing for uPAR in advance, once established in routine clinical practice.

[25] Schlichting et al., 2019 Cancer Causes Control 30(7):721-32
[26] Kaniski et al., 2017. Lung Cancer 103:66-74
[27] Pyke et al., 1993. Cancer Res 53:1911-5; Nielsen et al., 2007. Int J Cancer 120(10):2086-95; Morita et al., 1998. Int J Cancer 78:286-92

UK cases, no. resections, and resection rate for primary tumours, by cancer type

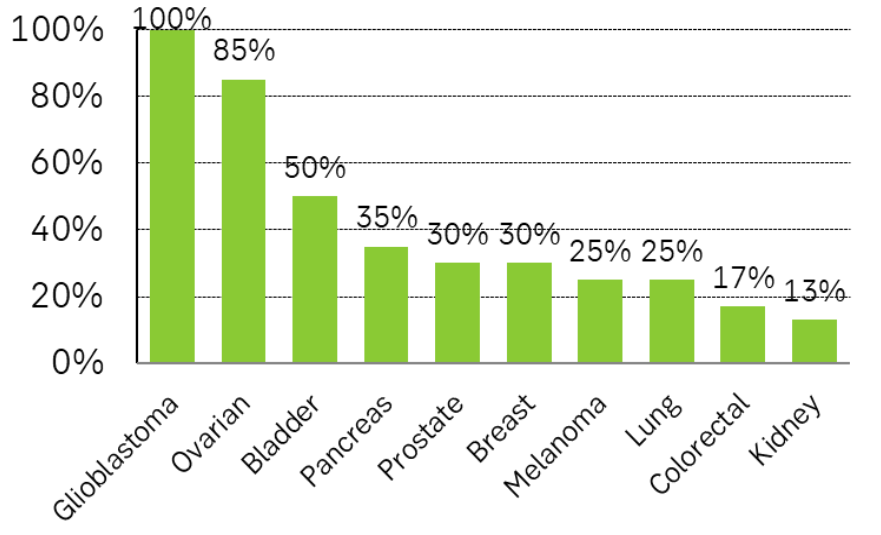


Source: NCRAS (ncin.org.uk); SEB

Resection rates for primary tumours

The gross and partial resection rates for glioblastoma and grade 3 glioma in the US are 58.2% and 42.5%, respectively, according to analysis of data from the SEER database[28]. Because surgeons in the US tend to be more aggressive than their European counterparts, we have assumed 50% and 40% rates for these respective cancer populations in Europe. The UK has an 81% resection rate. For lung cancer, data from the SEER database indicate a stable resection rate of 25% across all lung cancers[29], whereas the UK had a 14% rate across both NSCLC and SCLC.

Recurrence rate by tumour type



Source: FluoGuide; SEB

[28] Dong et al., 2016. Neuro-oncology Practice 3(1):29-38
[29] Lu et al., 2019. Cancer Management Res 11:943-53

Recurrence rate and multiple resections

Recurrent GBM has reoperation rates ranging from 3-30%[30], although we have found case series with reoperation rates of up to 50%, such as a Belgian single-centre retrospective analysis of 132 patients which reported that c. 50% had at least two resections[31]. Accordingly, we assume a 20% reoperation rate for GBM. For breast cancer, the rate of reoperation in the US[32] and UK[33] is 20% after breast-conserving surgery, whereas a French 10,761 patient, single centre retrospective analysis reported a 29% reoperation rate[34]. Reports of lung cancer reoperation rates were harder to find. One Italian retrospective reported a 2.5% reoperation rate for bronchogenic carcinoma[35].

Product life cycle

Given the development timeline set forth by management, we assume that FG001 will be launched in 2024 in high-grade glioma, and in 2026 in breast and lung cancer. Based on both patent life and orphan designation, we assume generic erosion will begin after 2034.

Peak market penetration

As the sole approved drug for FGS in glioblastoma, 5-ALA is the market leader, but if FG001 proves superior, it would become market leader, with only limited competition, and we therefore assume 70% peak penetration in GBM. For grade 3 glioma, we assume the same peak penetration, on the condition that FG001 is able to penetrate the blood-brain barrier. Because the competition is more intense in other cancers, including breast and lung cancer, we have assumed a 40% peak penetration of these markets, on the basis of a potential clinical profile that would position FG001 to be market leader. Because the clinical program is currently focused on bringing FG001 to market by the path of least resistance, and given the premium pricing we assume, we expect penetration of the high-grade glioma market to be slow, but assuming that a trial has demonstrated utility in photodynamic therapy by or around the time FG001 has launched in other cancers, ramp-up should be faster.

Pricing

The list price of 5-ALA in Ontario is CAD 2,265 per vial. EUR 980 in Spain in 2012[36], GBP 1,016 in the UK in 2016, AUD 3,990 in Australia in 2016, and CAD 2,265 in Canada in 2019. However, management believes that, by demonstrating superiority over 5-ALA, and potentially utility in photodynamic therapy, that it can motivate substantially higher reimbursement for FG001, which makes sense to us. We assume price per treated patient of USD 10,000 in the US and USD 6,500 in Europe.

[30] Robin & Kalkanis, 2017. Neurosurg Clin N Am 28:407-28
[31] Djamel-Eddine et al., 2019. Interdisc Neurosurg 18
[32] Landercasper et al., 2019. Annals Surg Oncol 26:3321-36
[33] Jeevan et al., 2012. BMJ 345:e4505
[34] Houvenaeghel et al., 2019. Cancer Manag Res 11:2507-16
[35] Voltolini et al., 2000. Eur J Cardio-Thor Surg 18(5):529-34
[36] Ontario Health 2020. Ontario Health Technology Assessment Series 20(9):1-92. PMID 32194883

Likelihood of approval

FluoGuide is an early stage biotech company that only recently entered clinical development. Based on typical pharmaceutical attrition rates, drugs that have yet to be tested in humans have modest odds of being approved, as both safety and efficacy are unproven. Therefore, we assume a 5% likelihood of approval for GBM, for which FluoGuide has been tested in xenograft models. Because the blood-brain barrier is disrupted in GBM, but intact in grade 3 glioma, it may not be possible for FG001 to bind uPAR and illuminate malignant tissue in the brains of patients with grade 3 gliomas, and we therefore assume a 2% probability of approval. Because uPAR expression in lung and breast cancer is established, we think the odds of approval are slightly better than in grade 3 glioma, but because we have yet to see preclinical or clinical data for either, we assume only a 3% probability of approval. The demonstration of clinical safety in the present phase 1/2 trial should trigger modest de-risking for breast and lung cancer, but until we start to see efficacy data for those diseases, we consider the upside from those opportunities to be limited.

Estimates

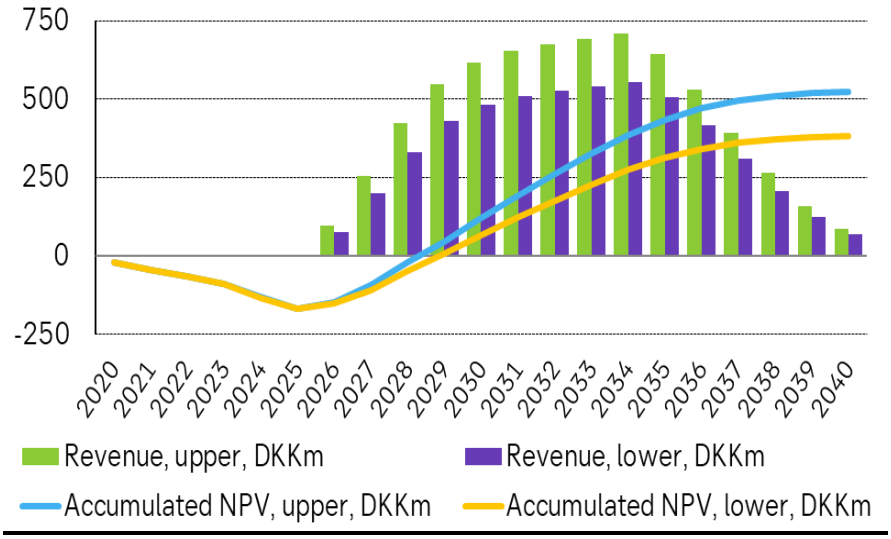
Detailed estimates

(DKK '000)	Q1/19	Q2/19	Q3/19	Q4/19	Q1/20	Q2/20	Q3/20	Q4/20E	2018	2019	2020E	2021E	2022E
Revenue	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Other operating income	0	0	0	100	150	0	1,019	0	0	100	1,169	0	0
Other operating expense	-74	-792	-4,657	-3,255	-3,543	-5,543	-3,230	-5,900	-52	-8,880	-18,216	-33,000	-45,000
Staff expense	-368	-552	-400	-545	-530	-1,040	-912	-1,200	0	-1,864	-3,682	-5,000	-6,000
EBIT	**-442**	**-1,343**	**-5,057**	**-3,700**	**-3,923**	**-6,583**	**-3,123**	**-7,100**	**-52**	**-10,644**	**-20,729**	**-38,000**	**-51,000**
EBIT margin, %	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*
Net financials	-511	-506	-48	-99	45	-23	-10	0	-1	-1,062	12	0	0
Tax	0	310	1,058	685	790	1,030	834	1,562	0	2,053	4,216	8,360	11,220
Net income	-953	-1,540	-4,047	-3,113	-3,088	-5,576	-2,299	-5,538	-53	-9,653	-16,501	-29,640	-39,780
Net margin, %	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*
EPS					**-0.38**	**-0.55**	**-0.22**	**-0.53**	**-0.08**	**-1.49**	**-1.65**	**-2.73**	**-3.17**

Source: SEB; FluoGuide

Valuation framework

Summary of valuation framework



Source: SEB

Risk-adjusted net present value (rNPV)

We arrive at our valuation range for FG001 by using a risk-adjusted net present value (rNPV) of future cash flows based on an explicit sales forecast for FG001 from the expected launch in 2024 until 2034 peak, as well as a generic erosion phase until 2041. Our valuation range encompasses a forecasted market penetration range with a midpoint of 70% for gliomas and 40% for resectable breast and resectable lung cancer operations, +/-5%, and a USD 10,000 price per procedure in the US, and an EU price of USD 6,500, or 65% of the US price.

rNPV range DKK 42-57 p.s.: sensitivity to price and market penetration

DKK		Price in the EU (top)/US (bottom)						
		1,625	3,250	4,875	6,500	8,125	9,750	11,375
		2,500	5,000	7,500	10,000	12,500	15,000	17,500
Change in peak penetration for all indications (in percentage points)	-15.0%	0	5	16	26	37	47	56
	-10.0%	0	9	22	33	46	58	70
	-5.0%	0	13	27	42	56	69	83
	0.0%	1	17	33	50	65	81	99
	5.0%	3	21	40	57	75	92	112
	10.0%	5	25	45	65	84	106	126
	15.0%	7	29	51	72	93	118	139

Source: xxx

Risk-adjustment based on probability of approval, *P*(approval)

We apply a 10% WACC to our FCF forecast, which we apply to all of our pre-commercial biotech coverage. Beyond that, as we wrote in the assumptions section, we apply a risk-adjustment of 2-5%, depending on indication, based on what we consider strong, promising preclinical data, but no clinical data as of publication date. The demonstration of clinical safety in the present phase 1/2 trial should trigger de-risking, on a modest basis relative to fully de-risked potential, but a very meaningful one, given our present risk-adjustment. However, until we start to see efficacy data from lung cancer and breast cancer diseases, we consider the upside from those opportunities to be limited, as compared to glioblastoma.

Appendix

Shareholder structure

Around 40% of FluoGuide's ownership is concentrated in the top three shareholders. Life Science IVS (controlled by FluoGuide's board member and Head of Scientific Advisory Board Andreas Kjaer) remains the single largest shareholder (20.2%), followed by Wexotec ApS (controlled by FluoGuide's Chief Executive Officer Morten Albrechtsen) holding 14.1% of votes and capital. Other major shareholders include Linc AB, holding 6.8% of shares in FluoGuide.

Shareholder structure (as of 30 June 2020)

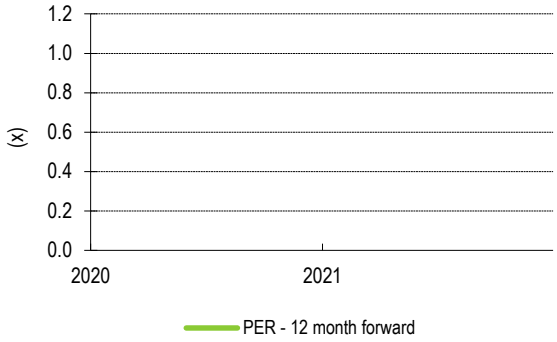
	Number of shares	Votes and capital (%)
Main shareholders		
Life Science IVS	2,124,891	20.2%
Wexotec ApS	1,487,394	14.1%
Linc AB	718,500	6.8%
Management and Board		
Grethe Nörskov Rasmussen	373,185	3.5%
Arne Ferstad	254,218	2.4%
PME Holding ApS (Peter Mörch Eriksen)	131,297	1.2%
Micaela Sjökvist	57,678	0.5%
Shomit Ghose	39,810	0.4%
Others	**5,343,053**	**50.7%**

Source: FluoGuide, SEB

Overview

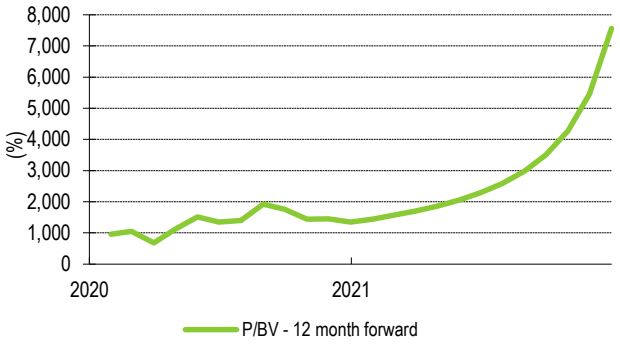
Investment considerations	In our view, FG001 targets an attractive market niche and the GBM market potential is large with an unmet need for discriminating surgical guiding imaging agents. Because uPAR is also expressed in other cancer types, FG001 holds the potential to expand to other solid tumours, such as breast cancer and lung cancer. With a direct and comparatively short path to market, including phase I/IIa and phase IIb/III clinical trials, FG001 may attain market approval already by 2023/24.
Company profile	FluoGuide was founded and incorporated in 2018 following years of extensive research within molecular imaging with PET, PET/MRI, and optical imaging, as well as targeted radionuclide therapies (theranostics) in cancer. FluoGuide develops surgical solutions that are expected to reduce suffering for the patient, increase the likelihood of cure as well as reduce costs for the health care system. The lead candidate, FG001, is a uPAR targeted guidance of cancer surgery, which has pre-clinical results for GBM. FluoGuide owns a patent family that protects FG001, and that has been issued in the US and Europe. The patents do not expire until 2034, providing a long period of protection from generic competition.
Valuation approach	We value FluoGuide using a NPV-based valuation, in which forecasts are risk-adjusted to reflect uncertainties regarding the outcome from various regulatory authorities.
Investment risks	Results from clinical studies may disappoint and lower the marketing potential of FG001 and clinical studies may be delayed. Currently ongoing and planned future clinical studies will entail significant costs for FluoGuide and acquisition of new capital may be needed. Failure to secure premium pricing, falling rate of surgical resection and decreasing routine use of imaging systems are all factors that may lower the market potential for FG001.

PER - 12 month forward



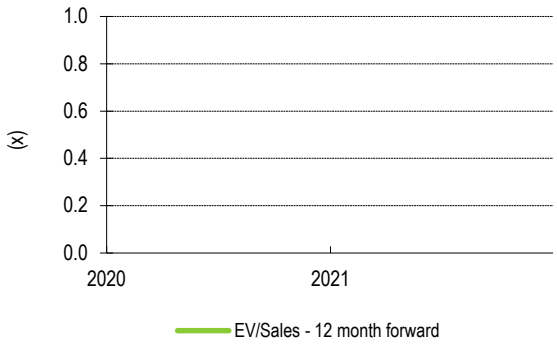
Source: SEB

P/BV - 12 month forward



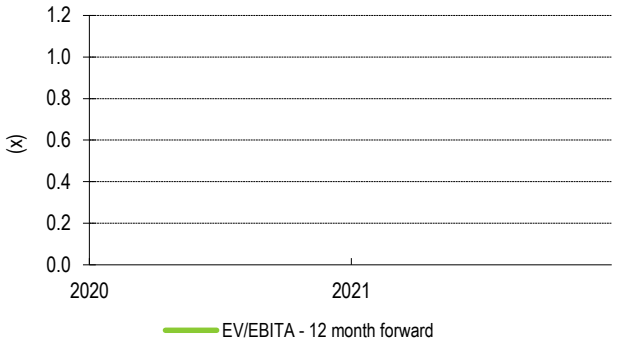
Source: SEB

EV/Sales - 12 month forward



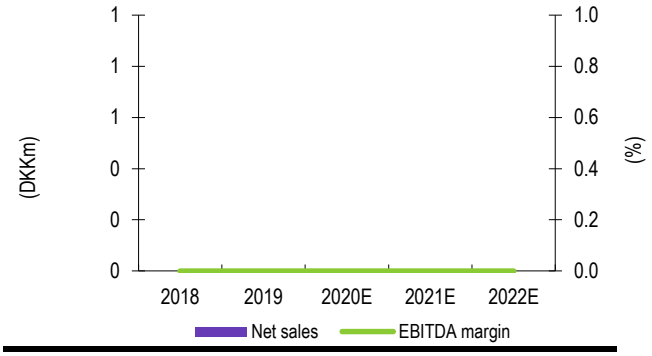
Source: SEB

EV/EBITA - 12 month forward



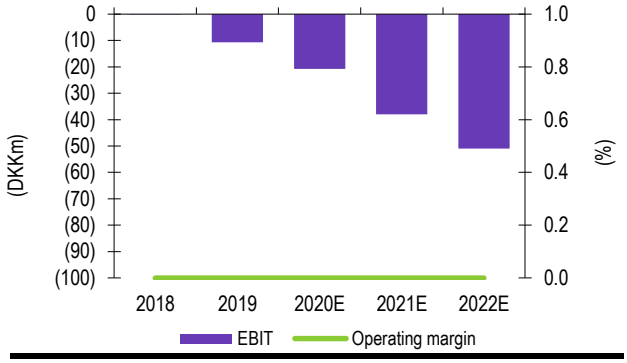
Source: SEB

Net sales & EBITDA margin



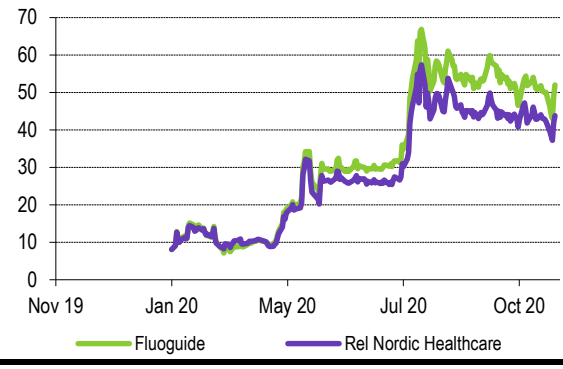
Source: SEB

EBIT & Operating margin



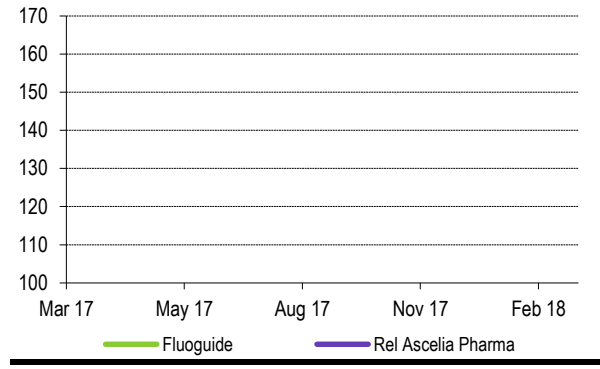
Source: SEB

Comparison with sector index - 1 year



Source: SIX

Comparison with Ascelia Pharma - 1 year



Source: SIX

Profit & loss statement - Fluoguide					
(DKKm)	**2018**	**2019**	**2020E**	**2021E**	**2022E**
Net Sales	0	0	0	0	0
Other revenues	0	0	1	0	0
Total revenues	**0**	**0**	**1**	**0**	**0**
Total expenses	(0)	(11)	(22)	(38)	(51)
Profit before depreciation	**(0)**	**(11)**	**(21)**	**(38)**	**(51)**
Depreciation - Fixed assets	0	0	0	0	0
Depreciation - Other assets	0	0	0	0	0
Amortisation - Goodwill	0	0	0	0	0
Amortisation - Other intangibles	0	0	0	0	0
Operating profit	**(0)**	**(11)**	**(21)**	**(38)**	**(51)**
Net interest expenses	0	0	0	0	0
Foreign exchange items	0	0	0	0	0
Other financial items	(0)	(1)	0	0	0
Value changes - Fixed assets	0	0	0	0	0
Value changes - Financial assets	0	0	0	0	0
Value changes - Other assets	0	0	0	0	0
Reported pre-tax profit	**(0)**	**(12)**	**(21)**	**(38)**	**(51)**
Minority interests	0	0	0	0	0
Total taxes	0	2	4	8	11
Reported profit after tax	**(0)**	**(10)**	**(17)**	**(30)**	**(40)**
Discontinued operations	0	0	0	0	0
Extraordinary items	0	0	0	0	0
Net Profit	**(0)**	**(10)**	**(17)**	**(30)**	**(40)**
Adjustments:					
Discontinued operations	0	0	0	0	0
Interest on convertible debt	0	0	0	0	0
Minority interests (IFRS)	0	0	0	0	0
Value changes	0	0	0	0	0
Goodwill/intangibles amortisations	0	0	0	0	0
Restructuring charges	0	0	0	0	0
Other adjustments	0	0	0	0	0
Tax effect of adjustments	0	0	0	0	0
Adjusted profit after tax	**(0)**	**(10)**	**(17)**	**(30)**	**(40)**
Margins, tax & returns					
Operating margin	0.0	0.0	0.0	0.0	0.0
Pre-tax margin	0.0	0.0	0.0	0.0	0.0
Tax rate	0.0	17.5	20.4	22.0	22.0
ROE	n.m.	n.m.	n.m.	n.m.	n.m.
ROCE	n.m.	n.m.	n.m.	n.m.	n.m.
Growth rates y-o-y (%)					
Total revenues	n.a.	n.a.	1,069.0	(100.0)	n.a.
Operating profit	n.m.	n.m.	n.m.	n.m.	n.m.
Pre-tax profit	n.m.	n.m.	n.m.	n.m.	n.m.
EPS (adjusted)	0.0	0.0	0.0	0.0	0.0

Cash flow					
(DKKm)	**2018**	**2019**	**2020E**	**2021E**	**2022E**
Net profit	(0)	(10)	(17)	(30)	(40)
Non-cash adjustments	0	(1)	12	4	5
Cash flow before work cap	**(0)**	**(11)**	**(4)**	**(25)**	**(35)**
Ch. in working capital / Other	0	0	2	0	0
Operating cash flow	**(0)**	**(11)**	**(3)**	**(25)**	**(35)**
Capital expenditures	0	0	0	0	0
Asset disposals	0	0	0	0	0
L/T financial investments	0	0	0	0	0
Acquisitions / adjustments	0	0	0	0	0
Free cash flow	**(0)**	**(10)**	**(3)**	**(25)**	**(35)**
Net loan proceeds	0	5	0	0	0
Dividend paid	0	0	0	0	0
Share issue	0	11	18	72	0
Other	(0)	(2)	0	0	0
Net change in cash	**0**	**3**	**15**	**47**	**(35)**
Adjustments					
C/flow bef chng in work cap	(0)	(11)	(4)	(25)	(35)
Adjustments	0	0	0	0	0
Int on conv debt net of tax	0	0	0	0	0
Cash earnings	(0)	(11)	(4)	(25)	(35)
Per share information					
Cash earnings	(0.01)	(1.66)	(0.45)	(2.34)	(2.78)
Operating cash flow	0.0	(1.63)	(0.26)	(2.34)	(2.78)
Free cash flow	0.0	(1.57)	(0.26)	(2.34)	(2.78)
Investment cover					
Capex/sales (%)	0.0	0.0	0.0	0.0	0.0
Capex/depreciation (%)	0	0	0	0	0

Source for all data on this page: SEB

Balance sheet - Fluoguide					
(DKKm)	**2018**	**2019**	**2020E**	**2021E**	**2022E**
Cash and liquid assets	0	2	18	64	29
Debtors	0	2	0	0	0
Inventories	0	0	0	0	0
Other	0	0	0	0	0
Current assets	**0**	**5**	**18**	**64**	**29**
Interest bearing fixed assets	0	0	0	0	0
Other financial assets	0	0	0	0	0
Capitalized development cost	0	0	0	0	0
Goodwill	0	0	0	0	0
Other intangibles	0	0	0	0	0
Fixed tangible assets	0	0	0	0	0
Other fixed assets	0	0	0	0	0
Fixed assets	**0**	**0**	**0**	**0**	**0**
Total assets	**0**	**5**	**18**	**65**	**30**
Creditors	0	1	0	0	0
Other trade financing	0	0	0	0	0
S/T interest bearing debt	0	0	0	0	0
Other	0	0	0	0	0
Current liabilities	**0**	**1**	**0**	**0**	**0**
L/T interest bearing debt	0	0	0	0	0
Other long-term liabilities	0	0	0	0	0
Convertible debt	0	0	0	0	0
Pension provisions	0	0	0	0	0
Other provisions	0	0	12	16	21
Deferred tax	0	0	0	0	0
Long term liabilities	**0**	**0**	**12**	**16**	**21**
Minority interests	0	0	0	0	0
Shareholders' equity	**0**	**5**	**6**	**48**	**9**
Total liabilities and equity	**0**	**5**	**18**	**65**	**30**
Net debt (m)	(0)	(2)	(18)	(64)	(29)
Working capital (m)	(0)	2	0	0	0
Capital employed (m)	0	5	6	48	9
Net debt/equity (%)	(843)	(52)	(293)	(133)	(342)
Net debt/EBITDA (x)	(0.0)	(0.0)	0.9	1.7	0.6
Equity/total assets (%)	9	87	33	75	29
Interest cover	0.0	0.0	0.0	0.0	0.0

Valuation					
(DKK)	**2018**	**2019**	**2020E**	**2021E**	**2022E**
No of shares, fully dil. (y/e)	5.0	7.2	10.5	12.5	12.5
No of shares, fully dil. avg.	5.0	6.5	10.0	10.9	12.5
Share price, y/e			52.0	52.0	52.0
Share price, high			73.4		
Share price, low			6.0		
Share price, avg			33.8		
EPS (reported)	(0.01)	(1.49)	(1.65)	(2.73)	(3.17)
EPS (adjusted)	(0.01)	(1.49)	(1.65)	(2.73)	(3.17)
Cash earnings/share	(0.01)	(1.66)	(0.45)	(2.34)	(2.78)
Dividend/share	0.00	0.00	0.00	0.00	0.00
Enterprise value/share			50	47	50
Book value/share	0.0	0.6	0.6	3.9	0.7
Adjusted equity/share	0.0	0.6	0.6	3.9	0.7
PER (adjusted)			n.m.	n.m.	n.m.
CEM			(116.7)	(22.2)	(18.7)
Dividend yield			0.0	0.0	0.0
EV/EBITDA			(25.6)	(15.5)	(12.2)
EV/EBITA			(25.6)	(15.5)	(12.2)
EV/EBIT			(25.6)	(15.5)	(12.2)
EV/Sales (x)			0.00	0.00	0.00
Price/Book value			90.70	13.46	75.61
Price/adjusted equity			90.70	13.46	75.61
Free cash flow/Market cap (%)			(0.5)	(4.5)	(5.3)
Operating cash flow/EV (%)			n.a.	n.a.	n.a.
EV/Capital employed (x)			0.0	0.0	0.0

Main shareholders				Management		Company information	
Name	**(%)**	**Votes**	**Capital**	**Title**	**Name**	**Contact**	
Andreas Kjaer		20.2	20.2	COB	Arne Ferstad	Internet	www.fluoguide.com
Morten Albrechtsen		14.2	14.2	CEO	Morten Albrechtsen	Phone number	+45 31 22 66 60
Bengt Julander		6.8	6.8	CFO	Henrik Moltke		
				IR			

Source for all data on this page: SEB

About this publication
This report is a marketing communication commissioned by Fluoguide and prepared by Skandinaviska Enskilda Banken AB (publ). It does not constitute investment research; as such, it has not been prepared in accordance with the legal requirements to promote the independence of investment research, nor is it subject to any prohibition on dealing ahead of the dissemination of investment research.

This statement affects your rights
This report is confidential and may not be reproduced, redistributed or republished by any recipient for any purpose or to any person. Redistributing this report to third parties may invoke legal requirements on the person engaging in such activities.

Producers and Recipients
SEB Research is approved and issued by Skandinaviska Enskilda Banken AB (publ) ("SEB"), a bank organized under the laws of the Kingdom of Sweden, on behalf of itself and its affiliates for institutional investors. When SEB Research is issued by an SEB subsidiary, the subsidiary itself is subject to this disclaimer.

Use
This material has been prepared by SEB for information purposes only. It does not constitute investment advice and is being provided to you without regard to your investment objectives or circumstances. The document does not constitute an invitation or solicitation of an offer to subscribe for or purchase any securities and neither this document nor anything contained herein shall form the basis for any contract or commitment whatsoever. Opinions contained in the report represent the authors' present opinion only and may be subject to change. In the event that the authors' opinion should change, we shall endeavour (but do not undertake) to disseminate any such change, within the constraints of any regulations, applicable laws, internal procedures within SEB, or other circumstances.

Good faith and limitations
All information, including statements of fact, contained in this research report have been obtained and compiled in good faith from sources believed to be reliable. However, no representation or warranty, express or implied, is made by SEB with respect to the completeness or accuracy of its contents, and it is not to be relied upon as authoritative and should not be taken in substitution for the exercise of reasoned, independent judgement by you. Recipients are urged to base their investment decisions upon such investigations as they deem necessary. To the extent permitted by applicable law, no liability whatsoever is accepted by SEB for any direct or consequential loss arising from the use of this document or its contents.

Distribution
This research report has been prepared by SEB or its affiliates and is being distributed by SEB offices in Stockholm, Copenhagen, Oslo, Helsinki, Frankfurt, London, Tallinn, Vilnius and Riga. Research reports are prepared and distributed in Lithuania by AB SEB bankas and in Estonia by AS SEB Pank in accordance with the requirements of the local laws and Financial Supervision Authority's conduct of business rules. This document may not be distributed in the United States, Canada, Japan or Australia or in any other jurisdiction where to do so would be unlawful. Addresses and Phone numbers for each office can be found at the end of the report.

The SEB Group: members, memberships and regulators

SEB is a member of, inter alia, Nasdaq OMX Nordic, Oslo Stock Exchange, the London Stock Exchange, NYSE Euronext, SIX Swiss Exchange, Frankfurt Stock Exchange, Tallinn Stock Exchange as well as certain European MTF's such as BATS-Chi-X, Turquoise and Burgundy. SEB is regulated by Finansinspektionen in Sweden and, for the conduct of investment services business, in (i) Denmark by Finanstilsynet, (ii) Norway by Finanstilsynet, (iii) Finland by Finanssivalvonta, (iv) Germany by Bundesanstalt für Finanzdienstleistungsaufsicht, (v) the UK by the Financial Conduct Authority and Prudential Regulation Authority (details about the extent of our regulation by the Financial Conduct Authority and Prudential Regulation Authority are available from us on request), (vi) Estonia by the Estonian Financial Supervision Authority, (vii) Lithuania by the Bank of Lithuania, (viii) Latvia by the Financial and Capital Markets Commission and Futures Commission.

SEB's research reports are prepared in accordance with the industry standards and codes of conduct applicable to financial analysts in the countries where they are based. In Denmark, Finland, Norway and Sweden, analysts act in accordance with the rules of ethics of each country's Society of Financial Analysts. Analysts comply with the recommendations and industry standards of the Danish, Norwegian and the Swedish Securities Dealers Associations and with those of the Federation of Finnish Financial Services. Analysts certified by the CFA Institute also comply with the Code of Ethics of the CFA Institute.

Prevention and avoidance of conflicts of interest

The remuneration of staff within the Research department is determined exclusively by research management and senior management and may include discretionary awards based on the firm's total earnings, including investment banking and markets (sales and trading businesses) income; however, no such staff receive remuneration based upon specific investment banking or markets transactions. SEB's Compliance department monitors the production of research and the observance of the group's procedures designed to prevent any potential conflicts of interest from affecting the content of research; the latter are described in greater detail in the "Statement of Policies for dealing with potential conflicts of interest surrounding our Research activities" which is available on our SEB Research website.

Your attention is also drawn to the fact that:

The current market price of the securities shown in this report is the price prevailing at the close of the business day preceding the date of publication, save where such price was more than 5% different from the price prevailing as at the time of publication, in which case it is the latter.

Unless explicitly stated otherwise in this report, SEB expects (but does not undertake) to issue updates to this report following the publication of new figures or forecasts by the company covered, or upon the occurrence of other events which could potentially have a material effect on it.

The securities discussed in this research report may not be eligible for sale in all countries, and such securities may not be suitable for all types of investors. Offers and sales of securities discussed in this research report, and the distribution of this report, may be made only in countries where such securities are exempt from registration or qualification or have been so registered or qualified for offer and sale, and in accordance with applicable broker-dealer and agent/salesman registration or licensing requirements.A copy of this report, not including the recommendation, has been provided to the issuer prior to its dissemination to check factual statements for accuracy; as a result, some amendments have been made.

A full list of disclosures for other companies mentioned herein (in which SEB has research coverage), can be found on our SEB Research website

Methodology
Final consideration as to any valuations, projections and forecasts contained in this report are based on a number of assumptions and estimates and are subject to contingencies and uncertainties, and their inclusion in this report should not be regarded as a representation or warranty by or on behalf of the Group or any person or entity within the Group that they or their underlying assumptions and estimates will be met or realized. Different assumptions could result in materially different results. Past performance is not a reliable indicator of future performance. Foreign currency rates of exchange may adversely affect the value, price or income of any security or related investment mentioned in this report. In addition, investors in securities, such as ADRs, whose values are influenced by the currency of the underlying security, effectively assume currency risk.

Company specific disclosures and potential conflicts of interest
A member of, or an entity associated with, SEB or its affiliates, officers, directors, employees or shareholders of such members (a) is not, and has never been, represented on the board of directors or similar supervisory entity of Fluoguide, (b) has from time to time bought or sold the securities issued by the company or options relating to the company, and (c) SEB does not hold any short / long position exceeding 0.5% of the total issued share capital of Fluoguide as of 31 Oct 2020.

The analyst(s) responsible for this research report (jointly with their closely related persons) hold(s) 0 shares in Fluoguide and do(es) not have holdings in other instruments related to the company.

Copenhagen
Bernstorffsgade 50
P.O. Box 100
DK-1577 Copenhagen V

Telephone: (45) 3328 2828

Frankfurt
Stephanstrasse 14-16
D-60313 Frankfurt am Main

Telephone: (49) 69 9727 7740

Helsinki
Eteläesplanadi 18
P.O. Box 630
FIN-00101 Helsinki

Telephone: (358) 9 616 28700

London
One Carter Lane
London, EC4V 5AN

Telephone: (44) 20 7246 4000

Oslo
Filipstad Brygge 1,
P.O. Box 1363 Vika
NO-0113 Oslo

Telephone: (47) 2100 8500

Stockholm
Kungsträdgårdsgatan 8
S-106 40 Stockholm

Telephone: (46) 8 522 29500

Tallinn
Tornimäe 2
EE-Tallinn 15010

Telephone: (372) 665 7762