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Minimally invasive, less conspicuous OAB option

Stimguard set to study its tibial nerve OAB system against Medtronic's Interstim device

By Katie Pfaff, Staff Writer

Stimguard LLC will begin enrollment for a head-to-head study of its Chronic Affarent Nerve Stimulator (CAN-stim) against Medtronic plc's gold standard Interstim device in treatment of urgency urinary incontinence from over active bladder (OAB) not controlled by medication, following FDA approval of the trial with an investigational device exemption (IDE). Privately held Stimguard's device can be

See Stimguard, page 5

Inside

Aims for June U.S. launch

Senseonics heads into FDA panel for implantable CGM

By Stacy Lawrence, Staff Writer

More than 20 years and roughly $175 million later, Senseonics Holdings Inc. is now headed before the FDA. Its aim is to market a novel, implantable continuous glucose monitor (CGM), which transmits data to a smartphone app, in the U.S.

See Senseonics, page 6

Surgivisio raising $10-15M in series B to market its surgical navigation system

By Bernard Banga, Staff Writer

PARIS – Surgivisio SAS, of La Tronche, France, is finalizing fundraising of $10-15 million in series B for the European marketing launch of the first 3-D imaging solution to include surgical navigation in real time.

See Surgivisio, page 8

Ketamine discovery may yield fast-acting antidepressants

By John Fox, Staff Writer

HONG KONG – A Chinese study has shown for the first time that the powerful antidepressant effects of ketamine are due to blockade of rapid neuronal firing in the brain's lateral habenula (LHb) region. Such blockade was found to disinhibit reward centers and relieve depressive symptoms rapidly in animal models.

See Ketamine, page 10

Radiologists say time has come to grapple with promise of AI, big data

By Mark McCarty, Regulatory Editor

The twin tools of artificial intelligence and big data have proven more cumbersome than anticipated to apply to several fields of endeavor, but a new article in the *Journal of the American College of Radiology* says radiologists – and by implication,

See Radiology AI, page 7

Contextual's next-generation genome sequencing platform gets financial lift from HK

By David Godkin, Staff Writer

The cash couldn't have come at a better time. This is a period of growth for Vancouver, B.C.-based Contextual Genomics Inc., and the C$12 million commitment it received in late February from Hong Kong's Pacbridge Capital Partners Ltd. could be just the thing to further validate and build worldwide markets for the genomics company's sequencing platforms.

"This is absolutely transformational," Chief Information Officer and Contextual Genomics co-founder Sohrab Shah told *BioWorld MedTech*.

See Contextual Genomics, page 9

BioWorld MedTech's Neurology Extra

Production Editor Andrea Applegate on one of med-tech's key sectors

Read this week's edition

Appointments and advancements

Ime Technologies, based in Geldrop, The Netherlands, has appointed Judith Heikoop as managing director. Heikoop brings experience in executive roles and a background as a researcher in metabolic disease, human genetics and women's health. The company develops electro spin processes and equipment for the fabrication of medical implants such as heart valves, blood vessels, nerves, tendons, skin and bone. Its technology can mimic human extracellular matrix in nanometer format and thereby produce fibers for implants for the human body.

Financings

Franklin Lakes, N.J.-based **Becton, Dickinson and Co.** reported the results of its previously disclosed offer to repurchase any and all of its outstanding 3.00 percent notes due May 15, 2026, in accordance with the terms and conditions set forth in the offer to repurchase, dated Jan. 8, 2018. As of the expiration date at 5 p.m. on March 1, 2018, a total of $460,687,000 aggregate principal amount of notes were validly tendered and not validly withdrawn, representing approximately 98.04 percent of the total outstanding aggregate principal amount of notes. Pursuant to the terms of the offer, holders who validly tendered and did not validly withdraw their notes prior to the expiration date are entitled to receive cash equal to 101 percent of the principal amount thereof plus accrued and unpaid interest to the date of purchase, subject to the rights of holders of notes on the relevant record date to receive interest due on the relevant interest payment date, which is equivalent to $1,015.58 per $1,000 principal amount of notes tendered. The settlement date of the offer is expected to occur March 6, 2018.

Other news to note

Brooks Rehabilitation, of Jacksonville, Fla., reported its partnership with Japanese medical and social innovation company, **Cyberdyne Inc.**, to introduce and make available the world's first advanced robotic treatment device that has been shown to improve a patient's ability to walk. Individuals with spinal cord injuries can now access FDA-cleared HAL, which is short for Hybrid Assistive Limb, at the Brooks Cybernic Treatment Center in Florida. The treatment center is currently the only facility in the U.S. offering this treatment.

Royal Philips NV, of Amsterdam, and **Hologic Inc.**, of Marlborough, Mass., reported a global partnership agreement to offer care professionals integrated solutions comprising diagnostic imaging modalities, advanced informatics and services for screening, diagnosis and treatment of women. The collaboration combines Hologic's innovative mammography technologies and Philips' leading portfolio of ultrasound, MRI, CT, and X-ray systems, advanced informatics and broad range of services, including maintenance, upgrade, training and operational performance management services. The multiyear, non-exclusive global partnership agreement allows for customized regional implementation to best meet the individual needs of each customer. The financial details of the agreement were not disclosed.

Teladoc Inc., Purchase, N.Y.-based provider of virtual care delivery services, reported its expanded collaboration with Microsoft. The organizations will be working together to advance the delivery of telehealth, with Teladoc's platform running on the Microsoft Azure cloud platform. As a result of the joint go-to-market strategy, hospitals and health systems across the U.S. will have greater access to the virtual care solution to meet their business needs.

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Our newsroom

Lynn Yoffee (News Director), Holland Johnson (Executive Editor), Mark McCarty (Regulatory Editor), Andrea Applegate (Production Editor)

Staff writers: Katie Pfaff, Bernard Banga, John Brosky, David Godkin, Stacy Lawrence, Alfred Romann, Tamra Sami

Business office

John Borgman, Director of Commercial Competitive Intelligence,
Donald R. Johnston, Senior Marketing Communication Director, Life Sciences

Contact us

newsdesk@bioworldmedtech.com

John Borgman, (831) 462 2510 | Donald R. Johnston, (678) 641-0970 | Lynn Yoffee, (770) 361-4789 | Holland Johnson, (470) 252-8448 | Andrea Applegate, (470) 236-3994 | Mark McCarty, (703) 966-3694 | Katie Pfaff, (267) 270-7054

Practical information

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BioWorld MedTech stock report for public med-tech companies

Company	Symbol	Close 2/23	Close 3/2	Change Week	Change YTD	Vol (000)
Abaxis	ABAX	68.65	68.64	-0.01	38.61	634
Abbott Labs	ABT	59.71	59.46	-0.42	4.19	32478
Abiomed	ABMD	268.45	275.13	2.49	46.81	1453
Accelerate Dx	AXDX	25.75	25.25	-1.94	-3.63	958
Accuray	ARAY	5.22	5.55	6.32	29.07	3227
Agilent Tech	A	70.7	67.51	-4.51	0.81	11118
Align Tech	ALGN	265.07	253.71	-4.29	14.19	4142
Allergan	AGN	162.09	144.02	-11.15	-11.96	27069
Allied Healthcare	AHPI	2.85	3.98	39.65	86.85	2358
Allscripts	MDRX	13.85	14.17	2.31	-2.61	9063
Alphatec	ATEC	3.3	3.22	-2.42	21.05	146
Analogic	ALOG	85.4	85.05	-0.41	1.55	661
Angiodynamics	ANGO	17.24	16.30	-5.45	-1.98	871
Anika Therapeutics	ANIK	51.69	51.94	0.48	-3.65	465
Antares Pharma	ATRS	2.35	2.19	-6.81	10.05	3891
Apollo Endosurg	APEN	6.59	6.44	-2.28	15.00	110
Athenahealth	ATHN	139.88	139.06	-0.59	4.52	1182
Atricure	ATRC	18	18.34	1.89	0.55	2113
Atrion	ATRI	547.8	569.70	4.00	-9.66	50
Axogen	AXGN	28.95	32.95	13.82	16.43	2777
Baxter Intl	BAX	68.36	66.28	-3.04	2.54	11400
Becton Dickinson	BDX	220.34	217.65	-1.22	1.68	5180
Biocept	BIOC	0.28	0.31	10.71	-55.07	17201
Biolife Solutions	BLFS	5.29	5.16	-2.46	-14.00	66
Bio-Rad Labs	BIO	254.31	263.04	3.43	10.21	1065
Bio-Techne	TECH	141.99	140.40	-1.12	8.38	706
Biotelemetry	BEAT	34.7	32.55	-6.20	8.86	1774
Boston Scientific	BSX	27.2	26.77	-1.58	7.99	31036
Bovie Medical	BVX	2.52	2.55	1.19	-1.92	162
Bruker	BRKR	31.79	29.90	-5.95	-12.88	1702
Cancer Genetics	CGIX	1.8	1.80	0.00	-2.70	418
Cantel Medical	CMD	115.34	115.12	-0.19	11.91	650
Cardinal Health	CAH	69.31	68.94	-0.53	12.52	9261
Cardiovascular Sys	CSII	22.38	24.11	7.73	1.77	1891
Caredx	CDNA	5.18	5.86	13.13	-20.16	467
CAS Medical Sys	CASM	1.14	1.13	-0.88	46.75	52
Celcuity	CELC	17.58	16.65	-5.29	-12.14	52
Cellectar Biosci	CLRB	1.19	1.17	-1.68	-14.60	357
Cerus	CERS	4.22	4.59	8.77	35.80	3776
Check Cap	CHEK	0.72	0.66	-8.33	-24.14	532
Chembio Dx	CEMI	7.3	7.65	4.79	-6.71	112
CHF Solutions	CHFS	3.08	3.19	3.57	-7.80	833
Cogentix Medical	CGNT	2.89	3.08	6.57	-2.22	297
Conformis	CFMS	1.42	1.39	-2.11	-41.60	2254
Conmed	CNMD	60.67	61.10	0.71	19.87	765
Cooper Companies	COO	230.54	234.38	1.67	7.57	1475
Corindus Vascular	CVRS	1.03	1.05	1.94	3.96	1240
CRH Medical	CRHM	2.83	2.80	-1.06	5.66	197
Cryolife	CRY	18.8	18.75	-0.27	-2.09	574
Cutera	CUTR	45.25	47.10	4.09	3.86	705
Cytosorbents	CTSO	7.9	7.80	-1.27	20.00	928
Danaher	DHR	99.33	96.22	-3.13	3.66	9241
Dariohealth	DRIO	1.44	1.45	0.69	-10.49	53
Daxor	DXR	3.63	3.58	-1.38	-21.66	2
Dentsply Intl	XRAY	57.67	56.96	-1.23	-13.47	11489
Dexcom	DXCM	56.36	54.89	-2.61	-4.36	5465
Digirad	DRAD	2.05	2.08	1.46	-19.38	197
Dynatronics	DYNT	2.85	2.80	-1.75	-5.08	17
Edap Tms	EDAP	2.47	2.38	-3.64	-17.07	283
Edwards Lifesci	EW	135.64	134.56	-0.80	19.39	4839
Ekso Bionics	EKSO	1.6	1.54	-3.75	-27.70	813
Electromed	ELMD	5.8	5.78	-0.34	-4.78	11
Endologix	ELGX	4.05	4.15	2.47	-22.43	2190
Enteromedics	RSLS	1.51	1.58	4.64	6.76	335

Company	Symbol	Close 2/23	Close 3/2	Change Week	Change YTD	Vol (000)
Enzo Biochem	ENZ	6.76	6.60	-2.37	-19.02	870
Fluidigm	FLDM	7.21	6.27	-13.04	6.45	1168
Fonar	FONR	26.2	25.05	-4.39	2.87	80
Foundation Med	FMI	77.65	82.20	5.86	20.53	1491
Fresenius Medical	FMS	54.57	51.55	-5.53	-1.90	759
Genmark Dx	GNMK	4.25	4.27	0.47	2.40	3391
Genomic Health	GHDX	32.78	31.94	-2.56	-6.61	1002
Glaukos Corp	GKOS	31.27	32.29	3.26	25.89	5299
Globus Medical	GMED	47.91	48.39	1.00	17.74	2405
Grifols	GRFS	22.77	20.97	-7.91	-8.51	5766
Haemonetics	HAE	69.99	71.57	2.26	23.23	2062
Halyard Health	HYH	47.91	46.73	-2.46	1.19	2317
Henry Schein	HSIC	68.05	65.19	-4.20	-6.71	9737
Hill-Rom	HRC	84.06	82.58	-1.76	-2.03	1811
Hologic	HOLX	39.21	38.21	-2.55	-10.62	8890
HTG Molecular Dx	HTGM	4.9	4.54	-7.35	123.65	4521
Icad	ICAD	3.28	3.63	10.67	5.52	259
ICU Medical	ICUI	232.45	242.00	4.11	12.04	591
Illumina	ILMN	233.84	229.19	-1.99	4.90	3020
Inogen	INGN	131.15	122.00	-6.98	2.45	1241
Inovio Pharma	INO	4.24	4.21	-0.71	1.94	3409
Insulet	PODD	75.55	73.07	-3.28	5.90	1670
Integer	ITGR	52.55	51.80	-1.43	14.35	1021
Integra Lifesci	IART	54.07	52.70	-2.53	10.11	2542
Interpace Dx	IDXG	1.05	1.01	-3.81	-0.98	2728
Intersect ENT	XENT	36.05	35.85	-0.55	10.65	1257
Intricon	IIN	19.7	18.15	-7.87	-8.33	224
Intuitive Surgical	ISRG	427.51	417.39	-2.37	14.37	2733
Invacare	IVC	17.85	17.25	-3.36	2.37	1334
Invitae	NVTA	6.53	6.84	4.75	-24.67	2206
Invivo Therapeut	NVIV	0.48	0.50	4.17	-35.06	383
Invuity	IVTY	3.5	4.40	25.71	-29.03	942
Iradimed	IRMD	13.4	13.00	-2.99	-14.19	31
Irhythm	IRTC	66.48	64.23	-3.38	14.59	768
Iridex	IRIX	7.44	5.83	-21.64	-23.49	148
K2M Group	KTWO	19.95	19.34	-3.06	7.44	2343
Labcorp	LH	172.37	172.23	-0.08	7.97	2522
Lantheus Holdings	LNTH	19.8	16.40	-17.17	-19.80	4790
Lemaitre Vascular	LMAT	35.79	35.15	-1.79	10.40	595
Lianluo Smart	LLIT	3.59	3.00	-16.43	71.43	322
Livanova	LIVN	87.87	87.69	-0.20	9.72	2391
Luminex	LMNX	20.35	19.42	-4.57	-1.42	848
Masimo	MASI	84.62	84.47	-0.18	-0.39	4128
Mazor Robotics	MZOR	63.19	65.13	3.07	26.22	1351
Medigus	MDGS	1.36	1.38	1.47	4.55	2
Medovex	MDVX	0.52	0.47	-9.62	-17.54	53
Medtronic	MDT	80.39	78.33	-2.56	-3.00	25533
Meridian Biosci	VIVO	14.05	13.90	-1.07	-0.71	1515
Merit Medical Sys	MMSI	46.75	44.80	-4.17	3.70	1882
Mesa Labs	MLAB	138.7	128.57	-7.30	3.44	68
Microbot Medical	MBOT	0.8	0.82	2.50	-19.61	924
Micron Solutions	MICR	3.51	3.55	1.14	1.43	78
Milestone Scientific	MLSS	0.9	0.90	0.00	-23.73	147
Mimedx Group	MDXG	7.83	7.59	-3.07	-39.81	17620
Misonix	MSON	10.25	9.90	-3.41	3.13	38
Myomo	MYO	3.92	4.91	25.26	30.93	6518
Nanostring Tech	NSTG	6.9	6.47	-6.23	-13.39	933
Natera	NTRA	9.25	9.24	-0.11	2.78	406
Natus Medical	BABY	31	31.60	1.94	-17.28	1192
Neovasc	NVCN	0.23	0.20	-13.04	-66.67	65267
Neurometrix	NURO	1.37	1.38	0.73	-18.82	1237
Nevro	NVRO	83.78	78.96	-5.75	14.37	1245
Novocure	NVCR	19.3	21.60	11.92	6.93	3538
Nuvasive	NUVA	47.86	48.03	0.36	-17.88	3894

Continues on next page

BioWorld MedTech stock report for public med-tech companies

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Company	Symbol	Close 2/23	Close 3/2	Change Week	Change YTD	Vol (000)
Nuvectra	NVTR	10.2	10.81	5.98	39.30	201
Nxstage Medical	NXTM	23.49	23.78	1.23	-1.86	1823
Obalon Therapeutics	OBLN	4.17	4.01	-3.84	-39.33	219
Oncocyte	OCX	3.45	3.10	-10.14	-33.33	56
Opko Health	OPK	3.8	3.37	-11.32	-31.22	35680
Optinose	OPTN	17.31	17.86	3.18	-5.50	211
Orasure Tech	OSUR	17.62	17.83	1.19	-5.46	2110
Orthofix Intl	OFIX	53.68	56.15	4.60	2.65	582
Orthopediatrics	KIDS	18.31	17.00	-7.15	-11.41	320
Oxford Immunotec	OXFD	12.13	11.47	-5.44	-17.90	1539
Pacific Biosci	PACB	2.46	2.38	-3.25	-9.85	3577
Pavmed	PAVM	1.58	1.71	8.23	-22.97	503
Penumbra	PEN	102.15	112.95	10.57	20.03	1803
Perkinelmer	PKI	77.02	74.73	-2.97	2.20	2447
Precision Therapeu	AIPT	1.08	1.10	1.85	7.84	1329
Presbia	LENS	3.06	3.13	2.29	-17.20	1
Pro-Dex	PDEX	6.95	6.65	-4.32	-2.92	22
Pulse Biosci	PLSE	18.5	17.76	-4.00	-24.75	347
Quest Dx	DGX	102.6	101.44	-1.13	3.00	5253
Quidel	QDEL	43.95	43.62	-0.75	0.62	847
Quotient	QTNT	4.53	5.26	16.11	6.26	1237
Radnet	RDNT	10.2	10.10	-0.98	0.00	588
Resmed	RMD	95.42	94.92	-0.52	12.08	2432
Restoration Robotics	HAIR	6.11	5.34	-12.60	16.09	121
Retractable Tech	RVP	0.9	0.88	-2.22	29.41	1412
Rewalk Robotics	RWLK	1.15	1.20	4.35	9.09	634
Royal Philips NV	PHG	39.03	38.25	-2.00	1.19	9189
RTI Surgical	RTIX	4.5	4.65	3.33	13.41	1137
Seaspine	SPNE	10.25	9.91	-3.32	-2.08	302
Second Sight	EYES	1.6	1.66	3.75	-13.09	4152
Senseonics	SENS	2.94	3.18	8.16	19.55	2720
Sensus Healthcare	SRTS	5.69	5.72	0.53	9.79	19
Sientra	SIEN	9.56	9.74	1.88	-30.73	780
Smith & Nephew	SNN	36.17	35.78	-1.08	2.20	4146
Staar Surgical	STAA	15.55	14.35	-7.72	-7.42	547
Steris	STE	91.78	89.76	-2.20	2.62	1198
Strata Skin Sci	SSKN	1.38	1.26	-8.70	1.61	55
Stryker	SYK	161.7	160.80	-0.56	3.85	5015
Surmodics	SRDX	27.15	32.90	21.18	17.50	319
T2 Biosystems	TTOO	4.51	6.36	41.02	54.37	3390
Tactile Systems	TCMD	31.25	31.76	1.63	9.59	1995
Tandem Diabetes	TNDM	2.86	3.89	36.01	64.83	9369
Tearlab	TEAR	0.29	0.33	13.79	-13.16	265
Teladoc	TDOC	37.95	41.95	10.54	20.37	6176
Teleflex	TFX	255.27	245.61	-3.78	-1.29	1659
Thermo Fisher Sci	TMO	211.71	206.44	-2.49	8.72	4814
Transenterix	TRXC	1.69	1.92	13.61	-0.52	13482
Trinity Biotech	TRIB	5.55	5.42	-2.34	6.07	79
Utah Medical	UTMD	90.3	88.70	-1.77	8.97	58
Valeritas	VLRX	3.05	2.98	-2.30	4.56	28
Varian Medical Sys	VAR	121.17	120.49	-0.56	8.40	2476
Veracyte	VCYT	5.76	5.98	3.82	-8.42	513
Vericel	VCEL	7.3	8.35	14.38	53.21	3173
Vermillion	VRML	1.35	1.54	14.07	-20.21	146
Viewray	VRAY	8.31	8.39	0.96	-9.40	2452
Viveve Medical	VIVE	4.24	4.24	0.00	-14.69	847
Vocera Comm	VCRA	27.03	27.34	1.15	-9.53	1025
Volitionrx	VNRX	2.99	3.12	4.35	6.12	1010
West Pharma	WST	86.58	85.74	-0.97	-13.10	1543
Wright Medical	WMGI	20.09	20.49	1.99	-7.70	9471
Xtant Medical	XTNT	5.9	6.41	8.64	-6.29	203
Zimmer Biomet	ZBH	118.85	117.05	-1.51	-3.00	3900

Notes

Trading volumes for Nasdaq, Amex and NYSE are recorded as the total number of shares traded (in thousands) on a weekly basis (cumulative Monday through Friday); the weekly and YTD changes are from IPO completion, where applicable.

Average percent change week: +0.49%
Range: -21.64% to +41.02%; Number of companies: 190
(not market weighted)

Average percent change year-to-date: +1.52%
Range: -66.67% to +123.65%; Number of companies: 190
(not market weighted)

10 biggest U.S. gainers for the week

Share price by percent		Share price by dollars	
T2 Biosystems	41.02	Atrion	21.90
Allied Healthcare	39.65	Penumbra	10.80
Tandem Diabetes	36.01	ICU Medical	9.55
Invuity	25.71	Bio-Rad Labs	8.73
Myomo	25.26	Abiomed	6.68
Surmodics	21.18	Surmodics	5.75
Vericel	14.38	Axogen	4.00
Axogen	13.82	Teladoc	4.00
Caredx	13.13	Cooper Companies	3.84
Novocure	11.92	Orthofix Intl	2.47

10 biggest U.S. losers for the week

Share price by percent		Share price by dollars	
Iridex	-21.64	Allergan	-18.07
Lianluo Smart	-16.43	Mesa Labs	-10.13
Fluidigm	-13.04	Intuitive Surgical	-10.12
Restoration Robotics	-12.60	Teleflex	-9.66
Opko Health	-11.32	Inogen	-9.15
Allergan	-11.15	Thermo Fisher Sci	-5.27
Oncocyte	-10.14	Nevro	-4.82
Grifols	-7.91	Illumina	-4.65
Intricon	-7.87	Lantheus Holdings	-3.40
Staar Surgical	-7.72	Agilent Tech	-3.19

Stimguard

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implanted in a physician's office with ultrasound guidance, avoiding a surgical procedure and general anesthesia required for the sacral device.

"The Stimguard device is a chronic implant that is [placed] outpatient in a doctor's office, but does not require coming back repetitively for treatments," Laura Tyler Perryman, co-founder and CEO of parent company, Stimwave Technologies Inc., told *BioWorld MedTech*. "It lasts for 10 years, and other products either last for just months or require surgery and replacement. Compared to Interstim, the CAN-stim device does not require surgery and does not require replacement of a battery unit like Interstim every three to five years. Eliminating the battery eliminates the risks associated with placing a lithium-ion battery in your body."

CAN-stim vs. Interstim

Unlike Dublin-based Medtronic's Interstim, Stimguard's device can be percutaneously placed to effect the afferent micturition, or neural urinary pathway at the tibial nerve, during an office visit. The minimally invasive neurostimulation device is attached to an external transmitter and activated wirelessly. By comparison, Medtronic's device system, considered the standard of care in OAB for decades, is made up of a sacral lead and battery unit which often needs to be replaced within five years, and is implanted during a fluoroscopy-guided operation.

Pompano Beach, Fla.-based Stimguard's device is intended to provide similar results with a more accessible and potentially less costly treatment.

"An electrode implanted at the tibial nerve in an office setting with the potential to provide the same outcomes as sacral neuromodulation will be a game-changing option for urgency urinary incontinence associated with OAB," said Kenneth Peters, an incontinence expert and consultant for Stimguard. "Stimguard's technology has the potential to provide similar outcomes as sacral nerve stimulation in an office-based procedure, which could drastically reduce the cost of care while allowing more patients to be treated, improving accessibility to a non-drug treatment option for many patients with OAB."

Less obvious device

Perryman added that CAN-stim also may provide a more appealing option to patients who are both put off by a general anesthesia operation and the size of the Interstim system.

"This approach is preferable to patients because it is office-based and you are awake while the device is implanted at the targeted nerve under local anesthesia," Perryman said. "The Interstim device requires surgery and general anesthesia, which is worrisome for many patients. Additionally, most OAB suffers are women, and the last thing women want is some battery device that is bulky and can show in their bathing suit or other warm weather clothing in their buttocks." Clinicians also avoid a time-consuming surgical procedure with Stimguard, she said.

Study evaluation

Stimguard will begin enrollment this month for its study intended to determine the effectiveness of its device's delivery of pulsed electrical energy to tibial nerves in impacting bladder function. Tibial nerves signal sacral nerves targeted in standard care. Trial enrollment for a planned 168 patients will last 12 months and include 20 U.S. sites. Patients will be evaluated at three months after implantation for episodes of incontinence in comparison to Interstim.

"The primary efficacy endpoint is defined as an equal to or greater than 50 percent reduction in number of urgency related incontinence episodes at three months post-implant of the CAN-stim system compared to SNS Interstim system therapy," said Perryman. "The number of urgency incontinent episodes per day is taken as an average of two three-day consecutive bladder diaries, with at least 24 hours between when the first diary ends and the second diary begins."

Secondary endpoints and observational endpoints during the study will look at comparison of the two systems in reducing the severity of urinary urgency defined by the Indevus Urgency Severity Scale, differences according to the Urinary Incontinence Quality of Life Scale, and comparison of incontinence episodes tallied daily in patients' voiding diaries. Patients' data indicating "moderately" or "markedly improved" results will be calculated using the Global Response Assessment tool, and patients receiving Interstim or CAN-stim will be asked to complete the Overactive Bladder Questionnaire Short Form. Adverse events for either group also will be compared. Trial results are expected to be used toward FDA clearance and submission to CMS.

Stimguard's CAN-stim device will be compared to Interstim as it is considered the standard treatment for OAB. "Interstim has been used for 20 years and does more than $600 million a year in sales, meaning it is the most well-established stimulation therapy for OAB," said Perryman.

"Allergan did a head-to-head study with Interstim for their Botox therapy as well, so it is already established as a standard of care. For a new therapy that is much less invasive and longer lasting, it seemed prudent to establish that the efficacy is the same as Interstim."

Incidence, competition

According to the Urology Care Foundation, about 33 million people in the U.S. deal with OAB. This amounts to about 30 percent of American men and 40 percent of women, however, the number is thought to actually be higher since patients may be embarrassed to discuss symptoms with their doctors or unware treatment options exist.

Earlier this year, Axonics Modulation Technologies Inc., of Irvine, Calif., also set its sights on Medtronic's top billing in the OAB space. Axionics r-SNM device is a rechargeable sacral stimulation device that can be implanted for about 15 years compared to Interstim's five years, and can be tracked and modified by a physician. The r-SNM device also is about 60 percent smaller than Interstim, according to the company. Axionics' r-SNM device is approved in Australia, Canada and Europe for urinary and fecal incontinence, OAB in Australia, and received FDA IDE pivotal trial (ARTISAN-SNM) November 2017, with approval anticipated in 2019. Interstim was approved to treat OAB in 1997. (See *BioWorld MedTech*, Jan. 18, 2018.) ♦

Senseonics

Continued from page 1

The Germantown, Md.-based company has an FDA Clinical Chemistry and Clinical Toxicology Devices Panel that is scheduled for March 29. The panel's recommendation, of course, will influence the FDA's subsequent decision on the CGM. If all goes well for Senseonics, it hopes to have an approval from the agency in hand and a U.S. launch underway by about June.

Panel considerations

The company expects the FDA panel will focus particularly on the safety of the implant for long-term use, as well as on the safety of the in-office procedure to inject the tiny CGM sensor under the skin. Real-world evidence based on existing ex-U.S. patients is playing a substantial role in the FDA submission for Eversense, alongside U.S. pivotal trial data.

"In my discussions, they have stated the panel will be focusing on long-term use and the in-office procedure for insertion/removal," Senseonics COO Mukul Jain told *BioWorld MedTech* about the company's interactions with the agency. "What we're looking for is for the panel to focus on the safety data that we have from the clinical study. We are going to bolster that with real-world evidence from the data that we are collecting as part of the European registry."

Senseonics first received a CE mark for its implantable CGM, known as Eversense, in May 2016. In September 2017, it received a second CE mark for a more recent iteration, called Eversense XL; the implantable sensor in this version can remain in the body for up to 180 days, an improvement over the original 90-day device.

In Europe, Eversense is marketed via established diabetes device player Roche to most countries; Rubin Medical distributes it in the Scandinavian region. Senseonics recently launched in Europe with a new iteration of its app, known as Eversense Now that allows remote viewing of the real-time glucose monitoring data generated by the system.

Real-world evidence

Jain said that Eversense has been used in "thousands, not hundreds" of European patients, but the company hasn't released any more specific figures. Senseonics reported $2.1 million in revenues during the third quarter.

The U.S. pivotal trial for Eversense, known as Precise II, was in 90 patients at eight sites. Over 90 days, there was a mean absolute relative difference (MARD) of 8.8 percent as compared to reference glucose values with twice-daily calibration. With once-daily calibration to fingerstick blood glucose, the MARD was 9.5 percent. Of the more than 16,000 paired data points between the sensor and reference data, 93 percent of the Eversense readings were within 20 percent of the reference.

The detection rate of hypoglycemia was 93 percent and for hyperglycemia was at 96 percent.

There were no reported infections or skin irritations reported, but eight subjects reported mild bruising.

The Eversense sensor requires twice-daily calibration with a standard fingerstick blood test. That's also the case with all FDA-approved CGMs, except Abbott's Freestyle Libre that uses a 10-day wearable sensor for the upper arm. A CGM from another competitor, Dexcom Inc., can be used for treatment decisions without additional fingerstick verification, but it must still be calibrated twice-daily via a fingerstick test.

Achieving a level of convenience and ease-of-use on par with a consumer device, while offering fingerstick-free accuracy at a relatively low cost is the Holy Grail of CGMs. But it's proven quite difficult to combine all of those aspects simultaneously.

Label expectations

The FDA released its description of the purpose of the upcoming panel. "The Eversense CGM system measures patients' glucose concentrations from subcutaneous interstitial fluid similar to approved CGM systems. All CGM devices currently or previously marketed used electrochemistry to measure glucose in interstitial fluids, last for three to 11 days and are inserted via a small-gauge needle by the end user," the agency stated. "The proposed CGM system uses a fluorescence-based measurement technique, requires minor surgery for subcutaneous implantation, and will have a 90-day sensor wear period."

Senseonics said it had discussed with the FDA its "minor surgery" description and that it had offered the term "procedure" to be used in its place. The Eversense sensor is also coated with a drug, dexamethasone acetate, which is intended to preserve the sensor accuracy within the body and prevent a foreign body response.

The tiny Eversense sensor is inserted under the skin, and later removed, by a physician. It is monitored via a worn transmitter that sends the real-time blood glucose data to a smartphone app for analytics and sharing.

Unlike in Europe, Senseonics aims to market Eversense in the U.S. without a partner. Last spring, it brought on Michael Gill as VP of Sales; He had most recently been the VP of the Americas in the Intensive Insulin Management Business at Medtronic Diabetes Care.

The plan is to initially target endocrinologists for prescribing Eversense. Senseonics has already received Category III CPT codes for the insertion and removal of the Eversense sensor. After a PMA approval, it intends to pursue a Category I CPT code. The former is temporary, while the latter is permanent and consistent with current medical practice.

On March 13, Senseonics will hold its year-end earnings call and plans to update investors on its progress toward manufacturing and commercialization for the U.S. market. It's also working now to submit to the FDA for the go-ahead to do a pivotal trial of Eversense XL, the 180-day version, that it hopes to start soon.

The roughly $425 million valuation for Senseonics has largely treaded water since it went public via a reverse merger in late 2015. To advance, the company likely will need to gain revenue traction and demonstrate clearly that it is on the path to profitability.

Up next for the Eversense technology, it is being featured as part of the National Institutes of Health funded International Diabetes Closed Loop pivotal trial. It's testing the use of Eversense in conjunction with an insulin pump from Roche Diabetes Care and software from Type Zero Technologies Inc., as a functioning artificial pancreas, also known as a closed loop system. ♦

Radiology AI

Continued from page 1

device makers – must begin now to sort through the challenges presented by these instruments if diagnostic imaging is to become a 21st century science.

The article appeared in a March 1 special issue of *JACR* under the title, "Artificial intelligence and machine learning in radiology: opportunities, challenges, pitfalls, and criteria for success." The authors say AI can ease a radiologist's workload by "identifying suspicious or positive cases for early review," and that radiomic data that are not visible to the naked eye may increase the diagnostic and prognostic value of imaging. The authors say, however, that fears that the blend of AI and massive volumes of data will put radiologists out of business are overblown.

The authors point out that picture archiving systems now house billions of images, but there is no system for centralized file sharing that would foster the requisite machine learning. There is also a need for reference data sets for use as validation tools for an AI system, but another source of noise in the current environment is a "high variability in imaging protocols between institutions," not to mention a considerable degree of variability in the execution of a protocol within a given clinical operation.

In addition to the prospect of greater diagnostic accuracy, such a system could sort through large volumes of images to help streamline the process of image examination for overtaxed imaging clinics, and the authors say observer fatigue still incurs the risk of failure to detect a true positive exam, particularly in the case of large-volume screening services. One rather interesting scientific problem is that AI may suffer from "inherent limitations" in distinguishing between normal and abnormal images, the authors state, thanks to the fact that biological data behave more like continuous random variables than discrete random variables, a predicament that will impose considerable demands on radiologists and device makers alike in the years ahead.

The right-now value of AI

Bibb Allen, chief medical officer of the American College of Radiology's Data Science Institute, told *BioWorld MedTech* that *JACR* will routinely include content dealing with AI and big data in the future, but he said the sensitivity-specificity dilemma won't disappear in this new world. Data science training "will help avoid some of those false positives," he said, and while there is a question as to where stakeholders and regulators will fall on the question of minimum levels of sensitivity and specificity, the value of these two instruments is not entirely defined by those two parameters.

"In the short term, AI has so much more potential for radiologists other than as detectors," Allen said, stating that the prioritization function creates economies of time and effort if only because a suspect image might prod the radiologist to direct additional studies without the patient having to leave the CT lab. Patients would benefit, too, thanks to the elimination of a trip to the clinic that would otherwise have been necessary.

Allen said a false positive is not necessarily a problem, noting that an emergency department physician would have examined the patient's scans regardless of whether a suggestion of pneumothorax proves correct. AI might pick up a subtle rib fracture that co-occurred with the pneumothorax, however, a fracture the radiologist might not have noticed on a stressful, high-volume weekend night in the ER.

Other uses of AI will require more labor-intensive activities up front, such as the construction of a data set for classification of lung nodules, but Allen said "having some of those things prepopulated for us, I think, makes us better radiologists," despite concerns that specialists could become overly reliant on the algorithm.

Allen confirmed that the data ownership problem will have to be resolved, although that resolution may end up being handled on a case-by-case basis for the time being. He said the ACR's Data Science Institute "is looking at solutions of validation and certification of algorithms" for FDA approval. One approach would be to set up a centralized process for images and corresponding data sets for all to make use of, but Allen said a federated process could be invoked as well.

In the federated model, individual practices would use their own data toward development of their own use cases, or they could contract with developers to handle the job. Developers in turn could contract with multiple institutions for their expertise in an effort to deal with technical issues such as patient diversity and the problems associated with differences in imaging equipment.

Validation of that algorithm is a bit more demanding, of course, and Allen said, "we're struggling with whether we can do it in a federated way, or would it have to be centralized?" A centralized repository offers some obvious advantages when it comes to validating the conclusions an algorithm draws from a data set, but he noted that hospitals might be reluctant to sell those data, in part because of all the confidentiality and privacy issues that would attach to such a practice.

Allen said publishers of algorithms could offer those algorithms to clinics via cloud computing, but the ability to upload images directly from the imaging system is a more economical proposition than a system that calls for a separate workstation for the upload. This separate workstation would not only be an additional footprint in the hospital's IT infrastructure, it would also be added steps for the physician. In any event, Allen said, clinical use of an algorithm "has to be something that's integrated into our workflow or nobody is going to use it."

Allen said payment for these algorithms would be handled as a practice expense under most fee-for-service models, but that a need for a novel CPT code for each algorithm would be impractical. While private payers are sometimes credited with being first to adopt a new technology, Allen indicated that ACR still sees public payers as the best place to start. "CMS is where we can influence all [payers] at once," he said. ♦

Surgivisio

Continued from page 1

Until now, orthopedic surgeons had to connect surgical navigation tools to the imaging device in order to carry out vertebroplasty. The procedures for calibration of instruments consume time and extend the duration of interventions.

"Thanks to this innovation, orthopedic surgeons will finally be able to follow their movements with great precision directly within the 3-D imaging of the patient," Stéphane Lavallée, founder and CEO of Surgivisio, told *Bioworld MedTech*.

The idea of Lavallée, an engineer specializing in computer-assisted surgery, was for 3-D to be obtained intra-operatively from computerized images for incorporation into a single machine. These images would come from a flat panel detector and a surgical navigation system. Founded in 2009 in Isère, near Grenoble, Surgivisio has invested several million dollars into the development of the first simple integrated operating system with 2-D/3-D imaging and real-time surgical navigation dedicated to mini-invasive orthopedic and trauma surgery protected by seven patent families. These patents notably focus on a method for reconstructing a 3-D image from 2-D X-ray images acquired with an X-ray imaging system, a device for minimally invasive attachment of a tracker and a registration phantom to a patient's bone, a fluoro-navigation system for navigating a tool relative to a medical image, a modular fluoro navigation instrument and a method for controlling movement of a motorized C-arm.

The machine, which weighs 450 kilograms, has been CE marked since July 2017. This surgical navigation platform with built-in 3-D imaging is presented in the form of a fully motorized C-arm with a flat panel imaging detector and integrating navigation system. Real-time tracking of the surgeon's movement in 3-D is reconstructed based on a series of radiological pictures that are automatically acquired and taken over the patient. Several algorithms enable auto calibration and auto registration of the machine. According to Lavallée, Surgivisio possesses the patented technology of "respiratory compensation, thus enabling acquisition of the 3-D image without stopping patient breathing whilst continuously looking at a very high quality image". Ultimately, the surgeon operates the system by a tablet interface, which is configured to receive his commands.

FIH intervention carried out at CHU Grenoble

The first human sacroplasty procedure to use the Surgivisio system was carried out three months ago at the Department of Orthopedics and Traumatology in Sport at CHU Grenoble Alpes (Grenoble Alps Regional Teaching Hospital) on an elderly patient suffering sacral fractures caused by osteoporosis. The surgical navigation system in real-time enables precise injection of cement into the pedicles of a vertebra that is difficult to access, the sacrum. The number of images taken per examination is between 90 and 180 as opposed to 380 to 760 with other systems, this is a radiation dose four times lower.

"The control scan carried out with Surgivsio in the operating room, just a few minutes after the intervention, confirmed the precision of the surgeon's act. The patient was awakened and left at the end of the day," said Professor Jérôme Tonetti, head of the Department of Orthopedics and Traumatology in Sport at CHU Grenoble Alpes, who performed the intervention. The Surgivisio system enables the surgeon's movements to be visualized accurately due to the voxel size precision, i.e., 0.35 milimeters. This is a strong argument in spinal surgery because according to the figures, 15 percent of pedicle screws are misplaced in conventional surgery.

Surgivisio system; Surgivisio SAS

> *"The Surgivisio system enables minimally invasive routine surgery in orthopedics thanks to more precise surgical acts.*
>
> Stéphane Lavallée
> CEO, Surgivisio SAS

'All percutaneous' soon in orthopedic surgery

According to Tonetti, "By allowing orthopedic interventions under routine surgical navigation, Surgivisio is opening the way to 'all percutaneous' in spinal and pelvic traumatology." Fifteen other French patients have already benefited from Surgivisio technology. The med tech based in the Isère region intends to play a role in the vertebroplasty market. "Our development prospects in orthopedic surgery are great," said Lavallée.

His company already uses some apps intended for pelvic trauma. It consists of making percutaneous fixtures of pelvic and acetabular fractures, notably iliosacral and iliopubic bolts. Other applications for the shoulder, extremities, the otorhinolaryngological and cranial area are anticipated. After commercial launch of the Surgivisio platform in Europe with the series B funds, Lavallée is already planning to raise funds in a series C round in 2019 to market the French technology on the U.S. market. ♦

Contextual Genomics

Continued from page 1

"Pacbridge recognized the potential for the global scaling of our business. It's a relationship that started very well right from the beginning."

For some, one last chance

It's not the first time Contextual has partnered with other med-tech companies to advance its fortunes. Last year, Australia's Sonic Healthcare and Brazil's Idengene Medicina Diagnóstica SA entered into agreements with Contextual to distribute Find It, a molecular hotspot assay that screens for more than 140 genome alterations in patients with solid tumor cancers. The latest deal with Pacbridge enables Contextual to roll out its next product called Follow It, which detects mutations in plasma from patients with widespread metastatic disease.

"The test identifies treatment options that these patients otherwise wouldn't have," said Shah. Another use would be in patients who are "treatment resistant" to certain drugs and who may suffer a relapse in treatment. This second test, said Shah, can detect emerging resistance to a drug early in the course of disease management and allow the physician to decide if a change in drug therapy is warranted.

"The Follow It mutation detection assay is very powerful because it's a blood draw, which allows us to isolate DNA that has its origins in the tumor cells and which release into the bloodstream," said Shah. "It's a much less an invasive diagnostic test than a biopsy and uses highly accessible biomaterial."

As next-generation sequencing technology, the Follow It assay is being designed with the same objectives underpinning the Find It hotspot assay, said Shah: to facilitate the collection of longitudinal patient data by monitoring tumor and blood, to do it inexpensively and permit rapid industrial scaling. Like Find It, Follow It is also a cloud based genome analytics platform providing complete molecular and computational quality assurance, mutation interpretation and report generation.

Another powerhouse joins the team

Sue Paish's decision to join the board at Contextual Genomics was reported on the same day as the cash influx from Pacbridge. Paish's reputation as a financial powerhouse solidified in 2013 after doubling the size of Lifelabs Medical Laboratory Services one year into her tenure as company president and CEO. There, she positioned the company for growth by stressing two sectors she hopes will serve Contextual Genomics well: genetics and technology.

"Contextual has taken the very broad concept of genetics and honed it into something that is very practical, very meaningful on the basis of the patient and physician," Paish told *BioWorld MedTech*. "They've created something that can actually change health outcomes for cancer patients."

A pragmatic approach to genomics technology also includes costs, Paish noted, amplified in Canada where equipment procurement occurs on the public dime. She believes avoiding costs through better patient outcomes is the strongest argument in favour of more genomics research and uptake of genomics technology in Canada and abroad.

> *"Contextual has taken the very broad concept of genetics and honed it into something that is very practical, very meaningful on the basis of the patient and physician. They've created something that can actually change health outcomes for cancer patients.*
>
> Sue Paish
> President and CEO, Lifelabs Medical Laboratory Services

"Contextual, because it has been at this for quite a while now, has developed cost effective testing that will be very attractive to the markets it is exploring."

Contextual makes its money from the original Find It hotspot assay by charging a fee for every patient test. This amounts to approximately 20 percent of the revenues obtained by the company's partners, Sonic Healthcare and Brazil's Idengene Medicina Diagnóstica SA. Still in development, the Follow It assay will likely employ the same pricing approach in partnership with Pacbridge Capital Partners and others, said Shah. ♦

Ketamine

Continued from page 1

That finding may help set the stage for developing new fast-acting antidepressants, researchers led by Hailan Hu, professor and principal investigator at the Zhejiang University (ZJU) School of Medicine and Interdisciplinary Institute of Neuroscience and Technology in Hangzhou, reported in the Feb. 14, 2018, issue of *Nature*.

Ketamine was originally developed as an anesthetic in the early 1960s. The subsequent discovery of the rapid antidepressant effects of the N-methyl-D-aspartate receptor (NMDAR) antagonist has since aroused great interest in mental health research.

"Ketamine has been known to induce rapid antidepressant effects for about two decades, having first been reported in 2000 by Berman et al. in *Biological Psychiatry*," Hu told *BioWorld MedTech*.

A single ketamine dose has been shown to elicit rapid and sustained antidepressant effects within just 30 minutes in both humans and in animal models of depression.

Ketamine also has a high metabolic turnover, with a half-life of around three hours, and it is currently in clinical trials for patients with major depressive disorder who are at high risk for suicide.

However, the potential drawbacks in humans include "potential for abuse and the transient induction of a schizophrenia-like state," noted Hu. Moreover, ketamine's exact mechanism of action had long remained elusive.

Neurons in the brain's mesolimbic system promote reward-seeking behaviors and pleasurable activities, whereas those in the LHb neurons act as an anti-reward center, being associated with harmful outcomes and suppression of reward-seeking.

In their new study, Hu and her ZJU team showed that the blockade of NMDAR-dependent bursting activity in the LHb mediated the rapid antidepressant actions of ketamine in three rodent models of depression.

"We used three models to induce depression, including congenitally learned helpless (cLH) rats, a lipopolysaccharide-(LPS)-induced rat model, and chronic-restraint-stressed (CRS) mice," noted Hu.

"The first of these models may reveal genetic predisposition for depression, while the other two may model depression induced by environmental factors such as inflammation, since LPS is a pro-inflammatory factor, and stress," she explained.

Electrophysiological study of rat brain slices revealed that the LHb neurons were more apt to fire in a pattern of rapid bursts rather than in steady volleys in depressed rats than in controls.

Moreover, when those neurons were hyperpolarized, with the cell's interior becoming more negative than the exterior, that further increased the chances of their firing in rapid bursts.

The researchers went on to show that depression-like behavior in the rats could be increased using genetic manipulation to drive hyperpolarization, hence burst firing in the LHb neurons.

"We found in the selectively bred cLH rats, as well as in animals exposed to stress or inflammation, that an astrocytic potassium channel was unregulated, which enhanced extracellular K++ buffering and neuronal hyperpolarization, resulting in burst firing and depression."

Pharmacological and modeling experiments then revealed that LHb bursting required both NMDARs and low-voltage-sensitive T-type calcium channels (T-VSCCs).

Furthermore, local blockade of NMDAR or T-VSCCs in the LHb was sufficient to induce rapid and significant antidepressant effects "within one hour after either systemic injection or local infusion [of ketamine] into the LHb," said Hu.

Taken together, those findings suggest a mechanism whereby ketamine quickly elevates mood by blocking NMDAR-dependent bursting activity of LHb neurons to disinhibit reward centers.

"This provides a new framework for how to think about the causes of depression and to design new drugs accordingly," said Hu. "In particular, we propose that drugs that block LHb bursting would be good candidates for rapid antidepressants.

"We are currently collaborating with hospitals to translate these findings in basic research into clinical use and hope in future to develop new cures for this devastating disease." ♦

Neurology Extra

Keeping you up to date on recent developments in neurology

By Andrea Applegate, Production Editor

Using Cas9 nickases to treat Huntington's disease

A new variant of the gene-editing CRISPR/Cas9 system is safer and more specific than versions previously used in early research towards a treatment for Huntington's disease, shows research published in the article "Precise excision of the CAG tract from the huntingtin gene by Cas9 nickases" Feb. 26, 2018, in *Frontiers in Neuroscience*. "In our study, we further improve the CRISPR/Cas9 approach by using a nickase version of Cas9," said Marta Olejniczak, group leader of the study and an associate professor at the Institute of Bioorganic Chemistry in Poland. "Because Cas9 nickases are known to be safe and specific, our approach provides an attractive treatment tool for Huntington's disease." Huntington's disease is caused by the abnormal repetition of a specific DNA sequence at the tail end of the huntingtin gene. This defective mutant gene causes production of a toxic protein that progressively accumulates and damages the patient's neurons. Researchers have tried many methods to silence the defective gene. This includes interrupting production of the toxic protein through DNA- and RNA-based approaches. Most recently, researchers have also begun work with one of the most promising gene-editing tools to date – the CRISPR/Cas9 system, which is far easier, faster and more specific than past tools. But it is still the early days of medical applications of CRISPR/Cas 9, which was only discovered in 2012. To make sure that this technique is as safe and effective as possible, Olejniczak's group has been testing out a new variant of the Cas9 protein component in cellular models from a Huntington's patient. This version of Cas9 was recently designed to act as a nickase – an enzyme that cuts just one DNA strand instead of two, which increases the precision with which Cas9 can edit specific sequences of DNA. "We demonstrated that excision of the repeat tract with the use of a Cas9 nickase pair resulted in inactivation of the huntingtin gene and abrogation of toxic protein synthesis in cellular models of Huntington's disease," said Olejniczak. "Our strategy is safe and efficient, and no sequence-specific side effects were observed."

Researchers use human neural stem cell grafts to repair spinal cord injuries in monkeys

Led by researchers at University of California San Diego School of Medicine, a diverse team of neuroscientists and surgeons successfully grafted human neural progenitor cells into rhesus monkeys with spinal cord injuries. The grafts not only survived, but grew hundreds of thousands of human axons and synapses, resulting in improved forelimb function in the monkeys. The findings, published online in the Feb. 26, 2018, issue of *Nature Medicine*, represent a significant step in translating similar, earlier work in rodents closer to human clinical trials and a potential remedy for paralyzing spinal cord injuries in people. The new work involves the use of human spinal cord-derived neural progenitor cells (NPCs). Because the NPCs were derived from an 8-week-old human embryonic spinal cord, they possessed active growth programs that supported robust axon extension and appeared to be insensitive to inhibitors present in the adult central nervous system. Two weeks after the initial injury (a period intended to represent the time required for an injured person to medically stabilize undergoing neural stem cell therapy), researchers grafted 20 million NPCs into the injury lesions in the monkeys, supported by a cocktail of growth factors and immune suppression drugs. Over the next nine months, the grafts grew, expressing key neural markers and sending hundreds of thousands of axons – the fibers through which nerve cells conduct signals to other nerve cells – through the injury site to undamaged cells and tissue on the other side. Several months into the study, researchers noted that the monkeys began to display partial recovery of movement in their affected forelimbs. Notably, the team documented regeneration of corticospinal axons, which are essential for voluntary movement in humans, into the lesion sites – the first such known documentation in a primate model. The authors said work remains to be done before initiating human clinical trials, including production of a candidate neural stem cell line from humans that meets requirements of the Food and Drug Administration, and additional studies of safety. The research group also continues to explore ways to further enhance the growth, distance and functionality of the regenerated cells. The title of the research article is "Restorative effects of human neural stem cell grafts on the primate spinal cord."

Genes linked to brain anatomy in autism

A team of scientists at the University of Cambridge has discovered that specific genes are linked to individual differences in brain anatomy in autistic children. Previous studies have reported differences in brain structure of autistic individuals. However, until now, scientists have not known which genes are linked to these differences. The Cambridge team analyzed magnetic resonance imaging (MRI) brain scans from more than 150 autistic children and compared them with MRI scans from similarly aged children but who did not have autism. They looked at variation in the thickness of the cortex and linked this to gene activity in the brain. They discovered a set of genes linked to differences in the thickness of the cortex between autistic kids and non-autistic children. Many of these genes are involved in how brain cells (or neurons) communicate with each other. Interestingly, many of the genes identified in this study have been shown to have lower gene activity at the molecular level in autistic post mortem brain tissue samples. The study, titled "Synaptic and transcriptionally downregulated genes are associated with cortical thickness differences in autism," was published Feb. 26, 2018, in the journal *Molecular Psychiatry* and provides the first evidence linking differences in the autistic brain to genes with atypical gene activity in autistic brains.